MEDICAL COMPLICATIONS in PHYSICAL MEDICINE and REHABILITATION
Medical Complications in Physical Medicine and Rehabilitation
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Preface

Those of us who care for patients with disabilities know all too well that medical complications can occur and interfere with our treatment programs and the therapy provided in inpatient rehabilitation units. The goal of this book is to serve as a practical resource to physiatrists who are providing daily inpatient care or who are sharing call on inpatients. The information should be useful to you whether you practice in an academic setting or have a private practice, since early identification and prevention of medical complications are important in whatever setting we practice. We have focused on the most common medical complications for major rehabilitation diagnoses in adults who we see in a large rehabilitation hospital. Although we have not addressed pediatric conditions in the book, the principles in this book are likely to be applicable to the pediatric patient.

The organization of this book is unique. The first half is a series of chapters written by physiatrists on eight major topics: musculoskeletal disorders, spinal cord injury, multiple trauma and burns, stroke, traumatic brain injury, neurological and rheumatological disorders, cancer rehabilitation, and amputations. Each chapter includes a discussion of many of the medical complications that can occur and a summary table of the major medical complications. The second half of the book is a series of chapters written by acute care specialists that discusses the diagnosis and management of the majority of those complications. Medical complications are written in such a manner as to help the physiatrist stay abreast of newer medical advances within a practical context.

We would like to thank the authors who are experienced physicians in the fields of physical medicine and rehabilitation, gastroenterology, cardiology, hematology, pulmonology, nephrology, and infectious diseases. Our hope is that you will find this an easy-to-use, practical guide to the management of medical complications in patients admitted to rehabilitation facilities.

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Medical Complications in Physical Medicine and Rehabilitation
Pthomegroup
As the population of the world continues to age, the geriatric segment will continue to grow. According to the U.S. census data from 2010, the working-age population aged 44 to 65 was 81.5 million persons, 26.4% of the entire population and a gain of 31.5% from 2010, whereas the population aged greater than 65 was 40.3 million or 13.0% of the population, which was a 15.1% gain from 2000. During that time, the overall population gained 9.7%. This confirms a “graying” of the U.S. population (1). With the increase in the active elderly, there will be an increase in persons with chronic conditions, including arthritis. The major types of arthritides include osteoarthritis (OA), rheumatoid arthritis, and gout. Of these, OA accounts for the largest proportion of those diagnosed with arthritis. The pathology of the disease includes subchondral sclerosis, osteophyte formation, and a decrease in function. In industrialized societies, OA has become the leading cause of disability. This brings an increase in health care utilization and a decrease in the quality of life.

The factors that affect this disease are related to age, obesity, joint position of the weight bearing joints, and joint abnormalities, including misalignment and previous trauma. Conservative estimates of the rates of OA suggest that from 1990 to 2005, the number of persons in the United States with OA has grown from 21 million to 26.9 million, an increase of 28.1% (2). It has been estimated that by 2030, over 67 million Americans over the age of 18 will be given a diagnosis of some form of arthritis by their doctor (3). This increase in arthritis is undoubtedly going to increase the need for rehabilitation at all levels of the health care system.

There are a number of treatments for OA. These are based on the effects they have on the patients’ function. Nonpharmacologic treatments include education, weight loss, activity modification, orthotics, and exercise. Because pain is the major factor to limit function, pain medications including acetaminophen, nonsteroidal anti-inflammatory drugs (NSAIDs), narcotic analgesics, and tramadol are often prescribed. Integrative complimentary medical interventions and nutraceuticals may also be helpful in select cases. Injection of corticosteroids can be used as a temporizing treatment, but does not affect the progression of the disease. Surgical interventions are the final treatment and should be used when nonsurgical treatments fail.
For over 40 years, total hip arthroplasty (THA) and knee arthroplasty (TKA) have led to an increase in function and quality of life, as well as pain control (4). Total joint arthroplasty (TJA) is used in patients with arthritides, fractures, and avascular necrosis among other diseases. Trends show an increase in their use in developing nations over the past few decades (5). There has been a broadening of the selection criterion for TJA and now includes more patients of advancing age as well as younger, more active patients. Using the National Hospital Discharge Summary and National Inpatient Sample data, it has been estimated that THA cases range from 202,000 to 230,000 per year and there are twice as many cases of TKA (6). These numbers are thought to underestimate the number of these procedures in that they are prone to coding errors and evaluate discharges rather than the number of procedures performed. As these procedures continue to increase, the need for rehabilitation will also increase. Unfortunately, these procedures are not risk free and, although they may lead to an increase in functional outcome in some patients, they have significant complications in others. Indeed, the majority of those who could benefit the most from these replacements because of medical issues are exactly that portion of the population that is most prone to complications.

We will focus on THA and TKA and discuss any differences the practitioner might encounter while treating these patients after surgery in the inpatient unit. We will also discuss possible complications, both acute and long-term, so the physician caring for these patients in the outpatient setting will be better aware of newer issues encountered with long-term care in this population.

**TOTAL HIP ARTHROPLASTY**

The goals for hip replacement surgery are to provide a long-lasting method to reduce pain and increase function in the patient. Surgery is usually performed after a trial of more conservative management for conditions that may cause hip pain and loss of function. There are three main components in a hip replacement, the femoral components, acetabular component, and often an ultrahigh molecular weight polyethylene liner (4). The femoral stems can be used with polymethacrylate to affix them to the underlying bone as seen in Figure 1.1, or they can be cementless, which requires a surface that requires bone ingrowth (see Figure 1.2). The materials most often used are titanium, a cobalt–chrome alloy that may include titanium, plastics, and/or ceramics (7). The former comes with porous and nonporous stems. Acetabular components may be anchored in place by several methods. These include polymethacrylate bone cement, the so-called “press fit” or metallic screws (8).

The choice of prosthesis is made by the surgeon based on a set of factors including life expectancy, cost, bone structure, and activity. These factors affect the postoperative rehabilitation and have some implications for possible complications. Rehabilitation is also affected by the surgical approaches—the anterolateral and direct lateral—that
FIGURE 1.1 Cemented left hip endoprosthesis with cement in the femoral medullary space.

FIGURE 1.2 Uncemented bilateral total hip arthroplasty.
tend to decrease the risk of postoperative dislocation. Unfortunately, these approaches require disruption of the glutei muscles and may prolong healing time and function because of abductor weakness. Whereas the posterior approach disrupts the abductors less, there is an increase in possible dislocation of the prosthetic hip. Minimally invasive techniques avoid this complication and offer increased strength in the early rehabilitation phase. There may be an added effect of decreased risk of dislocation, but it can be associated with an increase in intraoperative fractures that can restrict weight bearing for 3 weeks.

The choice of cemented versus noncemented femoral components has a significant role in rehabilitation. Cemented components allow for early weight bearing, whereas porous bone in growth type prosthesis will require a period of nonweight bearing to facilitate the in growth and stabilize the prosthesis/bone interface. The health of the underlying bone plays a major role in the choice of these two types of prosthesis.

TOTAL KNEE ARTHROPLASTY

The goals for TKA are the same as for the THA. The current longevity of the TKA suggests that a properly chosen and implanted prosthesis made with the current materials should last beyond 20 years, thus decreasing the morbidity associated with revision surgery. Unlike the THA, the TKA is routinely cemented, as seen in Figures 1.3 and 1.4, thus allowing for immediate postoperative weight bearing. The issues that impact the rehabilitation after TKA include patient’s overall health, type and extent of bone cuts, and soft tissue balancing. As far as the bone cuts are concerned, the recent addition of computer assisted total knee surgical techniques has increased the accuracy and precision of the bone resections and has allowed for a better outcome in these surgeries. Soft tissue rebalancing is important for overall outcome. Many patients have significant joint deformities (varus, valgus, rotation, and flexion) that, over time, have led to shortening of the ligaments on the medial or lateral sides of the knee or elongation of contralateral soft tissues. These anatomical abnormalities need to be addressed in the surgical plan to allow for a functional knee and to decrease pain.

The TKA is generally a Co/Cr femoral component with a polyethylene tibial component. There are two major designs of the TKA. The difference between the designs is based on whether the posterior cruciate ligament (PCL) is resected. Initially, it was thought that preserving the PCL allowed for more stability and also allowed better ease for stair climbing. It was felt this was because of preservation of the normal femoral rollback during knee flexion. The second type of knee is the posterior stabilized knee. This knee resects the PCL, but newer versions have stabilized the knee with a cam mechanism that mimics the function of the PCL. It is now thought that with the current knees, there is little difference in the range of motion (ROM)
FIGURE 1.3 Postoperative AP view of a total knee arthroplasty.

FIGURE 1.4 Postoperative lateral view of a total knee arthroplasty.
and stair climbing with both types of knees. Two new adaptations have evolved as the TKA recipients have become more active. One is a rotating platform TKA, which, as the name suggests, allows rotation of the femoral component on the tibial component. The other adaptation, which allows for better translation in the anteroposterior (AP) direction, is a variation on the meniscal bearing knee.

Surgical approach and patellar resurfacing are the other components of the TKA that need to be considered in the surgical plan. It appears at this time that the different approaches, which include medial patellar, vastus splitting, and sub patellar (4), are relatively equal in outcome and impact on rehabilitation. Those patients who do not undergo patellar resurfacing may have an increase in anterior knee pain and early joint effusions (4,9). Recent advances in minimally invasive knee replacement hold promise to further reduce the morbidity of this operation, but there appears to be a learning curve for the surgeons to perform this (10).

REHABILITATION OF TJA

One question that has not been fully elucidated is “When should TJA rehabilitation begin?” Studies supporting exercise programs focusing on strengthening and stretching the joint, ROM preservation of the joint, and aerobic conditioning are available in the literature (11–14). Some have suggested that preoperative physical therapy (PT) should be included in any TJA protocol. Unfortunately, there is a paucity of literature on this subject. In the case of THA, there is some evidence of effectiveness. Several small studies have shown that preoperative PT increases gait characteristics, strength, flexibility, and function (15,16). These were small unblinded studies that have several flaws. With respect to TKA, there is even less information. One study of 20 patients looked at preoperative therapy and showed only modest gains in isokinetic flexion (17). At this point in time, the authors do not feel that preoperative PT has been proven to be effective and we recommend considering this on a case by case basis before TJA. One should consider it in those patients with muscle imbalances and equilibrium problems.

Preoperative education has also been used to increase outcomes, patient satisfaction, and speed return of function. Unfortunately, here again there is little evidence in the literature to support its use in TJA. Despite this, the authors do recommend a preoperative education program for TJA, especially in patients who have limited family support and increased anxiety.

The overall goals of rehabilitation after TJA are to help prepare the patient for discharge to a safe environment. The usual criteria include comprehension and independent compliance with precaution, ambulation of greater than 100 feet with an assistive device, independent performance of a home exercise program, and proficiency and safety in performing activities of daily living, including toileting and transfers (4).
**Weight Bearing and ROM in THA**

After THA, the goals should include not only restoration of ROM, flexibility, and strength to the joint, but also prevention and treatment of complications associated with these surgeries. When prescribing therapy postoperatively to a THA patient, questions that need to be addressed include weight bearing restrictions and ROM restrictions. Weight bearing restrictions are usually based on the surgeon’s experience. There has been no clear answer in the literature to help guide standardization of weight bearing limits. The decision on weight bearing should take into account the patients’ age, medical condition, and bone health, as well as the type of prosthesis implanted, quality of fixation presence trochanteric osteotomy for femoral fracture. As a general rule, cemented THA will be able to bear weight immediately postoperatively. The degree of weight bearing in these cases ranges from partial weight bearing (PWB), about 70% of body weight to full weight bearing (FWB). Un cemented THA may require time for bony ingrowth and, therefore, require toe touch weight bearing (TTWB), which is less than 15% of body weight. The period of TTWB can range from a minimum of 6 weeks to 12 weeks. This practice has been ingrained in the practice of postoperative rehabilitation, but the literature does not back up this treatment plan. Whereas originally surgeons felt that there might be more of a problem with femoral subsidence in patients with FWB immediately after uncemented THA, Rao et al showed that FWB with uncemented hips did not relate to increased issues and subsidence at 2 years (18). Considering the delays in recovery by TTWB and based on a study by Beuhler et al that showed increased incidence of deep vein thrombosis (DVT) (19), some have suggested FWB for all cemented and proximal fitting uncemented THA implants without osteotomy, fracture, bone grafting, significant acetabular or femoral bone loss.

ROM restrictions after THA are employed to protect the integrity of the implanted hip. After a posterior or lateral approach, posterior dislocation is the main concern. Therefore, limitation of hip flexion to 90 degrees, hip adduction past midline, and internal rotation to 45 degrees is the norm. For those who undergo an anterior approach, there is an addition of no hip extension or external rotation greater than 45 degrees. Many feel these restrictions and patient education are key elements in the prevention of this complication. To enforce the importance of avoiding extremes of motion and largely to protect the soft tissue repaired, various postoperative restrictions have been proposed for patients undergoing THA since the early days of this procedure (20,21). Restrictions such as the use of an in-hospital abduction pillow, a pillow between the legs during sleep, a high chair, and an elevated toilet seat, along with the limitation of certain ROMs, and the avoidance of driving, or being a passenger in an automobile are frequently recommended; the value of these restrictions in postoperative rehabilitation has not been adequately evaluated. A prospective study demonstrated that the rate of early dislocation was acceptably low in patients who did not observe postoperative restrictions following THA (20,22). That study, however, was not randomized and lacked a comparison group. One prospective study in uncemented
hips included 265 patients and found no difference in the dislocation rate with or without ROM restrictions (20). They did note, however, that there was an increase in function and satisfaction in the unrestricted group. Unfortunately, there are very few of these studies in the literature, so it is hard to draw conclusions about efficacy of this education. The authors of this chapter currently recommend adhering to restricted ROM protocols as chosen by the surgeon.

**Weight Bearing and ROM After TKA**

As mentioned earlier in this chapter, most TKA are fixed in place with cement. This allows for FWB immediately postoperatively. Whereas the rehabilitation team works to restore strength and flexibility, reduce pain, and prevent other complications, ROM of the prosthetic knee is a major focus. Whereas in THA the protocol limits ROM, the typical TKA rehabilitation is to increase ROM. Passive and Active ROM is performed in the physical therapy area, but continuous passive motion (CPM) machines have been used in patient rooms to allow for greater early flexion, decreased knee pain, and decreased length of stay (LOS). There have been many studies of CPM since its inception, but they have been consistently unable to prove long-term benefits (23–26). As such, the use of CPM machines to improve and ensure adequate ROM in the knee after TKA is a controversial intervention. Broussou showed that use of CPM immediately after TKA resulted in positive effects on tissue healing, edema, hemarthrosis, and joint function (27). Patients utilizing CPM also exhibited improved short-term early knee flexion and decreased the LOS. However, Alkire found no statistically significant difference in flexion, edema, drainage, function, or pain between a group that was given CPM treatments and one that was given usual care after computer assisted TKA (28). Finally, Harvey and Broussou published a follow-up meta-analysis that concluded that “The effects of continuous passive motion on knee range of motion are too small to justify its use. There is weak evidence that continuous passive motion reduces the subsequent need for manipulation under anesthesia” (29).

Thus, it appears that whereas CPM does have a history of use and may facilitate early knee flexion after TKA, there appears to be no long-term benefit or cost savings. This suggests that hands-on therapy techniques and exercise education may be more helpful in this population. One should consider the whole patient in prescribing CPM and may find that it is more helpful in those patients with cognitive dysfunction and excessive stiffness after surgery.

**Postoperative Rehabilitation Prescription**

As with ROM and weight bearing, exercise programs for rehabilitation after TJA are lacking. As a result, exercise protocols may vary greatly among institutions.
These are often driven by the surgeon, rehabilitation specialist, and costs. A consensus report published in 1996 suggested that an exercise program consisting of ankle pumps, gluteal and quadriceps sets, and active hip flexion strengthening should be included in acute inpatient THA rehabilitation (30). Therapy should be started early and pain should be controlled to allow for participation. After THA, the patient should be encouraged to sit at the side of the bed, active and assisted hip flexion strengthening in supine and standing with support. Strengthening of the hip abductors can improve gait by decreasing contralateral hip sagging in the single leg stance phase of the gait (4). As long as there is no greater trochanteric osteotomy, hip abductor strengthening should be part of the rehabilitation protocol. Munin has found that hip abductor strength is positively correlated with immediate postoperative function (31).

TKA goals are to facilitate the rapid recovery of the knee ROM, strengthen the knee and hip musculature, and return to functional independence (32). Therapy is progressed rapidly from assisted ROM in sitting, usually on postoperative day (POD) 2 to isometrics of the hips and knees by POD 4 (4). Gait training should begin with crutches or walker, based on patient needs, balance, and strength. Proprioceptive training should be part of the protocol.

After discharge from rehabilitation for TJA, more therapy will be required to focus on increasing balance, gait mechanics and distance, navigation of stairs, and continued hip and knee strengthening. Studies evaluating the need for further therapy after discharge from the acute rehabilitation environment have also failed to consistently provide guidance as to the best way to treat these patients (4).

COMPLICATIONS DURING ACUTE REHABILITATION

Medical complications are common among patients undergoing inpatient rehabilitation, so the rehabilitation specialists need to be aware of them, know their treatments and prevention strategies. One study on patients with a stroke diagnosis found 60% incidence of at least one complication (33). A significant number of these medical complications may require a transfer to an acute facility. The complications can be direct or indirect. Those that might require transfer would more likely be as a result of indirect complications such as pneumonia, DVT with pulmonary embolism (PE), urinary tract infections (UTIs) that become systemic, hip fracture from fall, and gastrointestinal (GI) ulcer. Direct complications, which typically do not require transfer out of inpatient rehabilitation but can significantly impair or slow down the rehabilitation, include decubiti ulcers, hip dislocation, heterotopic ossification (HO), severe pain, skin infection (mainly from surgical wounds), syndrome of inappropriate adrenal hormone (SIADH), and loss of joint ROM.
Skin Issues

Development of pressure ulcers may be considered one of the most unfortunate complications seen by physical medicine and rehabilitation (PM&R) physicians. A pressure ulcer is a pressure sore or, what is commonly called, a “bed sore.” More commonly seen in patients with spinal cord injuries, insensate and immobile, pressure ulcers can range from a very mild pink coloration of the skin, which disappears in a few hours after pressure is relieved on the area, to a very deep wound extending to and sometimes through a bone into internal organs. Pressure ulcers are typically classified into four stages according to the severity of the wound.

The cause of pressure ulcers most often is because of pressure. Prolonged pressure past some threshold level leads to local tissue ischemia, and then necrosis, and breakdown of skin and underlying soft tissues. However, shear forces such as in too vigorous a transfer or taking off a sticky bandage when the skin is frail can also lead to skin breakage that results in ulcers. Hematomas can also lead to superficial skin breakdown as they resolve over time.

Pressure ulcers typically occur at pressure points, as the unrelieved pressure results in local ischemia and eventually skin and soft tissue necrosis. Therefore, the most common sites where pressure ulcers are seen include the sacrum, ischial bones, occiput, and heels. Pressure ulcers can be prevented in rehabilitation units by using frequent turns, pressure relief measures, and aggressive surveillance to catch any pressure ulcers in the earliest stage. Although treatment most often involves sustained pressure relief, pressure ulcers can impair the rehabilitation and even stop the therapies for a few days, weeks, or even months, depending on the severity. Pressure ulcers are feared because they are largely preventable in rehabilitation units and they are considered “never events” by Medicare and may result in reduced reimbursement to the hospital for the care provided to treat them.

The first step in resolution is to reduce, or even better, eliminate pressure on the affected area. Specialized mattresses and seating systems, which can maintain tissues at pressures below 30 mmHg, are available for beds and wheelchairs. These specialized surfaces include foam devices, air-filled devices, low-air loss beds and air-fluidized beds. Low air loss beds support the patient on multiple inflatable air permeable pillows. Air-fluidized beds pump air into permeable mattresses containing microspheric, uniformly sized, silicone coated beads. Wheelchair air seat cushions come with individualized inflatable cells that offer some pressure relief.

Direct treatment of pressure ulcers consists of a choice of dressings and devices that attempt to remove devitalized tissue and allow healthy tissue to heal. The frequency, amount, and use of more advanced treatments depend on the size of the sore, health and healing potential of the patient including nutritional status, and functional needs of the patient. Simple repeated wet–dry dressing changes with isotonic sodium chloride solution and intermittent debridement was the mainstay of treatment for many years. For smaller, more shallow, clean wounds, applying a gel agent that is changed every third
day can also be of value. More difficult, stage 2 and 3 wounds may require Sulfamylon, hydrogels, and xerogels applied daily. Many stage 3 and most stage 4 wounds do not respond to these treatments and require surgical grafts, often called “flaps.”

More recently, popular treatments of wounds include the use of negative pressure wound therapy (NPWT) (34). Many studies have been published regarding outcomes and methods of therapy used for wounds in adults. Even in the setting of pediatric wound healing there is evidence of efficacy for this treatment. One specific example is the study by Baharestani, who found efficacy with vacuum assisted closure (VAC) in pediatric wounds (35). Most studies showed efficacy of therapies in diabetic ulcers, more so than in pressure sores, but these therapies are still utilized frequently in rehabilitation hospitals. Vicario published two cases of grade 3 pressure sores in SCI patients that healed with NPWT (36).

Ultimately, just like the rehabilitation program, prevention and then treatment of a pressure ulcer requires a multidisciplinary approach. Experts from various disciplines—nurses, physical and occupational therapists, nutritionists, psychologists, and surgeons with specialty in wounds—work together with the patient and physiatrist for successful outcomes that will return the patient to active rehabilitation.

**Infectious Issues**

Another type of direct complication is skin infection. Most often, while rehabilitating patients with orthopedic diagnoses, skin infections are seen at the postoperative wound site. Thus, it is imperative that all wounds are checked daily by the rehabilitation physician. One patient group especially susceptible to such infection is post spine surgery patients. One study found that post laminectomy wound infection to be around 1% to 4%, but if there was instrumentation, the rate rose to 7% to 9% (37). Posterior cervical surgery carries a slightly higher rate of infection (38). Undetected, these infections could lead to discitis/osteomyelitis or, worse, sepsis that can become life threatening (39).

The primary pathogens in postoperative wound infections most often are the gram-positive cocci, specifically *Staphylococcus aureus*, *S. epidermidis*, and beta-hemolytic *Streptococci* (40). The organism most commonly seen in culture is *S. aureus*. Most concerning would be a methicillin resistant strain (MRSA). Of the gram negative rods, *Klebsiella pneumoniae*, *Escherichia coli*, *Pseudomonas aeruginosa*, and *Proteus* species are commonly seen in postoperative wounds.

Joint replacement patients commonly develop wound infection. Although occurring less often (1% incidence overall), patients in inpatient rehabilitation are typically more medically complex and thus have a higher risk of developing infection (41). The organisms are similar to those in the laminectomy patient, and treatment options are also similar. Although it is rare a prosthetic joint would have to be removed, taking the patient back to the operating room for a washout and interruption of the rehabilitation is a frequent necessity.
The constellation of treatments is based on the severity and type of infection. Superficial and less severe infections can be managed often with simple antibiotics. Deeper infections may require IV antibiotics for six weeks (40). Most severe infections and those not responding to antibiotics may require reoperation, debridement, full washout, or even removal of spine instrumentation or joint prosthesis. In some cases, re-implantation of hardware or prosthesis might be delayed until antibiotics have taken full effect. Nonetheless, treatment either slows down, postpones rehabilitation, or requires transfer of rehabilitation.

Therefore, the best treatment is prevention. Having staff follow strict hand washing protocol is essential. Checking wounds at least once per day during rounds should be routine. Finally, at risk patients such as those who are immunocompromised, diabetic, or malnourished must be monitored closely or isolated from other at risk patients. A multidisciplinary approach between the nursing staff, therapists, and a separate wound survey team works best in inpatient rehabilitation settings.

**Bone Issues**

Another possible complication of hip or knee arthroplasty is HO. HO is the formation of exogenous bone within a joint. Although rare, when HO occurs and if the bone is large enough, the HO can hamper ROM and cause pain. Patients at higher risk for developing HO after THA include men with bilateral hypertrophic OA, patients with a history of HO in either hip as seen in Figure 1.5, and patients with posttraumatic

![FIGURE 1.5 Severe heterotopic ossification of the hips prior to surgery.](image-url)
arthritis characterized by hypertrophic osteophytosis, and patients with ankylosing spondylitis. Patients at higher risk for developing HO after TKA include those with limited postoperative knee flexion, increased lumbar bone mineral density, hypertrophic arthrosis, excessive periosteal trauma, and those who require forced manipulation after TKA because of poor ROM at the joint (42).

Diagnosis of HO is challenging. The clinician can be fooled because the inflammatory component of the HO process often mimics joint infection. X-rays, unfortunately, are not helpful in identifying HO until the bone has started to form, leading to delayed treatment. Bone scan has been felt to be the most sensitive indicator of HO. Lab tests such as ESR can help track the condition and monitor treatment effectiveness.

Treatment typically is medical in the early stages and surgical in the end stages. Etidronate is the standard initial treatment of HO. Indocin also gets used frequently with good results. After 9 to 12 months, the exogenous bone from the HO becomes fully mature and can be excised surgically if it is limiting the function of the joint.

One of the most unfortunate complications seen in post THA patients on the rehabilitation service is dislocation as seen in Figure 1.6. Typically, this seems to occur overnight when the patient might move unaware of the precautions and wakes up with a painful, externally rotated hip. Immediate radiographs reveal the dislocation. Posterior approach patients have a much higher dislocation rate than anterior approach patients (43). Treatment most often requires a trip back to the operating room and possibly even a revision. De Palma published a study that showed of the 87 dislocated implants, all needed one or more closed reductions and 52 eventually required revision.
surgery. An early dislocation increases the cost of hemiarthroplasty, THA, and revision THA by 472%, 342%, and 352%, respectively.

Genitourinary Issues

The most common secondary complication seen in inpatient rehabilitation units is UTI. Clement found that the prevalence of UTIs in patients undergoing total knee or hip surgery was 14% (44). At times, urine can reveal abnormal cultures as the patient may be colonized with organisms because of having a Foley catheter inserted for 2 to 4 days postsurgery. However, given the presence of an implant that could become infected if urinary colonization becomes a urine infection, it is often better to treat any abnormal urine culture that shows greater than 100,000 colonies of a pathological microorganism in the culture with appropriate antibiotics.

Thromboembolic Issues

Complications that occur in patients undergoing acute inpatient rehabilitation after orthopedic procedures or with rheumatologic disorders can be indirect as well. These complications include DVT and PE and are not uncommon in the setting of decreased mobility, thus leading to the patients in the rehabilitation unit being at risk. A PE can be one of the most tragic events to occur in a rehabilitation service resulting in further disability or even loss of life. Therefore, it is important to recognize a DVT immediately after it occurs before the clot breaks off and goes to the lung. Additionally, patients who suffer a DVT but not PE can still develop postthrombotic syndrome (PTS). In one large study, 37% of patients with venous thromboembolism (VTE) developed PTS within 2 years of a diagnosis of DVT, with the occurrence of PTS linked to clinically relevant declines in measures of physical and mental health. They found the economic burden of PTS in the United States to be as high as $200 million annually (45).

The most basic check of the lower legs occurs every day as a vital portion of the physician’s examination of each patient in the rehabilitation unit. Calf redness, swelling and/or pain are three signs that a DVT is occurring. Many inpatient rehabilitation units employ “DVT survey teams” who check calves on every patient. However, it is still sometimes difficult to recognize the clinical sign of a DVT in orthopedic patients until it is too late. Some patients—especially those who have had joint replacement or who are obese—have swelling anyway. Therefore, prevention becomes a paramount focus of orthopedic and rheumatologic inpatient rehabilitation patients.

For many years DVT prevention consisted of a combination of mechanical and medical interventions. DVT is caused by a combination of venous stasis, hypercoagulability, and intimal injury; the first two are the most modifiable targets for prevention measures. The stasis occurs because of patient immobility postorthopedic
injury or surgery; this stasis can be reduced by intermittent pneumatic compression (IPC) devices. Typically, the clotting is reduced medically. Although physicians generally agree on the end goal, unfortunately much disagreement exists on how to achieve clot prevention in orthopedic patients. Treatment varies from a daily aspirin, to unfractionated heparin (UFH), and low molecular weight heparin (LMWH), to warfarin at full anticoagulation doses with INR between 2.0 and 3.0.

Even with application of one of the recommended DVT prophylaxis protocols, DVT and PE cannot be entirely prevented, reinforcing the importance of the physician’s daily evaluation of the orthopedic rehabilitation patient. One meta-analysis found the incidence of symptomatic postoperative DVT before hospital discharge as low as 1.09% for patients undergoing partial knee arthroplasty and 0.53% for those undergoing partial hip arthroplasty all of whom had adequate prophylaxis with LMWH or warfarin. One study utilizing a “fibrinogen uptake test” found the incidence of DVT in acute inpatient rehabilitation to be 48% after surgery for hip fracture, 54% after total hip replacement, and 63% after total knee replacement (46).

Ginzburg published a review of studies on multiple types of patients undergoing inpatient rehabilitation (47). They recommended “options” that the clinician can choose from as being acceptable methods of DVT prevention. Their recommendations in the category of “orthopedic surgery,” which included polytrauma, joint replacement, and hip fracture, are listed in Table 1.1. It is of some interest that one study by Santori et al found that mechanical prophylaxis was actually superior to UFH (48). One concern with medical treatments is bleeding; however, this was found to be an infrequent complication in all studies. Another major recommendation stemmed from a study by Westrich that showed that the prevalence of asymptomatic PE was significantly lower \((P < .05)\) with IPC (6%) or warfarin (8%) than with aspirin (12%) (49). The Ginzberg study does not recommend aspirin as an effective preventative measure of DVT prophylaxis for orthopedic patients involved in acute inpatient rehabilitation (47).

The newest agents currently still under study, but used often in Europe and Canada, are direct thrombin inhibitors rivaroxaban, apixaban, and dabigatran etexilate. The advantage of these agents is that they are oral agents with predictable pharmacokinetic profiles, allowing for a fixed-dose regimen without the need for coagulation monitoring. Whether these agents will supplant warfarin remains to be seen (50,51). However, more recent recommendations published by the American College of Chest Physicians (52) relating to

<table>
<thead>
<tr>
<th>TABLE 1.1 Anticoagulation Recommendations for Orthopedic Procedures</th>
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<tbody>
<tr>
<td>Enoxaparin: 30 mg b.i.d. or 40 mg q.d.</td>
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<tr>
<td>Dalteparin: 32 mg (5000 anti-Xa IU) q.d.</td>
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<tr>
<td>Fondaparinux: 2.5 mg q.d.</td>
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<tr>
<td>Unfractionated heparin (UFH): dosage adjusted to maintain activated partial thromboplastin time (aPTT) at high normal values</td>
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<td>Warfarin: dosage adjusted to maintain INR at 2 to 3</td>
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postorthopedic surgery patients in 2012 included them (see Table 1.2). They were against using inferior vena cava filter placement for primary prevention in patients with contraindications to both pharmacologic and mechanical thromboprophylaxis (Grade 2C).

If a DVT is suspected, immediate diagnosis is required so that treatment, which has a higher chance of preventing a subsequent PE, can be initiated. Diagnostic options include real time duplex ultrasound. If ultrasound is not available (this is rare in most rehabilitation settings), venography can be utilized. The limitation of ultrasound is that it occasionally misses a very proximal or pelvic DVT. Newer MRI protocols might be useful in such a situation. If the patient is short of breath and PE is suspected, specialized CT scans can now visualize the pulmonary defect from the PE even if Doppler studies are negative. In any case, once DVT or PE is suspected, the therapy should be sustained and the patient left at bed rest until the diagnosis can be sorted out and proper anticoagulation treatment initiated.

Once a DVT is identified, the medical treatment must be ramped up to prevent a PE or, if PE has been identified, to prevent worsening PE. Rehabilitation can resume when the patient is stabilized and the anticoagulant effect of treatment has had a chance to set in. Treatment recommendations include: enoxaparin: 1.0 mg/kg b.i.d. or 1.5 mg/kg q.d., UFH: dosage adjusted to maintain aPTT at 46 to 70 seconds, and/or warfarin: dosage adjusted to maintain INR at 2 to 3.

Evidence suggests that the prevalence of DVT after spinal surgery (without spinal cord injury) is higher than generally recognized, but with a shortage of epidemiological data, guidelines for optimal prophylaxis are limited. Bryson published a survey, which found that 73% of neurosurgical respondents and 31% of orthopedic surgeons employed LMWH after spine surgery. Neurosurgeons also selected antiembolism stockings more frequently (79% vs 50%) whereas orthopedic surgeons preferred mechanical prophylaxis (26% vs 9%) (53).

How long should thromboprophylaxis be maintained? One review of six randomized trials compared prolonged thromboembolic or bleeding outcomes (≥21 days)
with standard-duration (7 to 10 days) thromboprophylaxis. They found that prolonged thromboprophylaxis reduced the incidence of DVT and PE with an increase of minor but no major bleeding complications (54).

Another indirect complication from immobility, as a result of having had an orthopedic procedure, requiring inpatient rehabilitation is nosocomial pneumonia. Seen more often in spine patients, especially after cervical or thoracic procedures, pneumonia can often be mistaken for PE. Therefore, careful clinical assessment from the physiatrist is required to sort out the symptoms and signs. Early treatment with appropriate antibiotics is necessary to avoid bacteremia and seeding of implants in the spine or joints.

**Bleeding Issues**

Joint hematoma or continued drainage is another complication seen in rehabilitation units in patients after an orthopedic surgery. Most often this is a benign sterile issue that will resolve on its own with time. However occasionally, the fluid becomes a source for infection and, thus, if prolonged, may need surgical drainage.

The secondary question is what to do about anticoagulation related to this issue. Tasker published a meta-analysis and found that LMWH reduced nonfatal PE at the expense of hematoma formation (55). Other studies showed only minor bleeding risk with LMWH. If hematoma or prolonged sterile drainage persists on the rehabilitation service, the orthopedic colleagues should be consulted and the situation managed in a team approach.

**Pain Management**

Chronic pain is a combination of psychologic and physiologic responses to a noxious stimulus. Over time, pain from the original anatomic lesion that is not adequately treated affects psychologic variables and adds an overlay of anxiety and depression in these patients. This is clearly one of the big issues in treating a patient with rheumatoid arthritis and OA. These people may eventually lose some of their coping mechanisms for pain and this in turn leads to many challenges in the postoperative setting after TJA.

Pain can occur directly from the procedure, in joints and structures not involved in the procedure that may have arthritis or suffer increased strain from lack of mobility of the operated joint. The pain can hamper rehabilitation participation, lengthen the LOS on the unit, and cause stress to the patient and caregivers alike. Treatment requires the rehabilitation physician trained in pain management techniques to balance the need for pain control with the side effects of potentially strong medications that control the pain. The physiatrist will often spend a great deal of time and effort with each patient to strike that balance and encourage the patient to participate in the rehabilitation program despite pain issues they may have.
Early pain management is important to mobilize the patient. The goal is to control pain without making the patient too groggy to participate or recall the educational portions of rehabilitation. One review suggested less reliance on opioids for pain management after TJA (56). Whereas minimizing general anesthesia may decrease postoperative grogginess, nausea, and pain, once the patient arrives at the acute rehabilitation setting, the increase in activity may require adjunct treatments. Indwelling catheters may be helpful in the immediate postoperative period; however, they need to be removed as soon as possible to prevent complications.

In general, we prefer to have a scheduled long-acting narcotic with rescue dose of short-acting narcotics for pain relief. We administer anesthetic patches and use NSAIDs to keep the doses of narcotics as low as can be tolerated. This will minimize opioid associated gastroparesis but allow full participation in therapies. Care should be taken when administering NSAIDs in the setting of anticoagulation. COX2 inhibitors may be helpful because of their smaller effect on platelet function and decreases bleeding time as a result (57). Novel pain medications like tramadol may also be helpful in avoiding narcotics if the patient’s pain is moderate. Cold modalities have been shown to help control pain in the TJA patient (58). Studies have shown that body mass index and multiple comorbidities are associated with more pain (4,59).

LATE COMPLICATIONS

Immunologic Issues

Long-term, TJA is considered safe, nontoxic, and in the past it was thought that there was no issue with immune reactions to the prosthetic components. Over the past decade, this train of thought has been challenged. Some animal studies have suggested that parts of the replacement joints are potentially carcinogenic (60–62). A study by Jacobs et al described a variety of biologic responses to metallic implants (63). The study focused on THA components made with titanium-based alloys. Keel et al reports a case series of 12 cases with metal implant related tumors (62). The majority of these were in replacement surgeries; however, some were from intramedullary rods or plates. Figure 1.7 shows the radiographic features of implant related tumors whereas Figure 1.8 shows the pathologic specimen at the time of resection. The time from implant to diagnosis ranged from 1.7 to 11 years in a previous case series. When reviewing previous reports, Keel et al found the majority of the tumors to be in the hips. Since these reports, others have also reported on their experience with metal-on-metal hip resurfacing (64,65). This is an important complication to catch early as large high grade sarcomas like these carry a poor prognosis.

Whereas metal implant tumors are possible, they are not the only immunologic reaction to metallic implants. A study by Korovessis et al performed histologic evaluations of uncemented hips that were replaced because of loosening (66). They found
evidence of chromium–cobalt metallosis in all the 11 hips replaced. This process can be the result of a diffuse perivascularly oriented infiltration of lymphocytes, plasma cells, and eosinophils (67). A gross specimen of metallosis seen in Figure 1.9 shows the black necrotic tissue surrounding normal anatomy. This finding is seen with contemporary metal-on-metal prostheses. Whereas most of the studies have reported this in THA, they can also present in TKA. Figure 1.10 shows the radiographic changes in a TKA with metallosis. The physician should be aware that these complications exist and be able to consider them in appropriate patients with x-ray abnormalities.

**Leg Length Issues**

It is not uncommon to have some leg length discrepancy after TJA. For the most part this difference is minimal, <1 cm, and may not be apparent to the patient. For
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FIGURE 1.8 Gross specimen of an implant-related sarcoma of the hip.

FIGURE 1.9 Gross specimen of tissue reaction in metallosis removed from a knee.
some patients, however, this can be a significant source of dissatisfaction. With small perturbations in one’s gait, there can be an increase in pain in the lumbar spine and sciatica and sacroiliac joint, and an increase in gait abnormalities (68). Larger leg length differences can cause neural compromise, leading to a sciatic nerve injury in some. The rehabilitation specialist should assess whether this is a true leg length discrepancy or an apparent one. True leg length is determined by the distance from the anterior superior iliac spine to the medial malleolus and reflects the actual length of the extremity. Although leg length discrepancy cannot be eliminated after hip arthroplasty, it can be minimized through a series of steps both preoperatively and intraoperatively. These include physical examination to determine true and apparent leg length and radiographic evaluation to both assess leg length and to preoperatively template the surgical procedure (69). Figure 1.11 depicts such a mark up to help properly align a second THA.

One study found after THA, 56 (62%) limbs were long by a mean of 9 mm, and this was perceived by 24 (43%) patients after three months and by 18 (33%) after 12. The mean Oxford hip score in patients who perceived true lengthening was 27% worse
I. MEDICAL COMPLICATIONS

FIGURE 1.11 Preoperative mark up for a left total hip arthroplasty to help avoid leg length and alignment problems.

than the rest of the population after three months and 18% worse after 12. In 55 (98%) patients, lengthening occurred in the femoral component (68). Patients in whom the difference causes significant function problems or pain can be treated with a shoe lift, therapies for adductor stretching, and muscle rebalancing.

Cognitive Issues

Postoperative cognitive issues in the elderly have been recognized since the mid-1950s (70,71). The first International Study of Post-Operative Cognitive Dysfunction (ISPOCD 1) found that there was significant postoperative cognitive dysfunction (POCD) one week after surgery in over 25% of patients undergoing major non-cardiac surgery (72). This number dropped to just below 10% by the third month. They found a significant relationship between early (one week) POCD with advancing age, increasing duration of anesthesia, lesser educational level, second operation, postoperative infections, and respiratory complications. By three months, only age had a negative effect, but preoperative benzodiazepine use was found to be protective. Follow-up studies have confirmed that advancing age is a risk factor, but the type of anesthesia and the use of benzodiazepines are not. There appears to be evidence that duration of anesthesia may also be a risk factor (71). Patients undergoing THA have a significant risk for postoperative delirium, which is also a risk for POCD at three months (71,73).
Nerve Injury Issues

Peripheral nerve injury (PNI) after TJA is uncommon but can be a source of significant morbidity. THA has a higher incidence of nerve injury than TKA by about a 3:1 ratio (74). The latter has an incidence of around 1%; however, one study reported it as being as high as 10% (75,76). Early diagnosis can assist the patient by formulating the proper rehabilitation program and providing compensatory devices to maximize the recovery and function of the nerves. The cause of PNI is often unclear. Although one might think direct compression injuries the most likely cause, in most cases the surgery is not in an area where direct pressure on the nerve is possible. Distraction of the nerve (stretch injury) is another possibility, especially the femoral nerve in leg lengthening procedures. Vascular injuries or ischemia during surgery is another possibility. Finally, many injuries just defy explanation. In these cases, it is thought that a spontaneous neuropathy may be occurring, akin to the Parsonage–Turner syndrome, but of just one single nerve. Risk factors for nerve injury include diabetes mellitus, revision surgery, limb lengthening, female sex, increased surgical time, increased blood loss, revision surgeries, and congenital hip dislocation (4,74,77). In one study, overall incidence of PNI was not associated with peripheral nerve blockade or type of anesthesia; it decreased with age but increased with tourniquet time and bilateral procedures. Revision THA shows additional etiologies that include improper retractor placement, cement extravasations, cement-related thermal damage, patient positioning, manipulation, and postoperative hematoma (77). Risk factors for nerve injury include developmental dysplasia of the hip, female gender, posttraumatic arthritic bone spurs with preoperative compression, and revision surgery (77). Patients with PNI who underwent peripheral nerve blockade were less likely to have complete neurologic recovery (75).

Sciatic nerve injuries are more common than femoral nerve injuries in TJA. TKA has a low incidence of nerve injury overall, but the fibular nerve is the most common nerve injured. For THA, the fibular portion of the sciatic nerve or the fibular nerve proximally is the most likely to be affected. Possible causes of fibular nerve injury include traction, ischemia, direct trauma, cement, or hematoma (4). These patients often present with foot drop or other signs of deep fibular nerve injury. This may also include dorsolateral dysesthesias.

Fortunately, the prognosis for these injuries after THA is generally good. Electrodiagnostic studies can be used to clarify the location of the lesion and give prognostic information. Nerve conduction studies and needle EMG can identify whether the injury is demyelinating (neurapraxia) or axonal (axonotmesis). Axonal injuries carry with them a poorer prognosis for spontaneous recovery. Recovery in such cases is slow and often incomplete whereas demyelinating injuries usually recover fully. Clearly, the best recovery comes in those with the more mild deficits. Most of the deficits resolve over time, but can take up to 2 years to improve (4). PNI after
TKA has not been as well described. Proper treatment involves first identification by the physiatrist with electrodiagnosis for prognostication. Then the rehabilitation multidisciplinary team can design the therapy program to focus on either direct recovery for the neurapraxic injuries versus more of a compensatory strategy for the axonal and more slowly recovering injuries. Such strategies include bracing, home modification, and other assistive devices for activities of daily living.

**Complication Timeline for Orthopedic Surgery**

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<thead>
<tr>
<th>Complication</th>
<th>Onset of complication</th>
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<tbody>
<tr>
<td></td>
<td>Early/Acute</td>
</tr>
<tr>
<td>Hematoma</td>
<td>X</td>
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<tr>
<td>Pneumonia</td>
<td>X</td>
</tr>
<tr>
<td>Soft tissue infection</td>
<td>X</td>
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<tr>
<td>Pressure ulcer</td>
<td>X</td>
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<tr>
<td>DVT</td>
<td>X</td>
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<tr>
<td>PE</td>
<td>X</td>
</tr>
<tr>
<td>UTI</td>
<td>X</td>
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<tr>
<td>Cognitive dysfunction</td>
<td>X</td>
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<tr>
<td>Nerve injuries</td>
<td>X</td>
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<tr>
<td>Gastric ulcer</td>
<td>X</td>
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<tr>
<td>Hip dislocation</td>
<td>X</td>
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<tr>
<td>Heterotopic dislocation</td>
<td>X</td>
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<tr>
<td>Infection of the prosthetic joint</td>
<td>X</td>
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<tr>
<td>Pain</td>
<td>X</td>
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<tr>
<td>Postthrombotic syndrome</td>
<td>X</td>
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<tr>
<td>Metallosis/tumors</td>
<td>X</td>
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<tr>
<td>Leg length problems</td>
<td>X</td>
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**REFERENCES**


I. MEDICAL COMPLICATIONS


1. MUSCULOSKELETAL DISORDERS


Spinal Cord Injury

Kevin Dalal and Diana D. Cardenas

EPIDEMIOLOGY OF TRAUMATIC SPINAL CORD INJURY

Spinal cord injury (SCI) in the United States has a reported incidence of about 40 cases per million population per year or approximately 12,000 new cases per year. The true incidence is unknown since there is no mandatory national surveillance system. The prevalence in the United States as of 2013 is estimated to be 273,000 people with a range between 238,000 and 332,000 persons (1). Data from the National Model SCI Systems indicate that the average age at injury for those injured after 2010 is 42.6 years. The trend toward increasing age at injury has followed the increased median age of the general population in the United States since the mid-1970s. Male patients continue to comprise about 80% of all new injuries (1).

Etiology of SCI

The most common cause of traumatic SCI since 2010 continues to be motor vehicle crashes (36.5%), followed by falls (28.5%), acts of violence (14.3%), and sport injuries (9.2%) (1).

The most frequent reported neurologic category at hospital discharge is incomplete tetraplegia, followed by complete paraplegia, incomplete paraplegia, and finally complete tetraplegia.

Nontraumatic SCI is beyond the scope of this chapter; however, the medical complications in nontraumatic SCI are similar but less frequent with the possible exception of surgical wound infections (2). The etiologies of nontraumatic SCI include spinal stenosis, tumors, vascular events, infection, and noninfectious causes such as transverse myelitis, multiple sclerosis, and other rare conditions.
EARLY AND LATE MEDICAL COMPLICATIONS

Genitourinary Complications

During the period of spinal shock, the bladder is usually areflexic, and an indwelling catheter should be placed to allow drainage. The indwelling catheter allows for large outputs that are common in the acute state following SCI. Assessment of the genitourinary (GU) system after spinal shock ends will determine whether the individual has sustained an upper motor neuron (UMN) lesion versus a lower motor neuron (LMN) lesion. A UMN bladder typically develops when the lesion is located above the sacral segments and results in a hyperreflexic bladder. An LMN bladder is produced by a lesion in the conus medullaris or the cauda equine and is typically areflexic. Occasionally, a lesion in the conus medullaris spares the lowest sacral segments, and flaccid lower extremities are present with a hyperreflexic neurogenic bladder. Baseline evaluation of the function of the GU system during initial in-patient rehabilitation should include a renal and bladder ultrasound and, if clinically indicated, urodynamic studies (3).

Urodynamic studies will assist in determining the functional classification of the neurogenic bladder as well as assist in clinical recommendations for bladder management. Although intermittent catheterization (IC) is considered a healthier option, patients with tetraplegia and insufficient hand function (even with splints) may choose to continue with an indwelling urethral catheter because IC every 4 to 6 hours may make the individual dependent upon an attendant to perform the catheterizations. SCI males with the presence of detrusor-external sphincter dyssynergia (DSD), defined as contraction rather than relaxation of the external urethral sphincter during the contraction of the bladder, generally will not be able to adequately empty the bladder with reflex contractions and will typically develop high detrusor pressures due to the obstruction imposed by the contracting sphincter. In such patients, options include (a) sphincterotomy + external catheter; (b) IC with anticholinergics to reduce pressure and maintain continence; or (c) a chronic indwelling catheter (urethral or suprapubic). The goals of bladder management are to maintain continence, allow adequate emptying of the bladder, prevent accumulation of postvoid residual volumes above 150 to 200 mL or 500 mL if IC is used, avoid obstructed voiding, and enable the individual to be as functionally independent as possible.

Urinary tract infections (UTIs) are quite common in patients with SCI during the initial hospitalization for rehabilitation. The signs and symptoms of UTI may include increased spasticity, cloudy and odorous urine, urinary incontinence, autonomic dysreflexia (AD), general malaise, fever, and chills. Patients with complete injuries do not sense dysuria. The type of bladder management method will influence the incidence of UTIs and even the interpretation of urine culture results. IC is less likely to lead to recurrent UTIs especially during initial hospitalization; however, after discharge from initial rehabilitation, those having a caregiver perform IC may be more likely to have
febrile episodes of UTI (4). Indwelling catheters increase the risk of UTIs and are also associated with an increased risk of calculi, epididymitis, fistula formation, and the development of bladder carcinoma (5). The urine culture in someone with an indwelling catheter is likely to demonstrate significant bacteriuria any time a culture is taken even if the patient is asymptomatic. Therefore, other aspects of the urinalysis are of importance such as the presence of pyuria.

The patient has the potential to develop renal and bladder calculi. Renal calculi may be small and nonsymptomatic or may produce AD in those with lesions at or above T6. Large renal calculi may be a source of obstruction of the calyces and result in infection or abscess formation. Bladder calculi may be present in patients who have an indwelling catheter or who use IC and may produce gross hematuria and lead to UTI.

Epididymitis is another potential medical complication that may not produce any pain or discomfort in the patient with a complete lesion although there might be AD. Examination of the testes will reveal swelling, redness, warmth, and induration of the epididymis.

**GI Complications**

During the period of spinal shock immediately post SCI, a paralytic ileus is common, but should resolve within a week as the bowel regains intrinsic activity. However, appropriate bowel management is necessary to promote evacuation and prevent chronic constipation. Gastrointestinal (GI) bleeding is an uncommon occurrence, perhaps owing to the routine use of ulcer prophylaxis; however, when present, the signs may mimic other medical conditions. During the first 3 weeks of hospitalization, about 6% of patients develop GI complications, the most common of which are ileus, peptic ulcer disease, and gastritis (6). The GI problems that occur vary depending on the level and severity of the lesion. A UMN bowel results from a supraprenal lesion whereas injury to the related lower motor neurons or nerves results in an LMN bowel. If the individual has spasticity with a spastic external anal sphincter, it is likely that an UMN bowel exists.

All GI complications are more common in cervical level injuries than thoracic or lumbar level lesions, and the increased risk of GI bleeding and gastritis is thought to be due to loss of sympathetic innervations and unopposed parasympathetic stimulation of acid secretion.

A scheduled bowel program should be established as soon as possible and will depend on the type of injury. The UMN bowel program consists of judicious use of stool softener medications and insertion of a rectal suppository, followed by digital stimulation of the rectum until the bowels have reflexively evacuated stool. This should be performed daily or on an every-other-day basis. Lack of limb spasticity and a flaccid external anal sphincter usually indicates an LMN bowel. The LMN bowel program consists of judicious use of stool-bulking agents and manual disimpaction.
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of stool. Due to the flaccid characteristic of the bowel and sphincter, individuals may require daily or twice-daily disimpaction to maintain continence. With LMN bowel, digital stimulation or chemical stimulation in the form of rectal suppositories is of no value because of the last reflex activity. It should be noted that the neurogenic bowel with impaction is the second most common cause of AD.

Other GI complications that occur during the acute period include gastric dilatation, superior mesenteric artery syndrome, and pancreatitis. Pancreatitis may result from spasm of the sphincter of Oddi secondary to imbalance of the sympathetic and parasympathetic nervous systems. However, the acute pancreatitis that results from such a mismatch is not the same illness as hemorrhagic pancreatitis, which may be life-threatening and is not caused by the SCI itself. A rare complication that may occur is the superior mesenteric artery (SMA) syndrome. The SMA syndrome results from compression of the third portion of the duodenum by the SMA owing to loss of the fat layer between those two structures. Treatment may include a lumbosacral corset to push the abdomen upward, positioning with the head elevated after meals, frequent small meals, and replacement of weight lost.

Appendicitis may occur but not produce abdominal pain. As in the case of other GI complications, imaging and lab testing is key. Anorexia, nausea, vomiting, and an elevated white blood cell count often signify more serious GI complications such as appendicitis, cholecystitis, or even rupture of the appendix. The repeated use of antibiotics may result in C. difficile colitis. Diarrhea superimposed on the neurogenic bowel makes regulation even more difficult despite appropriate antibiotic treatment.

MUSCULOSKELETAL COMPLICATIONS

Heterotopic Ossification

Heterotopic ossification (HO), which forms between muscle planes, is the formation of mature lamellar bone in soft tissue. It may be contiguous with the skeleton but does not involve the periosteum (7). In the United States, the incidence of HO in SCI is 16% to 53%, and the incidence of clinically significant cases is 18% to 27% (8,9). In the acute phase, HO presents with erythema, swelling, warmth, and rapid loss of joint motion, and may cause severe pain during the process of formation. Such nonspecific symptoms may be on a differential list of other inflammatory conditions such as infection, cellulitis, deep vein thrombosis (DVT), and osteomyelitis (10).

Approximately 20% of patients will have some loss of range of motion (ROM), and 8% to 10% of patients with HO have severe functional limitations. Patients with neurologic lesions that are complete and of traumatic origin tend to have a higher incidence of HO. HO always occurs below the neurologically impaired segments. There is typically an association between the severity of spasticity and the extent of the HO.
The pathophysiology involves an inflammatory process with increased blood flow in the soft tissue. HO originates from dormant osteoprogenitor stem cells within the soft tissues. The stem cells are stimulated to differentiate into osteoblasts, which begin osteoid formation and develops ultimately into mature heterotopic bone. Research suggests that there may be a correlation between HO and human leukocyte antigens: HLA-B18, HLA-B27, and HLA-DW7 (11). The stimuli that trigger the osteoprogenitor cells have not been fully elucidated, but bone morphogenic proteins have been shown to stimulate HO under experimental conditions. There is also a component of neurologic control, which has not yet been explained.

Histologically, the timeline to maturation is as follows: in the first week after trauma, spindle cells proliferate. By the second week, the primitive osteoid has formed and primitive cartilage is being laid down. In weeks 2 to 5, trabecular bone forms. By week 6, immature undifferentiated tissues centrally surrounded by mature lamellar bone are present. HO formation peaks 4 to 12 weeks following SCI or surgery (12). Bone matrix is laid down and mineralized, and this sequence reaches a steady-state maturation by 6 to 18 months.

HO occurs only below the level of the lesion in SCI (12). The hips are the most commonly affected areas in SCI, and if left untreated, can result in loss of hip flexion, limiting sitting and interfering with transfers. The shoulders and elbows can also be affected in tetraplegics and result in loss of upper extremity function. Patients can also exhibit HO in more than one location, and it may reoccur in this population. Presenting symptoms in HO typically include progressive loss of ROM, localized swelling, redness, and warmth.

Complications of HO include joint ankylosis leading to decreased ROM, skin breakdown over the affected area, peripheral nerve entrapment, and DVT from compression of the veins by the HO.

The diagnosis of HO is most accurately made by a triple-phase bone scan. This test is the most sensitive test and can detect HO 2 to 4 weeks before x-ray. The three phases are blood flow, blood pool, and soft tissue uptake. The blood flow and blood pool are the most sensitive but are less specific than the soft tissue uptake. Plain films are not able to detect HO until 5 to 7 weeks after onset. A nonspecific laboratory test to detect HO is the serum alkaline phosphatase, which can detect early onset because it is a marker of osteoblastic and osteogenic activity that increases with bone deposition. In cases of HO, the alkaline phosphatase levels rise at 2 weeks, exceed normal values at 3 weeks, peak at 10 weeks, and then return to normal after HO is mature (6–18 months). It is nonspecific, however, as the serum alkaline phosphatase can also be elevated in cases of trauma, fractures, bony metastases, or liver disease.

Once the diagnosis of HO has been confirmed, treatment can commence with the first line of treatment being disodium etidronate, which can limit the extent of ossification if started early. The treatment course is 20 mg/kg for 2 weeks followed by 10 mg/kg for 10 weeks (13). Treatment is not effective in treating ossification once it
is present on x-ray; it can only prevent further deposition of calcium into the matrix. Indomethacin has also proven to be of value in the treatment of HO and may be used in those patients without contraindications and is sometimes useful if the process continues despite disodium etidronate.

If ankylosis and loss of function occur, the only treatment is surgery. Surgical outcome is not optimal as there is a high rate of recurrence. Patients with massive HO, severe spasticity, lack of local motor control, and impaired cognition have a higher recurrence rate following resection (14). This recurrence can be mitigated with radiation and/or etidronate. This option is reserved for patients with seating problems, skin breakdown, excessive pain, or loss of function. Surgery is typically delayed until the HO is mature. The maturation state can be confirmed once the serum alkaline phosphatase returns to normal and when bone scan reaches a steady state. There is typically an association between the severity of spasticity and the extent of the HO.

PULMONARY COMPLICATIONS

Diseases of the respiratory system are the leading cause of death in patients with cervical spinal cord injuries. The mortality from respiratory issues is dependent on the level and duration of injury, but are also affected by age, preexisting cardiopulmonary disease, and associated trauma affecting the pulmonary system (15).

The challenge of respiratory management in the SCI patient involves atelectasis, secretion management, and hypoventilation. The loss of intercostal muscle innervation places more demands on the diaphragm, which leads to atelectasis. Due to the poor cough and clearance of secretions, SCI patients have difficulty clearing secretions. In the early stages, these secretions are particularly copious due to unopposed vagal tone. This can lead to downstream complications, such as acute respiratory distress syndrome (ARDS), hypoxemia, hypercapnia, and may necessitate intubation.

Thus, in the early days of injury, when the patient is in acute rehabilitation, pulmonary toilet is a priority. An incentive spirometer should be available bedside and used intermittently throughout the waking day. Suctioning is to be administered on a PRN basis for secretions attributable to the unopposed vagal tone. The timing of suctioning can be guided by bedside pulse oximetry as patients may not be able to express distress or cough. When suctioning, a curved tip should be used to improve access to the left lung, which is more frequently affected due to the oblique entry of the left main-stem bronchus. If this proves inadequate, a bronchoscopy to clear refractory plugging may be necessary.

Atelectasis affects 45% of all SCI patients and typically responds to high tidal volumes. Though there is theoretically a higher risk of barotrauma, the overall morbidity and mortality is improved by decreasing the risks and sequelae of persistent atelectasis and trapped lung (16). Pneumonia is most likely to develop in an atelectatic
area of the lung. Other complications include pulmonary embolism, which is usually attributable to the patient’s increased risk of DVTs.

Many SCI patients have chest injury, rib fractures, and other contusions associated with their original trauma. Such concomitant injuries place the patient at high risk for pneumothorax, which may also occur due to high pressure ventilation. A low volume may lead to atelectasis as discussed. Pneumothorax should be treated with high tidal volumes (>1000 mL) and to mitigate the risk, the pressure should be maintained below 40 cmH$_2$O. This improves the likelihood of weaning off the ventilator. The predicted healing of these secondary injuries must be taken into account along with the superimposed impairments of any concomitant neurologic compromise, which may also affect lung function in these patients. The combination of atelectasis, pulmonary effusion, and pneumonia can lead to empyema. In these complex cases, a chest tube may be placed for drainage. Such complications increase the danger of trapped lung, caused by scarring or fusion of the parietal and visceral pleura. The organization of this exudate in the pleural space can cause a peel around the lung.

Pneumonia is the leading cause of death during all postinjury time periods, ranging from 19% in the first postinjury year to 12.7% after the first postinjury year (17). If the level of injury is C1–4, this incidence is as high as 60% lifetime. Differentiating pneumonia from atelectasis is challenging because their presentations occupy a similar cohort of cervical/high thoracic injuries presenting with low-grade fevers and poor secretion management. On average, the onset for pneumonia is 25 days post-op with a duration of 15.5 days (18). The principle mechanisms of inflation—movement, cough, and clearance are compromised by the deficits to the diaphragm and intercostals. A tracheostomy can introduce a foreign body that further magnifies susceptibility.

Although prophylactic antibiotics are not recommended, immunizations are, namely Influenza annually and \textit{S. pneumoniae}, every 5 years. Once diagnosed, the treatment protocol mimics that of the noninjured population. Sputum cultures are checked, and the patient is initiated to broad-spectrum antibiotics until susceptibilities allow the caregiver to tailor the treatment to the identified infection. Even if the diaphragm is intact, T1–6 injured patients have an increased risk of pneumonia when compared to lower thoracic or thoracolumbar injuries because of intercostal muscle weakness and the concomitant impaired ability to cough.

SCI patients are particularly susceptible to aspiration. One reason is that many have clinically altered mental statuses in the time frame immediately following their anesthesia. Usually, the aspiration is caused by gram-negative bacteria and anaerobes. If there is no aspiration, there is a high risk of community-acquired infections, with the highest being \textit{S. pneumoniae} and \textit{H. influenzae}. If there is aspiration suspected, anaerobe coverage should be started, and if the patient has a tracheostomy tube, it should be replaced and the patient treated presumptively for methicillin-resistant \textit{Staphylococcus aureus} (MRSA) until cultures suggest otherwise. Of course, strict adherence to contact and/or air-borne precautions are necessary to prevent dissemination to other patients.
I. MEDICAL COMPLICATIONS

Assisted Cough

If a patient cannot maintain a vital capacity of 1.5 L, they should receive maximal insufflation by a manual resuscitator or portable volume ventilator to achieve adequate cough flows. If volumes can be reached, the expiratory muscles may be assisted manually via anterior compression assist or costophrenic abdominal thrust. Initially, the nurses can perform these techniques, as the patient and their caregivers learn how to perform it in the home setting.

Glossopharyngeal Breathing

If the bulbar innervation is intact, the patient may be able to accomplish glossopharyngeal breathing as a means of air-stacking to force air past the glottis. In this maneuver, the patient uses the glottis to assist in the inspiratory effort by gulping boluses of air into the lungs. The glottis closes with each gulp, and one breath typically consists of 6 to 9 gulps of 40 to 200 mL each. Limitations to this technique include the inability to implement it in the presence of an indwelling tracheostomy tube. Even when capped, air tends to leak around the outer walls of the tube.

Mechanical Assistance

A patient who cannot maintain a vital capacity of at least 1.5 L is a candidate for mechanically assisted ventilation. An insufflator–exsufflator, which generates alternating positive and then negative pressure to a patient’s airway, assists in clearing retained bronchopulmonary secretions. This method can generate 600 L/min of expiratory flow.

An intrapulmonary percussive ventilator is a mechanized form of chest physical therapy that delivers high flow jets of air to the airways at the rate of 100 to 300 cycles/min via a mouthpiece.

Intermittent Positive Pressure Ventilation

The high-level SCI patient, because of the inability to control secretions and breathing, which exceeds the capacity of the denervated diaphragm, is frequently treated with tracheostomy and intermittent positive pressure ventilation (IPPV). The indication for IPPV is a forced vital capacity (FVC) <10 mL/kg or 25% of predicted value, a daytime PaCO₂ of >50 mmHg, and a Pimax <50 cmH₂O.

Noninvasive Ventilation

Through a regimented treatment plan using mechanical/manual cough techniques, progressive cuff deflation, and adjustment of volumes for insufflation and speech, it
may be possible to wean many patients to noninvasive ventilation. This requires a total commitment on the part of the caregiver as well as the patient. One potential means of noninvasive ventilation is bilevel positive airway pressure (BiPap), in which a biphasic positive airway pressure system is employed via a nasal mask. Unlike continuous positive airway pressure (CPAP), BiPap differentiates between inspiratory and expiratory positive airway pressure.

Ventilatory Assistance

Intubation or noninvasive means should be employed if there is respiratory distress or vital capacity <15 mL/kg. Intubation is recommended when the noninvasive means fail to reverse an intractable atelectasis, hypoxemia, hypercapnia, or persistent rapid, shallow breathing, tachycardia, or hypotension. Frequently, the decision between noninvasive vs. invasive is facility driven. Intubation, however, is clearly favored if there is a brain stem injury which impairs glossal control.

If noninvasive ventilation is not an option, a tracheostomy may be preferable to an endotracheal tube as there is less chance of damage to the vocal cords, it gives the patient the potential to eat, and it is easier to clear secretions with a suction catheter. Also, it is possible to deflate the tracheostomy cuff to allow speech, which is an integral part of any potential weaning process. However, deflation does increase the risk of aspiration.

Patients can be started with a tidal volume of 12 to 15 mL/kg of ideal body weight and then titrated up. C3–4 tetraplegics who receive high tidal volume (>20 mL/kg body weight) ventilation can wean approximately 3 weeks faster than the lower tidal volume group. The concern over barotrauma in the high tidal volume group appears to be overstated, especially when considering the increased weaning success of this group. Oxygen is titrated to maintain greater than 92% saturation. If peak pressure is less than 40 cmH2O, then tidal volume can be increased by 100 mL/day. The end-tidal pCO2 is maintained at 28 to 35 mmHg by adding or subtracting appropriate dead space.

The ventilation of spinal cord patients cannot be managed using the same algorithms as would be used in neurologically stable vent patients. One important area of differentiation is that of peak pressure. Peak pressure is not to exceed 40 cmH2O. Tidal volume should be increased to a maximum of 25 mL/kg ideal body weight (IBW) until the patient is afebrile and has minimal secretions and the chest x-ray is clear. The peak flow should not exceed 120 L/min.

As discussed at the beginning of this section, atelectasis after the ventilator starts means that the tidal volume is too low. The risk of pneumothorax can be mitigated by carefully monitoring the inspiratory pressure. If there is mucus plugging, pressure of up to 40 cmH2O can be tolerated to generate 10 to 12 cmH2O at the alveolus (19). Remember that using larger volumes also increases surfactant production.

Another area of differentiation in the ventilator management of tetraplegic patients is the use of positive end expiratory pressure (PEEP). PEEP is used very frequently in
ventilation but may not be optimal in SCI. PEEP increases the mean airway pressure and predisposes to barotrauma, and PEEP does not allow for surfactant release (20). Mean airway pressure is lower if patients are ventilated with large volumes without PEEP.

The lower the level of the SCI, the more feasible a weaning program becomes. A vital capacity of >1 L on admission is favorable for weaning high-level injuries. Weaning should take place according to a protocol and should start for 2 to 5 minutes TID and increase slowly as tolerated to 10 minutes TID, to 20 minutes TID, to 30 minutes TID, and increasing by the hour to 3 hours TID and then to 4 hours BID, 5 hours BID, then 12, 14, 18, 20, 22 hours QD. Steps may be skipped as appropriate. Weans should take place in the bed with the cuff deflated and talking permitted. Oxygen should be titrated to >92%. Weans can take place in the wheelchair once the patient tolerates weans for >30 minutes.

A long-term consequence of prolonged ventilator usage is chronic hypocapnia. Chronic ventilated patients may show an arterial blood gas (ABG) with a low PCO$_2$ value. The kidneys compensate and pH remains between 7.4 and 7.45. There are minimal side effects to a mild alkalosis unless there is a history of seizures or heart disease.

**Sleep Apnea**

Sleep apnea is a common occurrence in SCI patients, with variable prevalence reported from 15% to 60%. The sleep apnea is typically obstructive, but a small percentage may be central in nature. Relationships exist between sleep apnea and a higher level of injury, vital capacity, obesity, neck circumference, and the effect of antispasticity or pain medications. The loss of thoracic sympathetic outflow may contribute to nasal stuffiness, which may exacerbate the sleep apnea.

The complications of sleep apnea include hypertension, pulmonary hypertension, cor pulmonale, congestive heart failure, daytime sleepiness, and poor judgment. The workup should include an overnight oximetry recording followed by a formal sleep study. Treatment is with CPAP or BiPap. Pharmacologic treatment with tricyclic antidepressants (TCAs) are also an option.

**Diaphragmatic Pacing**

Patients who have disruption of central control over phrenic nerve motoneurons and malfunctions of the respiratory control center may be candidates for diaphragmatic pacing. Patients with respiratory muscle paralysis secondary to phrenic nerve damage, parenchymal lung disease, or acute respiratory failure are not candidates. The lower motoneurons of the phrenic nerves have to be sufficiently intact, and the patient should have stabilized their neurologic level for at least 3 months. Diaphragmatic pacing has become a laparoscopic procedure and has become much cheaper than previous electrophrenic pacing with much less risk to the phrenic nerves.
Over the course of 3 to 4 months, a progressive program of bilateral pacing can eventually lead to full-time ventilator support. Adjustments during the course of training include lengthening pulse duration, adjusting threshold ramp, and changing inspiratory time. These modifications allow for increasing tidal volumes, decreasing upper airway resistance, and smoothing contractions. The diaphragm must be conditioned, like any other muscle, to tolerate the pacing. More realistically in some cases, patients may be able to “rest” on the ventilator at night, while being paced during the day.

Unfortunately, even if patients tolerate 24 hours support, they typically require a permanent tracheostomy and backup ventilator just in case of equipment failure. They must also have personnel on hand who are trained in managing this equipment.

### CARDIOVASCULAR COMPLICATIONS

**Cardiovascular Fitness**

Patients with SCI are susceptible to various cardiovascular conditions and complications, both in an acute as well as chronic setting. In cervical and high thoracic injuries, the interruption of the sympathetic outflow tracts affects cardiac and vascular function. There is reduced sympathetic efferent output in complete SCI, which can mean the loss of the mechanism to compensate for cardiovascular stresses of active exercise. For instance, sympathetic vasoconstriction with increased venous return or increased heart rate and contractility are not available in these patients. The maximal heart rate is significantly reduced. The exercise capacity, as represented by the VO$_2$ max is reduced and leads to deconditioning. Overall fitness is compromised as there is reduced muscle mass under voluntary control.

SCI patients have a sedentary lifestyle due to impaired mobility. Arm endurance and resistance exercise is typically not sufficient to counteract the lost motion of the legs in terms of maintaining overall fitness. Basal energy requirements should be reduced from those calculated for able-bodied individuals from 10% for low paraplegia to 25% for those with high tetraplegia. Ideal body weights may be 10 to 20 lbs lower than the general population. The denervation of the skeletal muscle, prolonged inactivity, and increased adiposity lead to decreases in insulin sensitivity. High density lipoprotein (HDL) levels are lower in chronic SCI when compared to the general population. Together, sedentary lifestyle and lower HDL suggest an increased risk for coronary heart disease in SCI patients.

**Hypotension/Bradycardia**

Regulatory control of the sympathetic nervous system is lost and there is concomitant loss of sympathetic activity below the level of injury (21). As a result of reduced
sympathetic activity, there is reduced vasomotor tone, which directly leads to low baseline pressure in SCI patients. There is a lower epinephrine and norepinephrine levels in both new and chronic SCI patients. Additionally, due to the autonomic imbalance of having predominant parasympathetic and decreased sympathetic activity, there is a resultant bradycardia. This condition typically resolves after 2 to 6 weeks. Atropine can be administered if severe and recurrent episodes occur during tracheal stimulation (as a result of unopposed vagal stimulation causing reflex bradycardia). Temporary pacemakers may be considered if severely recurrent.

Orthostatic Hypotension

Orthostatic hypotension is defined as a >20 mmHg drop in systolic blood pressure (BP) on upright position or any symptomatic fall in systolic BP in upright posture. Positional changes can cause changes in BP and pulse in any patient, but these effects are particularly pronounced and concerning in the SCI patient. Specifically, orthostatic hypotension is likely to occur in lesions below the origin of major splanchnic outflow at T6. The lack of sympathetic vasoconstriction in large splanchnic and skeletal vascular beds conspires with the gravitational effects of venous pooling and the lack of compensation in other vascular beds. The pooling in the distal extremities leads to reduced filling pressures and end-diagnostic filling volumes and stroke volume. To compensate, there is tachycardia due to reflex vagal inhibition, but this is not sufficient to overcome the reduced sympathetic response.

Over time, the orthostatic hypotension tends to stabilize and improve. For one, reduced flow to the kidneys activates afferent glomerular dilation, which stimulates the renin–angiotensin system. Other reasons for improvement include vascular wall hypersensitivity and increased skeletal muscle tone. Even in cases where the readings do not markedly improve, the patient may become tolerant to the symptoms.

Though the SCI itself is not a modifiable risk factor, there are additional measures, which can be taken to avoid exacerbating the potential for orthostatic hypotension. For one, the care team should avoid any sudden positional changes, especially in patients that have endured prolonged recumbency prior to starting therapy. Once in therapy, the patient can be gradually acclimated to upright postures by using progressive tilt table trials. Also, the patient can be maintained in a head-up position during sleep. Other nonpharmaceutical management practices include increasing salt intake and using compression stockings. Useful equipment modifications include having a wheelchair with reclining and elevating leg rests.

Other contributing factors include a hot environment, dehydration, heavy meals, sepsis, and certain medications such as diuretics, antidepressants, alpha-blockers, and narcotics.

If the patient is continuing to exhibit symptomatic orthostatic hypotension, it may be appropriate to pursue a short-term trial of fludrocortisone or midodrine.
Fludrocortisone’s pressor action is due to sodium retention over several days. Arteriole sensitivity to norepinephrine is increased. One cannot use this medication in cases of CHF due to fluid retention and weight gain. Midodrine is an alpha-1 adrenoreceptor agonist that directly increases pressure by arteriolar and venous constriction.

**Autonomic Dysreflexia**

Whereas orthostatic hypotension features a rise in heart rate and a postural change in BP, an emergent case of AD has the exact opposite effect, with increased BP and a failed attempt to compensate with bradycardia. AD is one of the most urgent complications of higher-level spinal cord injuries and a delay or negligence to immediately recognize its hallmark signs and symptoms may result in preventable morbidity. The morbidity is associated with the marked hypertension causing retina/cerebral hemorrhages, myocardial infarction, or seizures. Mortality is rare. AD is reported to occur in 48% to 85% of SCI patients injured at or above T6 (22). There have been cases reported as low as T10.

In spinal cord injuries above the level of the splanchnic sympathetic outflow or T5–7, the patient may exhibit a massive imbalanced reflex sympathetic discharge under certain conditions. This typically occurs after the phase of spinal shock, once reflexes have returned despite the patient’s injury. During this period of susceptibility, a noxious stimulus below the level of lesion produces an afferent impulse, which generates a generalized sympathetic response, which leads to vasoconstriction below the neurogenic lesion.

The vasculature below the diaphragm, or splanchnic beds, receives innervation from the T5–7 levels, whereas the heart receives innervation from the T1–4 levels. With lesions at or above the T6 level, the splanchnic vascular bed becomes involved, which provides the critical mass of blood vessels required to cause an elevation in BP.

A strong sensory input is carried to the spinal cord via intact peripheral nerves. Most commonly, these stimuli originate from the bladder and bowel. This strong sensory input ascends in the spinothalamic and posterior columns to stimulate sympathetic neurons located in the intermediolateral gray matter of the spinal cord. As a result, there is widespread vasoconstriction, most significantly in the splanchnic vasculature.

The brain detects this hypertensive crisis through intact baroreceptors in the neck, delivered to the brain via cranial nerves IX and X, which are obviously intact in spinal cord injuries not involving head trauma. The brain attempts to abort the sympathetic surge by sending descending inhibitory impulses, which do not get to most of the sympathetic outflow levels because the SCI at T6 and above impedes this signal. Thus, that critical mass of blood vessels in the splanchnic vasculature supplied by T5–7 can continue to constrict unopposed by compensatory mechanisms from the brain.
In a further attempt to compensate for this unregulated pressure, the brain attempts to lower the peripheral BP by lowering the heart rate. Because the parasympathetic innervation of the heart is regulated by the vagus nerve, which is CN-X, this nerve is also spared in SCI and allowed to perform its function. However, this compensatory bradycardia is inadequate; this can be attributed to Poiseuille’s law; namely, the pressure in a tube is affected to the fourth power by a change in radius (the initial vasoconstriction) and only linearly by a change in flow rate (compensatory bradycardia).

In summary, a noxious stimulus triggers an intact spinal reflex of sympathetic outflow, which leads to peripheral arterial vasoconstriction and resultant hypertension. Compensatory parasympathetically modulated bradycardia tries but fails to compensate for this phenomenon. Below the level of the injury, where the vasoconstriction is predominant, the patient exhibits skin pallor, bladder sphincter contraction, GI sphincter contraction, and penile erection. Above the level of injury, the parasympathetic vasodilation is allowed to occur and manifests as flushing, sweating, pounding headache, nasal congestion, and mydriasis.

The immediate management is to sit the patient up, remove any restrictive clothing and remove the inciting stimulus, thereby aborting the reflex hypertension. The most common stimulus is irritation or over-stretch of the bladder wall. This can be caused by a blocked catheter, an overfilled collection bag, noncompliance with catheterization program, urinary retention, or a UTI. Therefore, the first treatment is to catheterize the patient who is on an IC program. Lidocaine jelly should be administered to the catheter prior to placement. If the patient has an indwelling or external catheter, then check the urinary drainage system and straighten any kinks in the tubing, and bring the drainage bag below the level of the bladder. If the catheter is plugged, it can be flushed with 10 to 15 mL of normal saline. If the AD does not resolve immediately, the etiology may not be due to an overdistended bladder and other etiologies should be investigated.

If symptoms persist, another frequent stimulus is irritation or overdistension of the GI tract such as one would find in constipation or impaction, or occasionally hemorrhoids. Disimpaction should not be attempted unless systolic blood pressure (SBP) <150 mmHg as the act of disimpaction may actually exacerbate the dysreflexia. In these cases, pharmacologic intervention to exogenously lower the BP should be tried prior to disimpaction.

Although bowel and bladder irritation are the most common etiologies for AD, any direct irritant below the level of injury can cause AD. Frequently, this can be caused by the lack of perception of prolonged pressure by a foreign object such as an object in the chair, in the patient’s shoe, a bullet fragment, pressure sore, ingrown toenails, burns, or tight clothing. More rarely, sexual activity, menstrual cramping, and labor/delivery have been shown to manifest as AD. Extremity findings, which may also cause AD include HO, occult fractures, spasticity, or DVTs. Certain procedures may initiate dysreflexia, among them urodynamic studies, cystoscopy, or electro-ejaculation.
When evaluating an SCI patient’s BP to gauge severity during episodes, it is important to recognize that a tetraplegic patient has a lower resting BP and that an increase of 15 to 20 mmHg above this baseline may represent an episode of AD, even though this BP may not be considered a hypertensive crisis for an able-bodied individual. Pharmacologic intervention in the treatment of AD should only be considered if the SBP >150 mmHg. The most immediate management is ½” of nitropaste, which can be easily removed. Alternatively, the patient may take a calcium channel blocker, nifedipine 10 mg bite-and-swallow, which is effective in lowering the BP without further impacting the bradycardia negatively (23). Yet other options include clonidine and, in patients who cannot swallow, hydralazine IM or IV. It is not recommended to take medication chronically for prophylaxis as the most effective cure is to eliminate the trigger, which may be masked if the patient is chronically managed on antihypertensive medication, which can lead to further morbidity.

### Venous Thromboembolism

DVT in acute SCI is a frequent occurrence due to the additive impact of platelet aggregation, increased factor VIII, and stasis (24). The diagnosis of peripheral vascular disease is frequently delayed or missed altogether due to the lack of the cardinal symptom of intermittent claudication. Further down the path of morbidity, symptoms of advanced limb ischemia, such as rest pain or numbness, may also be present. It is essential that peripheral pulses and skin be routinely examined to monitor for ischemic changes. Inpatients and postoperative SCI patients are placed on low molecular weight heparin (LMWH) or on an analogue for DVT prophylaxis. If the patient is paraplegic, this treatment is maintained for 8 weeks, and in tetraplegics, this treatment should be sustained for 12 weeks. If a DVT is present, conversion to warfarin treatment and maintenance for up to 6 months is warranted.

### Cardiac Ischemia and Acute Events

It may be challenging to diagnosis SCI patients with acute coronary syndrome (ACS) because of the lack of predictable chest pain. Treatment may be delayed and secondary prevention overall may be inadequate. Extant comorbidities in SCI patients may mimic certain cardiac conditions as well on cursory physical exam. For instance, dependent edema may be mistaken for heart failure and atelectasis may be mistaken for left ventricular failure. SCI patients also have nonspecific ST-segment and T-wave changes. As far as routine testing is concerned, traditional treadmill stress testing is typically not possible in this population for obvious reasons. Performing arm exercises instead of leg exercises gives suboptimal sensitivity. For these patients, pharmacologic stress testing is preferred.
Medications to treat cardiovascular conditions should be started at a lower dose with careful BP monitoring. Because many SCI patients also have erectile dysfunction, the prescriber must be careful when giving Viagra if the patient is already taking nitrates. Additionally, the use of ACE inhibitors may complicate SCI-related urologic problems.

SKIN COMPLICATIONS

Decubitus Ulcer

A decubitus ulcer is an area of unreleased pressure over a defined area, typically over a bony prominence, resulting in ischemia, cell death, and necrosis. Decubitus ulcers are typically preventable and represent a tremendous expenditure and source of morbidity in both acute and chronic SCI patients. The costs are not purely economic, as an ulcer forces the patient to be restricted physically, socially, and even vocationally. Model systems data shows that 32% to 40% of all patients develop pressure ulcers during initial rehabilitation (25).

Decubitus ulcers are staged from I to IV and this stratification incorporates both macroscopic and morphologic criteria, based on erythema of the skin and depth of the ulcer. Stage I is nonblanchable erythema, which is not resolved in 30 minutes. The epidermis remains intact, and the condition is reversible with intervention. A dressing is typically not necessary as there is no drainage or disruption to the outer epidermis, but weight shifts and turning need to be aggressively pursued to prevent progression. Patients with dark pigmentation may not clearly manifest a stage I ulcer.

A stage II ulcer represents a partial loss of skin thickness involving the epidermis and possibly the dermis. The ulcer may appear as blisters with erythema, an abrasion, or a shallow crater.

A stage III ulcer represents destruction of full-thickness of skin through the dermis into subcutaneous tissue, which may extend down to, but not through, the underlying fascia. The ulcer presents clinically as a deep crater with or without undermining adjacent tissue.

A stage IV ulcer is loss of full-thickness of skin with deep tissue destruction through subcutaneous tissue to the fascia, muscle, bone, joint, or supporting structures. Undermining and sinus tracts may also be associated with stage IV pressure ulcers.

A potential wound cannot be assessed if there is an overlying eschar present. It is recommended that eschars be debrided to properly stage the underlying tissue and allow for healing. Otherwise, this type of wound is considered unstageable.

To properly assess a decubitus ulcer, one must remember to measure its length along the longest axis of the ulcer and width at the widest point at 90 degrees to the axis of the length. The depth to the ulcer bed should also be measured. If there is undermining under a ridge of epidermis, the degree of undermining should also be
documented. Tunneling should be probed and measured and documented in terms of its direction with respect to a clockface.

Decubitus ulcers primarily target the bony prominences, which are the most susceptible to shear and friction forces. While the patient is hospitalized, the sacrum, heels, and ischium are the most commonly affected areas, in that order. This is likely attributable to the prolonged time spent in a dependent, supine position. After 2 years, the ischium becomes the most common site, probably because, by this point in time, the patient is spending extended periods of time up in a wheelchair, thus targeting the ischia, which sustain the most pressure during sitting. Similarly, when trying to offload the sacrum or ischium by lying on the side, the greater tuberosities are then placed at risk. The prone position has the greatest surface at the lowest pressure but is also the least tolerable position for many patients because of the positioning of the face and neck. Based on measurements of transcutaneous partial pressure of O$_2$ and interface pressure, positioning at 30 degrees when lying on the side is the most effective.

**Risk Assessment**

Two commonly used scales for risk assessment in pressure ulcers are the Braden and Norton scales (26). The Braden scale has six subscales: sensory perception, moisture, activity, mobility, nutrition, and friction/shear. Each group is rated 1 to 4 (highest to lowest) with the lower total representing the greatest risk. The Norton scale uses five variables to assess risk: activity, mobility, incontinence, physical condition, and mental condition. However, neither of these commonly used scales are SCI specific; so it is important to consider certain facets of a SCI in assessing risk. To quantify these SCI specific issues, the Salzberg scale may be of greater utility as it considers level of activity, level of mobility, completeness of injury, urine incontinence, AD, pulmonary disease, renal disease, traumatic paralysis, and lung infections.

**Pathophysiology**

Besides issues of impaired tissue function and loss of mobility and sensation, there are other pathophysiologic factors in SCI that can predict the development of pressure ulcers. SCI patients have decreased levels of lysyl hydroxylase below the level of injury. This is an enzyme, which catalyzes the hydroxylation of lysine to hydroxylysine, which is necessary to the formation and stabilization of collagen. Decreased or disrupted collagen formation jeopardizes skin turgor and structural integrity. The increased excretion of the metabolite glucosyl-galactosyl hydroxylysine after traumatic SCI stops in the second year postinjury.

Below the level of injury, SCI patients have decreased adrenergic receptors, which then alter the vascular response. After pressure is removed, there develops a
slower reflow rate, which leads to lower tissue oxygenation. Also, the elastin content of skin decreases postinjury. This can exacerbate the mechanical load on the skin and cause it to thin out.

**Pressure Ulcer Prevention**

When a patient is in the acute inpatient setting, a turning program must be put in place immediately. Initially, the patient is turned every two hours. This interval may be increased to four hours as tolerated prior to discharge. During dependent transfers, it is essential that the care-staff not pull the patient across the bed to the chair, but use a sheet underneath the patient to assist with sliding. This lowers friction and reduces the chances of shearing the skin during transfers.

Static support mattresses may be an option if the patient is considered at high risk for developing an ulcer or if the patient has an active ulcer on which they are not placing any weight. These static supports include foam-filled (Eggcrate, Geomatt, Comfortline), air-filled (Roho, Sof-care, First Step) or gel-filled (KCI) overlays. However, it is more likely, that it would not be possible to position the patient without putting pressure on the ulcer. In such cases, or if the ulcer is not healing, another option is a dynamic support surface. These include low air loss overlays, low air loss beds, and air fluidized beds. Air-fluidized beds are effective for excess moisture, and have a bactericidal effect; however the beds make bed mobility and transfers exceedingly difficult.

Similarly, wheelchair cushions may be constituted of foam, gel, air, or alternating air. The RoHo, with its individualized air villi, is effective in prophylaxis and management of extant ulcers but is prone to breakdown and is expensive. When a patient is up in the chair, they should be mindful to tilt to shift their weight every 15 minutes for 30 seconds. The shifts may be anterior with head between knees, lateral while leaning over an arm rest, or upwards by extending elbows on the armrests. If a patient does not have the arm strength to shift weight independently, it would be appropriate to consider a wheelchair with a power tilt-in-space feature. This offloads the weight of the trunk and head from being directly above the ischium and, thus, allows for transiently increased perfusion via passive pressure distribution. Tilt-in-space is preferable over simple reclining because reclining induces a shear force on the posterior thighs. A back support system for the wheelchair is essential to maintain the architecture of the back as a simple sling-back will promote kyphosis and pelvic obliquity, and increase ulcers on buttocks and the sacrum.

Nutrition is also an important consideration in preventing decubitus ulcer occurrence. Risk is increased with a lower calorie, lower protein diet. The Agency for Health Care Policy Research recommends individuals without ulcers consume 1.25 g protein/kg/day. If an ulcer is present, this can increase to 1.5 g/kg/day. Vitamins C and E assist in the hydroxylation of proline and lysine, which are important factors in
collagen formation. Prealbumin is the most sensitive indicator for monitoring nutritional status because of its short half-life (2 to 3 days). Total protein and albumin have also been associated with pressure ulcer development. Any open wound, secondary to inflammation or infection, will lead to catabolic reactions with a concomitant loss of body protein. Because SCI patients have decreased levels of the anabolic hormones, HGH, and testosterone, the anabolic agent oxandrolone has been shown to restore weight and increase healing rate.

**Treatment**

There are three phases of wound healing; inflammation, tissue formation, and remodeling. Wounds can become persistent, secondary to chronic inflammation, because of wound exudate, bacteria, and devitalized tissue. Nonviable tissue is unable to draw appropriate oxygenation and will not spontaneously heal without more aggressive management. Debridement can be chemical, mechanical, autolytic, or surgical. Mechanical debridement involves using woven gauze in a wet to dry technique. Wet to dry are not considered moist saline dressings, as they are intended for debridement. In autolytic debridement, devitalized tissue is hydrated to allow reactive enzymes to digest denatured tissues. Agents typically used for this include hydrogels, which are moisture retentive tissues. These wounds must be frequently cleaned to wash out the degraded fragments.

**Autolytic debridement** specifically targets nonviable tissue and is less traumatic to surrounding healthy tissue. Enzymatic debridement involves the use of chemically prepared agents such as accuzyme or collagenase, but these are much more expensive than hydrogels and work faster. Each visit should feature cleaning with isotonic saline flush, and if the wound is dirtier, a commercial cleanser such as Dermagran, Biolex, or Ultra-Klenz can be implemented. The irrigation stream should use between 10 and 15 psi of pressure, which can typically be accomplished with a 35 mL syringe and a 19-gauge needle.

If no improvement is seen within two to four weeks, using topical antibiotics, such as a two-week trial of silver sulfadiazine, may be considered. Systemic antibiotics are only considered in the event of bacteremia, sepsis, cellulitis, or osteomyelitis. The objective of dressings is to keep the ulcer bed moist and the surrounding tissue dry. Moist saline gauze heals as well as hydrocolloid occlusive dressing and is faster than wet-to-dry. However, hydrocolloids do not consume as much nursing time.

Adjunctive therapies also play a role in assisting in the wound healing process. Hyperbaric oxygen can assist in accelerating the healing process by driving up the oxygen tension and promoting angiogenesis and creating a hostile environment for certain bacteria. Electrical stimulation can be considered in stage III and IV wounds, which have been otherwise unresponsive to conventional methods. If there is a large
amount of exudate and necrotic tissue, then hydrotherapy can be useful in clearing out this excess debris, but it should not be implemented on clean wounds. A frequently used method to assist in accelerating wound closure is vacuum assisted treatment. By filling and sealing the exposed area with foam and applying subatmospheric pressure (125 mmHg below ambient), there is increased blood flow to the wound as well as the adjacent tissue.

Surgical treatment is reserved for stages III and IV, and may be necessary for closure of larger wounds. Different surgical modalities include direct closure, skin grafts, skin flaps, musculocutaneous flaps, fasciocutaneous flaps, and free flaps. Of these, the musculocutaneous flaps are the most desirable option because they have their own blood supply and, thus, can withstand pressure and shear. In cases of osteomyelitis, this flap is favorable because of the highly vascularized muscle tissue brought into the area. For sacral involvement, a gluteus maximus flap is recommended. For the ischium, there are several options, including a posterior thigh fasciocutaneous flap, an inferior gluteus maximus myocutaneous flap, a hamstring advancement flap, or a tensor fascia lata flap. To treat ulcerations over the greater trochanter, a tensor fascia lata fasciocutaneous flap is the procedure of choice.

Postoperatively, the patient is on strict bed rest on a low air loss mattress for a period of 2 to 6 weeks followed by a progressive sitting program. The head of the bed should be elevated no greater than 15 degrees to reduce shear. Recurrence rates can range from 13% to 56% (27). One factor which may compromise recovery includes smoking. Both nicotine and carbon monoxide are vasoconstrictors, which impair oxygen delivery, increase viscosity and oxidase release by neutrophils. Spasticity may cause an internalized shear by promoting joint movement, especially during the recommended period of postop immobilization. Contamination from urine and stool can colonize the affected area and delay healing as well.

**Recurrence**

Patients who have had previous ulcers may be particularly susceptible to a recurrence. Having a previous ulcer that has healed and closed can give the patient the feeling that they have “cured” their condition. However, it is important to realize that the granulation of wound healing is scar tissue. Scar tissue is fundamentally of an inferior quality to native tissue and, thus, has poorer structural integrity and is more prone to breakdown.

Once a wound has developed, a strict seating restriction protocol should be put in place. Gradually, the time allowed for sitting can be increased as it becomes evident that the affected area is allowing perfusion. If the decubitus is stage III or greater, a total sitting restriction may be appropriate until it can be appropriately treated and show improvement.
POSTTRAUMATIC SYRINGOMYELIA

A syringomyelia is the development and progression of a cyst filled with cerebrospinal fluid (CSF) within the spinal cord. The cyst can be caused by intramedullary tumors, a blockage in CSF circulation, and spinal dysraphism or idiopathic. A rare etiology representing less than 10% of cases is that of previous SCI. In the United States, approximately 3% to 4% of persons with traumatic SCI are affected.

The symptoms are often the insidious progression of pain and loss of sensorimotor function. If left untreated, posttraumatic syringomyelia (PTS) can result in a loss of function, chronic pain, respiratory failure, or even death. PTS can occur at any age and may begin at any time after SCI. The average interval between SCI and onset of syrinx is 7.6 years, but the range is vast, from 6 months to 26 years. The average interval between diagnoses is 10.7 years, implying a 3.1-year delay in onset of symptoms and the diagnosis.

Cavity formation is followed by enlargement and extension of the cystic cavity. Tethering of the spinal cord results in CSF circulation around the traumatized segment of the spinal cord; this occurs as a sequela of bleeding-induced arachnoiditis, scarring, spinal canal stenosis, or kyphotic deformity. An incomplete spinal canal decompression may predispose the person to tethering and CSF obstruction (28).

Rostral or caudal cyst extension may occur because of turbulent CSF flow or a one-way valve phenomenon, which allows CSF into, but not out of, the cyst cavity. The “slosh and suck” theory proposes that increased epidural venous flow during activities such as coughing and sneezing, which produce valsalva effects, results in increased pressure, which cannot be dissipated because of disruptions in CSF flow around the spinal cord (29). This pressure may force CSF into the cyst, resulting in expansion and extension.

Pain is the most commonly reported symptom, and it is variable in character; it can be localized or diffuse, a dull ache or a burning, stabbing sensation. Also, there may be increased weakness, numbness, increased spasticity, and hyperhidrosis. Other symptoms include decreased reflex micturition, progressive orthostasis, AD and relatively painless joint deformity or swelling as in a Charcot joint (30). On physical examination, spasticity is typically increased over previous examination, and deep tendon reflexes are increased over prior examinations. An ascending sensory level with sensory dissociation can be observed. Selective loss of pain and loss of temperature sensation are very sensitive indicators. If the syrinx has progressed to the brainstem, numbness may involve the face. Progressive weakness and wasting can occur but may be a late finding. There can be a complete or partial Horner’s syndrome or other evidence of dysautonomia such as labile BP or hyperhidrosis. Signs may be unilateral (31).

The differential diagnosis is extensive due to the breadth and variability of symptoms. These may include radiculopathy, spinal tumor or infarct, epidural abscess or hematoma, tethered cord, progressive noncystic myelopathy, AD, or cervical spondylosis.
I. MEDICAL COMPLICATIONS

Diagnosis is made by MRI. T1 and T2 sequences can help differentiate between CSF and normal spinal cord tissue and areas of spinal cord edema, myelomalacia, and gliosis. Serial examinations are necessary to evaluate changes in cavity size over time. Interestingly, there is a lack of correlation between cavity size and the severity of clinical symptoms (32). A CT myelogram can also delineate the extent of the syrinx cavity, arachnoid scarring, and tethering of the spinal cord. This study demonstrates the extent of obstruction to CSF flow. Plain films are only helpful in determining spinal stability or other disruptions in architecture.

Serial quantitative strength measurements with grip tests or hand held myometry can confirm the progression of weakness. The calculation of central motor conduction time using motor evoked potentials is useful in monitoring PTS, whereas standard EMG and NCS are less sensitive and specific (33).

The goal of physical therapy is to preserve ROM and function. Exercises that can induce a valsalva reaction must be avoided until normal CSF flow can be restored. In occupational therapy, splinting may be appropriate to maintain functional positions to prevent contracture formation.

If a case progresses to the point of neurologic deterioration, pain, or AD, then surgery is necessary to treat the syrinx to prevent further expansion and to collapse syrinx cavities. It is controversial whether asymptomatic yet enlarging syrinxes merit surgical treatment as well. Surgical options include simple drainage, shunting procedures, and decompressive laminectomy with expansion duraplasty. No surgical procedure has been uniformly successful in relieving symptoms or resolving radiographic abnormalities. Shunting of syrinx cavities has a high complication rate including failure or blockage and recurrent cyst expansion. They may leave the patient in worse condition in the long term by inducing or provoking gliosis inside the spinal cord. Syringopleural shunts have an improvement rate of 53.5% and a direct clinical deterioration of 15.7% (34). This procedure is appealing from a surgical approach because both the proximal and distal operative sites can be approached without repositioning the patient. Duraplasty with dural grafting and adhesiolysis may be performed with the goal of reestablishing unrestricted subarachnoid CSF flow.

ENDOCRINE COMPLICATIONS

Calcium Metabolism/Osteoporosis

Bone and calcium metabolism can be affected by the unloading of gravity bearing skeletal regions. The first phase involves increased osteoclastic activity and commences immediately following immobilization. This peaks at days 3 to 5 and leads to a loss of trabeculae. Resorption returns to normal after approximately 10 days. After a prolonged period of chronic skeletal unloading, the second phase involves a slower
loss of bone and is marked by decreased osteoblastic activity. Eventually, there is a decreased pool of osteogenic cells in the bone marrow.

Calciuria can begin occurring within 10 days of the injury and reaches its maximum between 1 and 6 months postinjury (35). In the case of able-bodied people on voluntary bed rest, the calciuria can be two to four times higher. Hypercalcemia occurs with increased resorption and increased fractional excretion from the kidney. Exacerbating factors include multiple fractures and young age during which there is high bone turnover and resorption (36). Other risk factors include recent paralysis, male gender, complete injury, high cervical level, dehydration, and prolonged immobility.

Complete SCI patients have increased suppression of the parathyroid hormone (PTH)–vitamin D axis. Hypercalcemia in the SCI patient may manifest with nausea, vomiting, anorexia, fatigue, lethargy, polydipsia, polyuria, and dehydration. The condition can be monitored by following the calcium and albumin levels. The condition can be treated with NS 100 to 150 mL/hr to help promote calcium excretion. Once rehydration has been achieved, Lasix may be employed to further promote calcium excretion. There has not been a tremendous amount of success in improving bone mass. Disuse is an obvious etiology, but nutritional deficiencies of calcium and vitamin D may also be a cause. Because SCI patients have a proclivity for developing nephrolithiasis, many are treated with calcium/dairy restriction, which further exacerbates the process of bone resorption. Other contributory factors in SCI patients may be decreased sunlight exposure as well as the frequent use of anticonvulsants, which increase the metabolism of vitamin D. This decrease in calcium and vitamin D intake leads to an increased PTH, which leads to increased bone resorption. SCI patients have decreased 1,25-hydroxyvitamin D (1,25 D), which has an inverse relationship with PTH as well. However, 1,25 D is increased in chronic SCI, which correlates with PTH, thus suggesting a secondary hyperparathyroidism.

The potential, downstream impact of this increased bone loss is osteoporosis. Paraplegics typically lose mineral density in the pelvis and legs whereas tetraplegics lose bone more diffusely. There is not a predictable loss of density in the vertebral column. The primary reason for this is that the vertebral column continues to bear weight in spite of the injury (37). Secondly, the column can actually exhibit an artificial increase in bone mineral density, otherwise known as neuropathic osteoarthropathy (38). This increase in BMD is attributed to the loss of disc space, bone sclerosis, fragmentation, osteophytosis, and subluxation. However, it is possible that postural imbalances in SCI patients may lead to asymmetric vertebral body loads, which may accelerate an osteoporotic process in specific areas.

Bisphosphonates may be used as a treatment measure, as they reduce osteoclast number by inhibiting osteoblast recruitment, adhesion, life span, and osteoclast activity. Alendronate has proven effective in cases of increased bone turnover but is not totally defined in SCI.
I. MEDICAL COMPLICATIONS

Thyroid Hormone

SCI has been shown to lead to changes in thyroid levels. After acute SCI, there is a transient reduction in T3 and T4 for 2 to 6 months. Higher cord lesions manifest a greater depression in levels. The stress of acute illness may lead to pituitary suppression of thyroid stimulating hormone (TSH) release with transient increase during the recovery phase. Functional recovery is shown to improve if exogenous T3 or TRH is given soon after SCI. Symptoms of hypothyroidism, such as constipation and weight gain, are commonly present regardless of hormone levels. Hyperthyroidism, when present, may also be difficult to discern due to the concomitant existence of hyperactive reflexes and resting tremors. Because SCI patients are at risk for a multitude of acute and chronic conditions, they are prone to sick euthyroid syndrome. In this condition, TSH is not elevated and thyroid replacement does not improve prognosis. In one study, the level of T3 correlates with the level and duration of SCI. Lowest T3 levels are present in those with acute tetraplegia and highest in those with paraplegia who ambulate. This finding suggests impaired conversion of T4 to T3 (39).

Sympathetic Denervation

An important consideration when evaluating endocrine abnormalities is the transient sympathetic denervation of organs such as the pancreas, adrenal medulla, and the juxtaglomerular apparatus of the kidney. Sympathetic denervation is rare and short-lived after SCI and typically occurs during spinal shock. Sympathetic activity usually recovers after several weeks in a disorganized, unpredictable manner. The sympathetic chain arises from T5–12, and thus, lesions above T12 can affect these organ systems. The lack of sympathetic input to the adrenal medulla results in decreased release of catecholamines. The adrenal medulla is the only source of epinephrine and is unable to mount a pressor response in the acute injury phase. The disorganized sympathetic inhibition after SCI leads to an increase in plasma, renin, angiotensin II, and aldosterone. As a result, angiotensin II, in its function as a vasoconstrictor can raise BP, whereas aldosterone stimulates sodium retention. Both of these processes can serve to reverse the hypotensive effect of decreased sympathetic output in the SCI patient.

Trauma to the pituitary/hypothalamus axis, though above the level of injury, has to be considered because 40% to 50% of SCI patients present with a head injury. There should be an increased index of suspicion in patients with multitrauma and low specific gravity urine. The adrenocortical axis is also affected. There is a high prevalence of impaired adrenal reserve in chronic SCI. In persons with tetraplegia, serum and urinary catecholamine levels are less than normal. During paroxysms of AD, serum catecholamine levels may rise relative to that patient’s baseline but, still, would not typically exceed the baseline of able-bodied persons.
Growth Hormone

Growth hormone (GH) and its secondary messenger, insulin-like growth factor-1 (IGF-1) are decreased in SCI. Baclofen has been noted to increase GH release and normalizes plasma IGF-1 in SCI patients. GH administration may benefit patients with SCI in a fashion similar to its benefit on elderly patients with relative GH deficiency. The result is an increase in lean body tissue and decreased fat mass, a decrease in low-density lipoprotein (LDL) and an increase in HDL. The metabolic rate increases after only 2 weeks, which is likely as a result of the impact on the thyroid hormone.

The use of exogenous oral steroids may be of some benefit in limited therapeutic interventions, such as in cases of respiratory compromise. The lean tissue mass of SCI patients mimic trends found in aging, and there is a correlation between body fat composition and the level of the SCI. The body weight per se does not change, but successively higher complete lesion areas are associated with decreasing lean body mass and body cell mass. The percentage of body fat in SCI may be 60% higher in correlated twin studies. Oxandrolone has been shown to improve diaphragm thickness, spirometry measures, maximum inspiratory and expiratory pressures, and fat free mass and accelerate the healing of burns and refractory pressure ulcers. Oxandrolone does have the potential for a host of side effects including edema, with and without congestive heart failure, and hepatic abnormalities. In addition, genitourinary effects include oligospermia, female virilization. Premature closure of epiphyseal growth centers can occur in the younger patient.

Reproductive Endocrinology

Men with SCI may have relative or absolute androgen deficiency, which is likely attributable to prolonged sitting and euthermia of the scrotal sac. A study of 20 otherwise healthy SCI patients, shows reduced serum totals and free testosterone levels without significant increase in gonadotropin concentrations (40). In a tested subset, stimulation of the testes for 2 days with chorionic gonadotropin produced testosterone similar to that found in able-bodied counterparts.

Semen analysis shows decreased sperm counts and impaired motility. Carnitine is an index of epididymal function and is decreased in SCI patients. A lack of spermatogenesis is common in SCI patients. Nonpsychogenic, reflex erectile function is possible in up to 80% of SCI patients, especially in incomplete spinal cord injury patients. It is important to remember that hypogonadal men may be predisposed to osteoporosis and anemia; so the secondary benefits of correcting this condition may be significant. In females, estrogen replacement may be a valuable consideration, as this would improve lipid profile, lower LDL, raise HDL as well as prevent osteoporosis, which is more prevalent in the paralyzed population.
I. MEDICAL COMPLICATIONS

Chronic Pain

Another common complication in SCI is chronic pain. This may be sensed above, at, and/or below the neurologic level. The prevalence of chronic pain has been estimated to be about 81% at 1 year after SCI (41). The two major categories of pain are neuropathic and nociceptive pain. Nociceptive pain is divided into three categories: (a) musculoskeletal pain (eg, glenohumeral arthritis, lateral epicondyritis, rotator cuff tendinosis), (b) visceral pain (eg, myocardial infarction, abdominal pain because of bowel impaction), and (c) other nociceptive pain (eg, surgical skin incision) (42). Neuropathic pain that results from the spinal cord damage itself occurs in about 40% of patients (43). Neuropathic pain may be classified as: (a) at-level SCI pain (produced by spinal cord compression, nerve root compression, and cauda equina compression); (b) below-level SCI pain; and (c) other neuropathic pain (eg, carpal tunnel syndrome) (42).

Treatment of neuropathic pain in SCI is challenging. General approaches include physical therapy, exercise, behavioral interventions, pharmacologic agents, alternative medical approaches—such as acupuncture, relaxation techniques, self-hypnosis—and surgical/invasive approaches. Pharmacologic agents that have been used include antidepressants, anticonvulsants, opiates, nonsteroidal anti-inflammatory drugs (NSAIDs), and others. Of the antidepressants, amitriptyline, TCA, was not found effective in pain relief in the first double-blind, placebo-controlled trial of TCAs in persons with SCI and chronic pain (44) but was found effective in a more recent study if there was concurrent depression (45). TCAs have a number of side effects such as urinary retention and constipation that may lead to significant problems in the presence of a neurogenic bladder and bowel; however, the dose for pain relief is typically lower than that for depression in those without depression who do respond to the drug. The newer selective serotonin reuptake inhibitors (SSRIs) may produce an increase in spasticity as well as insomnia and do not seem clinically effective for treatment of chronic SCI pain. In a study of neuropathic pain in SCI or stroke, it was found that with doses of 60 and 120 mg/day duloxetine, a serotonin–norepinephrine reuptake inhibitor (SNRI), was not effective in reducing pain intensity (46).

Anticonvulsants are increasingly used as first line drugs for the management of neuropathic pain. Gabapentin may be helpful at higher doses but may produce sedation and dizziness that impede its tolerability. The starting dose of gabapentin is 100 mg three times a day, and the dose may be gradually increased to a maximum of 3600 mg/day in three to four divided doses as tolerated. In 2012, the FDA approved pregabalin for the treatment of neuropathic pain after SCI; it thus became the first anticonvulsant with such approval. Pregabalin binds to alpha2-delta auxiliary subunit types 1 and 2 of voltage-gated calcium channels and reduces excitatory neurotransmission partly via modulation of glutamatergic signaling (47). A recent large multicenter randomized controlled trial demonstrated efficacy of pregabalin at doses from 150 to 600 mg/day with significant improvement in reduction of pain interference (48). The major side effects of pregabalin are somnolence, dizziness, and edema. Slow titration
of the dose is key to minimizing the occurrence of side effects. The lowest maximum
dose that provides pain relief is recommended for all such medications.

Although opiates are potentially habit-forming, there are some patients who
report neuropathic pain relief with such medications. It is important to establish a
strict agreement with the patient regarding dosing because tolerance may develop and
the patient may seek an ever increasing dosage and develop a substance use disorder.
Tramadol may be helpful if pregabalin, gabapentin, or TCAs are found to be insuffi-
cient and slowly titrated from 50 mg three times daily to a maximum dose of 400 mg
daily (49). Nonpharmacologic modalities such as acupuncture, relaxation techniques,
exercise, and self-hypnosis may be useful for some patients.

### Complication Timeline for Spinal Cord Injury

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<td>Atelectasis</td>
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<td>Pneumonia</td>
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<td>Orthostatic hypotension</td>
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<td>Autonomic dysreflexia</td>
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<td>Chronic pain</td>
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REFERENCES

2. SPINAL CORD INJURY


Rehabilitation, including the restoration of functional independence and the prevention of secondary complications, is a primary goal for patients having multiple trauma and burn injuries especially since there has been an increasing survival rate in this patient group over the past several decades owing to improved systems of care for the management of acute trauma (1,2). Trauma is a significant cause of disability in adults of working age and thus there is a tremendous annual economic burden resulting from multiple trauma and burn injuries in the United States, including both the direct health care costs and the lost productivity, which is estimated at 406 billion dollars (1,3,4). Each year trauma accounts for 42 million emergency department visits, of which 450,000 are due to burn injuries (4,5). Burn injuries account for about 1% of trauma admissions and 2% of the annual costs which amounts to approximately 7.5 billion dollars each year (3,6). There are 2 million multiple trauma hospital admissions, with 45,000 for burns (4,5).

Burn injuries include 44% caused by fire/flame, 33% from scalds, 9% caused by hot surface contacts, 4% from electrical injury, 3% chemical burns, and 7% resulting from other causes (5). The majority of burn injuries, about 68%, occur from accidents at home, 10% occur from occupational injuries, 7% from motor vehicle/street or highway accidents, and 15% as a result of other causes (5). Burns are classified according to the depth of injury of the skin. First-degree burns are limited to the epidermis, which is the outermost layer of the skin. First-degree burns present with reddening of the skin but no blistering and resolve with application of a moisturizer. Second-degree burns damage the dermis, which is the deeper layer of the skin and can be categorized as superficial, intermediate, or deep depending on the depth of dermis involved. Second-degree burns present with reddening of the skin and blistering; pink tissue beneath the blister would indicate a more superficial dermal injury whereas a deep red color would indicate much deeper dermal involvement. Second-degree burn wounds may heal when there is residual healthy dermis beneath the injury, however, the deeper the dermal involvement, the higher the risk for subsequent contractures. Deep second-degree burns may require operative intervention to prevent contractures. Third-degree burns involve the full-thickness of the skin including the nerves that supply the skin,
and present with a whitish glistening color, are firm to the touch, and usually do not involve pain. Third-degree burns require surgical excision and grafting as these burns can heal only by contracture as there is no viable dermis remaining. Fourth-degree burns extend into the structures beneath the skin such as the muscle and nerves and thus result in a much higher risk of amputation.

Chemical burns can be very deep and in some cases lethal. Alkali agents such as those found in common cleaning agents, such as drain cleaners, cause a liquefactive necrosis of the skin. Alkali burns proceed deeper and deeper into the tissues until the chemical agent is completely irrigated away. Alkali burns result in much deeper wounds than burns caused by an acid as acids usually cause a limited coagulative necrosis of the skin. One of the most dangerous acids in burns is hydrofluoric acid, which is found in certain cleaning agents and is also used by glass workers. Hydrofluoric acid removes calcium from the tissues with which it comes into contact leading to life-threatening cardiac arrhythmias and necrosis of muscle and deep tissues.

Electrical injuries are classified as high or low voltage by whether the involved current is greater or less than 1000 volts. Electrical burn patients often present with a small but deep burn wound at the entrance and exit sites of the current. The typical electrical burn wound care is minimal at the skin’s surface but this belies the extent of the underlying injury which often goes deep to the bone. Electrical burns usually result in deep tissue injury because electrical current conducts a great deal of heat while passing through bone. This heat often damages the surrounding muscles, tendons, nerves, and blood vessels leading to dysfunction of an extremity and significant deep tissue necrosis. The inflammation of the deep tissues resulting from an electrical burn may lead to a compartment syndrome during the acute care hospitalization causing secondary tissue ischemia resulting in worsened injury. Electrical current may cause significant morbidity including spine fractures, delayed bowel perforation, cataract formation, and cardiac complications that may be life-threatening.

Burn patients, though they have many special needs related to the thermal injury, are still considered trauma patients and, thus, require the same evaluation and workup as any other trauma patient with the potential for multiple injuries. Multiple trauma may include fractures/extremity injury, internal injuries, head and spinal injuries and amputation/crush injuries resulting from motor vehicle crashes in approximately 62.5% of cases, falls in 25%, and 12.5% because of other causes (2). At least 26% of trauma patients will require comprehensive inpatient rehabilitation services following treatment in acute care (2). Many trauma patients are transferred from acute care to inpatient rehabilitation programs earlier than in previous years resulting in an increased risk for medical complications occurring while in the inpatient rehabilitation units.

Medical complications in trauma patients during inpatient rehabilitation may result from the direct or indirect effects of their injuries including physical and/or psychological problems. In multiple trauma patients there may be missed injuries that may be diagnosed during inpatient rehabilitation, and there may be late effects of trauma
including heterotopic ossification of joints, development of internal organ adhesions/bowel obstructions, and posttraumatic cholecystitis. In addition, trauma patients are at high risk for all the usual complications of immobility, which are discussed elsewhere in this book, including skin ulceration, deep venous thrombosis, pulmonary embolism, and pneumonia. Falls and pain management are also concerns in all trauma patients. Specific concerns in burn patients include proper nutrition and the prevention of catabolism or hypermetabolism, secondary hypoparathyroidism, hypertrophic scarring/joint contractures, heterotopic ossification, peripheral neuropathy, wound infections and the need for secondary amputations, and posttraumatic stress disorder or depression. Table 3.1 summarizes the potential common inpatient rehabilitation complications that may occur in trauma patients. This chapter addresses all of these potential complications of trauma inpatient rehabilitation with the exception of the complications specifically associated with traumatic brain or spinal cord injuries, amputations, and immobility, which are discussed elsewhere in this book.

**MULTIPLE TRAUMA**

**Missed Injuries**

Missed diagnoses of injuries in multiple trauma patients in emergency and acute care departments is a significant clinical and medico-legal problem with an incidence ranging from 8% to 38% of major trauma cases (7–9). Common risk factors for missed diagnoses in trauma patients during acute care are summarized in Table 3.2.
The patients at the greatest risk for missed injury diagnoses include those having neurologic compromise, low initial Glasgow Coma Scale scores, higher mean Injury Severity Scores, prolonged stays in the acute care hospital and intensive care unit, required pharmacologic paralysis, being young in age, and having other more severe concomitant injuries, including chest or pelvic trauma, and the absence of/or overlooked signs of soft tissue injury (9,10). The incidence of missed diagnoses may be lessened in trauma centers that use a “tertiary examination” in which a repeated head-to-toe examination and review of all laboratory and radiologic studies is performed within 24 hours of the trauma admission (7,8). However, even with the tertiary examination protocol in place, missed traumatic diagnoses still occur during the acute care hospitalization and may not become evident until a patient is transferred to an inpatient rehabilitation unit.

The most commonly missed injuries involve the head and neck followed by the chest and the extremities (10). Missed injuries may include fractures, internal injuries, and neurologic injuries, including brain/spinal trauma and traumatic neuropathies. The most frequent locations for missed fractures include the foot, knee, elbow, hand, wrist, hip, ankle, and shoulder (11). The most common reason for missed diagnoses of fractured extremities is subtlety of the fracture; however, only one third of missed fractures are attributed to imperceptible radiographic lesions (11). On the inpatient rehabilitation unit, signs of possible fractures, which may have been missed being diagnosed during a patient’s trauma acute care, may include pain, swelling, erythema, ecchymosis/bruising, overlying lacerations, and a palpable deformity. If a fracture is suspected in an inpatient rehabilitation patient, orders should be immediately given to immobilize the affected joint/extremity and for avoidance of active or passive range-of-motion exercises and weight bearing at least until the results of a STAT radiograph are obtained. Missed internal injuries may present 3 to 96 days posttrauma with a median time of delay in diagnosis of approximately 7 days (12). Possible reasons for missed internal injuries include obscured trauma history, radiologic misinterpretation, no
reliable radiologic findings, admission to an inappropriate hospital service/department, surgical inexperience, peritoneal adhesions, and incomplete surgical exploration (12). The most commonly missed internal injuries involve the colon (13), but these may also involve the spleen, liver, pancreas, diaphragm, urinary bladder, stomach, and retroperitoneal hematomas (12,13). Most internal injuries will be diagnosed prior to transfer from acute care to inpatient rehabilitation, however, some internal trauma may occasionally be missed. Symptoms and signs of possible missed internal trauma may include persistent complaints of abdominal or thoracic discomfort/pain, nausea, vomiting, poor appetite, fever, malaise, and guarding/rebound tenderness on abdominal palpation. Trauma surgical follow-up should be obtained if these symptoms or signs are present and otherwise unexplained.

Neurologic injuries, including traumatic neuropathies and brain injuries, especially concussions/mild traumatic brain injuries (MTBIs), may not become evident until the multiple trauma patient is transferred to an inpatient rehabilitation unit. Concussion/MTBI, an acute trauma-induced alteration of mental function lasting less than 24 hours with or without a preceding loss of consciousness, is a common consequence of assaults, crashes, and accidents involving motor vehicles, bicycles, pedestrians, construction, and sports (14,15). Because of the subtle nature of the initial symptoms and the often negative findings in the emergency department brain CT scans and neurologic examination, especially in association with more pressing life-threatening traumatic injuries, the diagnosis of MTBI is often missed. Individuals having MTBI may present in the inpatient rehabilitation unit with the symptoms given in Table 3.3. A diagnosis of MTBI may be made in the inpatient rehabilitation unit based on a review of the patient’s history if there was posttraumatic amnesia/confusion of up to 24 hours with or without a preceding loss of consciousness (14,15).

**TABLE 3.3 Possible Symptoms/Signs of Common Missed Injuries**

- **Fractures**—pain, swelling, erythema, ecchymosis, overlying lacerations, palpable deformity
- **Internal injuries**—persistent abdominal/thoracic discomfort, nausea, vomiting, poor appetite, fever, malaise, guarding/rebound tenderness
- **Traumatic neuropathies/plexopathies**—pain, weakness, numbness, paresthesias, foot/wrist drop
- **Concussion/mild traumatic brain injury**—spectrum that may include headaches, dizziness, insomnia, imbalance/incoordination, emotional irritability/lability, depression/anxiety, impaired memory/executive function
- **Skull/facial trauma/cranial neuropathies/ophthalmic injury**—overlying scalp/facial lacerations/bruising, “raccoon eyes/Battle’s sign,” otorrhea/rhinorrhea, impaired vision, facial weakness/numbness, double vision, impaired smell/taste, difficulty chewing
- **Vocal cord paralysis/paresis**—hoarse voice, dysphagia
- **Subglottic tracheal stenosis**—labored respiration or rhonchi after endotracheal tube deccanulation
Patients with symptoms of MTBI who may have had an initial negative brain CT scan, may have positive findings on brain MRI scans for up to 2 to 3 months after trauma including findings consistent with areas of axonal shear injury or small contusions (14). Acute care diagnosis of MTBI improves prior to inpatient rehabilitation transfer in patients with an initial Glasgow Coma Scale score of 13 or 14, pathology noted on the initial brain CT scan, known loss of consciousness, and/or posttraumatic amnesia (16). However, one series showed that radiologic findings consistent with mild and moderate traumatic brain injuries, particularly findings of contusions, may be missed in up to 67% of CT scans, especially when the scans are read by inexperienced radiologists (17). Mild and moderate traumatic brain injuries may also be missed in individuals having concomitant spinal cord injuries. The reported incidence of concomitant brain and spinal cord injuries ranges from 25% to 60%, especially if the mechanism of injury was a motor vehicle collision or a fall (18,19).

Traumatic neuropathies may also present during inpatient rehabilitation and may be due to fractures, dislocations, crush or stretch injuries, and various other late posttraumatic causes of nerve compression, including heterotopic ossification, hematomas, scar tissue, and pseudoarthrosis. It is not unusual for the symptoms and signs of a posttraumatic neuropathy to present in an inpatient rehabilitation unit in patients who may be recovering from brain injury and other multiple traumas. These patients may become aware of persistent pain, weakness, or numbness that on careful examination is consistent with the pattern of innervation of a particular nerve or neural plexus. The most frequently injured nerve in upper extremity trauma is the radial nerve (20). The supraclavicular and infraclavicular portions of the brachial plexus may be injured in association with injuries involving the shoulder, humerus, clavicle, and the axillary artery. Supraclavicular brachial plexus injury occurs approximately 75% of the time in association with stretch injuries as compared to infraclavicular injury (21). Space-occupying pseudoarthrotic lesions resulting from clavicle nonunion may also cause brachial plexus injury (22). Trauma at the wrist may be associated with the development of the carpal tunnel syndrome, which could manifest with symptoms and signs of median neuropathy in the hand, including pain, weakness, and loss of two point discrimination (23).

Peripheral neuropathies may also occur in the lower extremities at the pelvis, hip, knee, leg, ankle, and foot secondary to the direct effects of trauma as well as perioperative and postoperative causes such as excessive tension or inappropriate placement of retractors, instrument or implant related complications, postsurgical/posttrauma limb malpositioning, heterotopic ossification, hematoma, and scarring (24–26). The most frequently injured nerve in lower extremity trauma is the peroneal nerve (20). Sciatic nerve injury may result from acetabular pelvic fractures and may present with a range of symptoms that could include a foot drop (24). Other common traumatic neuropathies of the leg, knee, ankles, and foot include the piriformis syndrome, iliacus syndrome, saphenous neuropathy, lateral femoral cutaneous neuropathy...
3. MULTIPLE TRAUMA AND BURNS

■

(meralgia paresthetica), tibial neuropathy, common/deep and superficial peroneal neuropathy, tarsal tunnel syndrome, Baxter’s neuropathy, jogger’s foot, sural neuropathy, and Morton’s neuroma (25,26). The diagnosis of a posttraumatic neuropathy involving a limb may be confirmed by electromyography/nerve conduction and MRI studies. Prevention in the inpatient rehabilitation unit includes proper positioning of injured limbs and adherence to appropriate weight bearing/range of motion precautions. Treatment may involve various orthopedic or neurosurgical interventions.

Facial trauma and skull fractures may result in various clinical problems, which may not become apparent until a patient is in an inpatient rehabilitation unit, including vision loss, cranial neuropathies, extra-ocular muscle entrapments, and spinal fluid fistula leaks. Trauma is the second leading cause of blindness and patients with significant eye injuries may present initially with grossly normal eye examinations and good visual acuity (27). Traumatic optic neuropathy often occurs in association with fractures involving the zygomaticomaxillary complex and cranial bones and LeFort type-2 fracture; additional risk factors include history of loss of consciousness, injury to the superolateral orbital region, fracture of the optic canal, evidence of orbital hemorrhage, and evidence of blood in the ethmoid sinus region (28). The diagnosis of cranial nerve (CN) injuries after trauma is often delayed in about 60% of patients because of other life-threatening trauma, altered mental status, and/or associated bone or soft tissue injuries that may initially mask the symptoms (29). The most frequently injured cranial nerves in order of frequency from the most common are CN-7 (facial nerve), CN-1 (olfactory nerve), and CN-6 (abducens nerve) (29). CN-7 injury presents with ipsilateral facial weakness and occurs in association with temporal bone fractures. CN-1 injury results in an impaired sense of smell and taste and occurs with occipital bone fractures. CN-6 injury presents with double vision on lateral gaze and occurs in association with orbital fractures. Fractures at the superior orbital fissure may result in ophthalmoplegia as a result of variable injuries to CN-3 (oculomotor nerve), CN-4 (trochlear nerve), and CN-6, which would present with a patient’s complaint of double vision (30). Ophthalmoplegia resulting in diplopia may also occur with extra-ocular muscle entrapments, which may variably involve the medial, lateral superior, or inferior rectus muscles, associated with orbit fractures. Maxillary bone fractures are associated with CN-5 (trigeminal nerve) injury, which may present in a patient with facial pain, facial numbness, and difficulty in chewing foods. Neurology and/or neurosurgical consultation may be beneficial for patients with suspected CN injuries; and in some cases decompression surgical procedures may be helpful. In cases of suspected optic neuropathy, ophthalmoplegia, or other orbital trauma, an ophthalmology or neuro-ophthalmology evaluation is indicated.

Skull base fractures may be associated with extensive dural membrane laceration which may lead to the development of a cerebrospinal fluid (CSF) fistula. Trauma to the anterior skull base frequently involves the paranasal sinuses and may result in
CSF leakage from the nose (rhinorrhea); anterior fossa fractures may also involve the orbit, optic, and olfactory nerves (31). Periorbital ecchymosis, known as the raccoon eyes sign, is associated with anterior skull base fractures in nearly 50% of cases (32). Fractures involving the middle and posterior skull base often involve the petrous portion of the temporal bone and are associated with risk for facial palsy, hearing loss, and CSF leak from the ears (otorrhea) (31). Bruising over the mastoid process, known as Battle’s sign, is frequently associated with middle cranial fossa skull base fractures. CSF fistulas presenting as rhinorrhea or otorrhea are independent predictors of a significant risk for the development of posttraumatic meningitis infections. Neurosurgical consultation is indicated as soon as possible in these patients (33).

Trauma patients with a history of prolonged intubation/mechanical ventilation are at risk for vocal cord injury, which may not become apparent until the patient is admitted to an inpatient rehabilitation unit. Signs of a vocal cord paralysis/paresis include hoarse voice and dysphagia. Any patient suspected of having a vocal cord injury will need an otolaryngology evaluation, speech-language pathology interventions, and appropriate dietary modifications. These patients may also be at risk for subglottic tracheal stenosis, which may present in the inpatient rehabilitation unit with labored respiration or rhonchi following the decannulation of a tracheostomy tube. Otolaryngology evaluation is also indicated when subglottic tracheal stenosis is suspected. The possible symptoms and signs of common injuries that may not be diagnosed in trauma patients until they are transferred to an inpatient rehabilitation unit are given in Table 3.3.

**Posttraumatic Cholecystitis**

*Posttraumatic cholecystitis* is a potentially life-threatening complication that can develop in patients in the inpatient rehabilitation unit more than 3 to 15 weeks after trauma (34,35). Presenting signs and symptoms may include right upper-quadrant pain and/or tenderness, anorexia, nausea, vomiting, and fever. Approximately 10% of patients having severe multiple injuries develop cholecystitis (36). Independent risk factors for the development of cholecystitis in severe multiple trauma patients include a history of fasting, total parenteral nutrition, hypotension/shock, pressor support, blood transfusions, narcotic medications, positive pressure ventilation, pneumonia, tachycardia, and sepsis (34,36–39). Risk for cholecystitis may be even greater in trauma patients having these risk factors in addition to co-morbidities including diabetes, congestive heart failure, cardiac arrest, or cancer (37). Acute and chronic acalculous cholecystitis occur almost twice as commonly as cholecystitis with cholecystolithiasis, particularly in younger patients having higher injury severity scores (36). Acalculous cholecystitis results from bile stasis in the absence of gallstones. Ultrasound of the gallbladder is the most accurate diagnostic modality in correlation with clinical symptoms and laboratory data (36,37,39). A patient suspected of having posttraumatic cholecystitis should
be immediately transferred from the inpatient rehabilitation unit back to the acute care for further evaluation and treatment. Cholecystostomy and/or cholecystectomy are the mainstays of treatment (36,37).

Paralytic Ileus/Bowel Obstruction

Paralytic ileus is a serious complication that may occur in the inpatient rehabilitation unit as a multifactorial complication of multiple traumas, which may progress to an acute surgical abdomen involving partial or complete bowel obstruction. Symptoms and signs may include abdominal pain and distention, abdominal guarding or rebound tenderness to palpation, abnormal/diminished or absent bowel sounds (40), constipation, nausea, vomiting, and loss of appetite. Ileus with possible bowel obstruction may be seen on plain abdominal x-rays as multiple dilated loops of bowel having air-fluid levels (41). Ogilvie’s syndrome, also known as colonic pseudo-obstruction, is a particularly severe form of ileus involving the cecum and right/ascending colon (42). Physical causes of ileus and Ogilvie’s syndrome may include recent trauma or surgery of the spine and/or the retroperitoneum or peritoneum (42,43). Pharmacologic causes for ileus and Ogilvie’s syndrome may include the use of narcotics, H-2 blockers, phenothiazines, calcium-channel blockers, tricyclic antidepressants, and epidural analgesics (42). Narcotics are a leading pharmacologic cause of paralytic ileus (44). Potential metabolic causes include hypocalcemia, hyponatremia, hypokalemia, hypomagnesemia, and hypophosphatemia (42). Any patient suspected of having a paralytic ileus or bowel obstruction should be transferred back to an acute care ward for further evaluation and treatment. Conservative treatment includes bowel decompression by a nasogastric tube or colonoscopy, whereas surgery is the mainstay of treatment for those patients having persistent paralytic ileus despite decompression and for those patients having a mechanical bowel obstruction due to various causes that may include peritoneal adhesions.

Falls

As many as 10% of patients have at least one fall while in an inpatient rehabilitation unit, with most falls occurring during the day time in a patient’s room (45). Approximately half of all falls occur during the first week of inpatient rehabilitation (45). Trauma patients who are at the greatest risk for falls during inpatient rehabilitation include those having brain or spinal cord injuries, amputations, greater medical complexity, multiple co-morbidities, cognitive impairment, neurologic impairments, and low total or cognitive functional independence measure (FIM) scores (45,46). A history of prior falls and/or the use of certain medications such as anticonvulsants, sedatives/tranquilizers, and antihypertensive medications may also increase the risk
Clinicians should identify patients at risk for falls on admission to inpatient rehabilitation and a fall prevention plan should be initiated accordingly. Nursing/medical interventions to reduce risk of falls and associated injuries may include a low bed, a bed alarm, a pelvic belt for wheelchair use, frequent toileting/bladder training program, frequent checking on the needs of patients with communication impairments, strict supervision of all transfers/ambulation, and patient/family education. As many as 20% of hospitalized patients 65 years or older having falls will reportedly suffer a new fracture (48). The risk of intracerebral hemorrhage is low in anticoagulated patients having falls without evidence of new external head trauma (49) but the risk increases if there is loss of consciousness (49), change in mental status, or external signs of head trauma resulting from the fall. Those trauma patients on antiplatelet medications or on warfarin anticoagulation with signs or symptoms of head trauma following a fall are at higher risk for intracranial bleeding (49–51), especially if the INR at the time of the fall is 2.43 or more (52) and should be referred for an emergency brain CT scan. Any trauma patient having a reported fall while in the inpatient rehabilitation unit needs to be evaluated for signs of serious injury, therapies should be temporarily suspended, and appropriate imaging studies should be ordered as necessary.

Inadequate Pain Management

Proper management of pain in trauma patients is essential to maximize functional recovery and to prevent adverse side effects. Inadequate pain management occurs when pain is under-treated or over-treated and when there are adverse effects from analgesic medications that could have been prevented. Pain that is not adequately treated may result in the development of associated anxiety and depression, which will often interfere with functional recovery. The relationship between pain, anxiety, and depression is well established in head trauma patients and particularly those having poor functional recoveries after a concussion (14). In patients having under-treated pain, a reduced capacity to perform physical and complex cognitive tasks may be due to the direct distraction of pain, and/or related to associated fatigue, sleep deprivation, depression, anxiety, and poor motivation. Similarly the sedative side effects of certain analgesic medications in overtreated pain will also interfere with a trauma patient’s physical and cognitive functions. Adverse effects from analgesics, including sedation, may result from interactions with other medications or as a direct side effect. A diligent bowel protocol is necessary in trauma patients receiving narcotic analgesics to prevent constipation, which can progress to paralytic ileus and bowel obstruction (42,44,53). Common gastrointestinal side effects of narcotics that would interfere with a trauma patient’s ability to participate in rehabilitation therapies also include nausea and vomiting. The use of opioids in the elderly and in patients having impaired renal function must be approached with caution as the half-life of these drugs and their active metabolites may be significantly increased (54).
To prevent problems associated with inadequate pain management in the inpatient rehabilitation unit, nurses must be extremely careful in receiving and implementing pain medication orders while physicians should carefully verify orders in the medical administration record as well as keep in mind the potential side effects and interactions of the drugs. Also, whenever a pain management specialist physician is involved, all analgesics should be exclusively ordered by that physician (53). Use of nonopioid analgesics, unless otherwise contraindicated, should be considered in trauma patients. Rehabilitation nursing staff should be provided in-service education regarding the facility’s pain management interventions so that they are better able to assess the efficacy, potential side effects, and goals of treatment (53). Rehabilitation physicians may assess and reassess the adequacy of pain management strategies at the weekly interdisciplinary team conferences.

BURNS

Pruritus/Special Pain Concerns

There are special concerns regarding the management of pain and itching in burn patients during inpatient rehabilitation, which is summarized in this section. Throughout the healing phase of burn wounds, most patients complain of itching. The incidence of postburn pruritus has been reported to range from 80% to 100% (55–58). This phenomenon can be persistent and very distressing to patients in the rehabilitation unit resulting in anxiety, depression, and impaired sleep (59–62). The itching process can begin a few days after the burn injury and it may persist for a few weeks to several years (59,63,64). The prevalence of pruritus in burn patients at discharge from acute care to inpatient rehabilitation is reportedly 93% (59). Pruritus usually occurs with partial thickness wounds whereas deeper burns and those that have been grafted are less likely to itch (57,64). Other risk factors in postburn pruritus include young age, dry skin, and hypertrophic scarring (59,65). Postburn itching may occur in the area of the burn wounds, grafts, and/or donor graft sites (59).

Postburn pruritus is multifactorial in etiology resulting from histamines, activation of neuropathic pathways, and from the stimulation of opioid receptors (65). The primary mediator of the itching process in burns is believed to be histamine. Inflammatory wounds and postburn healing scars, usually in the hypertrophic phase, attract large numbers of mast cells (65,66). The mast cells produce histamine, whereas other inflammatory cells produce several chemical mediators of inflammation that include kinins, substance P, platelet activating factor, chymase, and tryptase all of which potentiate the action of histamine (66). Wound manipulation and increased body temperature, which may result from exercise activity and heat, leads to degranulation of the mast cells and exacerbation of the itching (66). Postburn itching caused by inflammation can be reduced by antihistamines, but histamine antagonists do not
reduce pruritus in all burns, which suggests other mechanisms that may be targeted for treatment (65). Histamine antagonist medications as the only treatment are reportedly only effective in 20% of postburn pruritus (66). Several investigators consider postburn itch to be a form of neuropathic pain as itching and pain share mediation through C-fiber nerve endings (65,66). Itching can be elicited by a light stimulus applied to the superficial surface of the skin, whereas a stimulus applied deeper in the skin, such as a hypodermic needle, produces pain. It has been demonstrated that when the pain pathway is cut, itching also goes away (66), which may be why deep burns are less likely to itch (57,64). Thus medications that target neuropathic pain are also included in the treatment of postburn pruritus (55). Importantly, opioid receptor stimulation and opioid medications may also play a role in contributing to itching in burn patients (65).

There have been limited clinical trials to guide treatment protocols for postburn pruritus because of a lack of validated measurement tools that would allow for a better understanding of the severity and pathophysiology of the itching process as well as allow for a better comparative evaluation of the available therapeutic modalities (52,56). The usual therapeutic treatment modalities involve the use of antihistamines and emollients, which are not effective in all patients (55,66). The emollients that may be used include simple moisturizers, aloe vera, lanolin, liquid paraffin, coconut oil, and various other vegetable oils (66). The process of the application of emollients to the skin is perceived by burn care personnel to be therapeutic against itch (67). The therapeutic mechanism of emollients may involve the desensitization of the skin through the mechanical process of their application (66) and the moisturizing of dry skin. Massage therapy has also been shown to reduce postburn pain, itch, and psychosocial symptoms including anxiety, depression, and insomnia (60,62,68). Massage therapy may also be helpful in reducing hypertrophic scars (62). The most commonly used antihistamines, with H1 receptor antagonist actions, include diphenhydramine, hydroxyzine, certrizine, and pheniramine maleate. However, several studies have shown that these antihistamines have limited efficacy in reducing postburn itching (52,57,69,70). The antihistamines may also cause intolerable drowsiness. The anticonvulsant medications gabapentin and pregabalin are known to have analgesic effects for pain of neuropathic origins. These medications have been demonstrated to eliminate, or reduce to tolerable levels, moderate and severe itching in postburn patients, while also reducing anxiety (69). Mild itching may be best treated with a combination of antihistamines, massage, and/or pregabalin (69).

Burn wounds can be very painful with the most severe pain seen in partial thickness wounds where the epidermis has been removed exposing the underlying dermis. Although eschar-covered burns may be insensate, when the eschar separates, the exposed viable tissue is painful when manipulated. Narcotics are the most commonly used agents in the initial debridement and management of burn wounds. They are effective in conjunction with a short acting benzodiazepine anxiolytic for continued dressing
changes, wound care, physical and occupational therapy, and to help with sleep. Stool softeners such as docusate sodium (Colace) should be given in conjunction with the narcotic agents to prevent the constipating effects of these agents, which can lead to a paralytic ileus. As the wounds epithelialize and become less tender to touch and less painful with manipulation, nonsteroidal anti-inflammatory drugs (NSAIDs) can often be substituted and used to help wean burn patients off narcotic pain medications unless otherwise contraindicated. Burn patients may need to be readmitted to acute hospital care, if pain during inpatient rehabilitation is not controlled with oral medications, for improved control to allow for appropriate wound care to prevent infection, scarring, and loss of function. Oral medications also useful for the treatment of burn pain include gabapentin and pregabalin, especially when pruritus is also a problem. Gabapentin is tolerated with no significant adverse effects in children (52,55,71). Antidepressant medications may also be useful in relieving postburn pain during inpatient rehabilitation, particularly in electrical injury (72). Nonpharmacologic modalities useful in burn pain relief include massage therapy and cognitive behavioral treatment (72). A summary of the treatment options for burn pain and pruritus is given in Table 3.4.

### Table 3.4 Pruritus/Pain Treatment Options in Burns

<table>
<thead>
<tr>
<th>Pruritus</th>
<th>Pain</th>
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<tbody>
<tr>
<td>Antihistamines</td>
<td>Opioids</td>
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<tr>
<td>- Diphenhydramine</td>
<td>Nonsteroidal anti-inflammatory drugs</td>
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<tr>
<td>- Hydroxyzine</td>
<td>Antidepressants</td>
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<tr>
<td>- Cetirizine</td>
<td>Gabapentin</td>
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<tr>
<td>- Pheniramine maleate</td>
<td>Pregabalin</td>
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<tr>
<td>Emollients</td>
<td>Massage</td>
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<tr>
<td>- Simple moisturizers</td>
<td>Cognitive-behavioral therapies</td>
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<tr>
<td>- Aloe vera</td>
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<tr>
<td>- Lanolin</td>
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<td>- Coconut oil</td>
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<tr>
<td>- Vegetable oils</td>
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<tr>
<td>- Liquid paraffin</td>
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- Gabapentin
- Pregabalin
- Massage
I. MEDICAL COMPLICATIONS

Hypermetabolism/Catabolism

Full-thickness burn injury causes a loss of the skin’s ability to retain heat, fluids, and sodium, which is an immediate concern in acute burn patients, and also a concern in postacute care. The volume of fluid needed to initially resuscitate an acute burn patient can be calculated by many different formulas that take into consideration the total body surface area of the burns, which allows for an estimate of the necessary daily sodium and fluid replacement. Larger surface area burns will require a large volume of fluid resuscitation, which may lead to deep tissue edema requiring fasciotomy to prevent ischemia to an extremity and a decompressive laparotomy to prevent ischemia to the internal organs. Although these surgical procedures are immediately lifesaving, these lead to an increased risk for greater insensible fluid losses, ileus, intra-abdominal sepsis, fistula formation, and complications associated with a large ventral hernia, and set patients up for long term hypermetabolic/catabolic states. To reduce the volume of fluid given for resuscitation, vitamin C infusions in adults, colloid infusion, and the use of higher content sodium solutions can reduce the total volume infused and decrease the associated risks.

Severe burn injury is often followed by a profound catabolic/hypermetabolic response that persists for 12 to 24 months after the trauma (73,74). Factors that increase the likelihood for a hypermetabolic response that will persist for at least one year after trauma include open wounds that occur from the direct effect of the burns and/or the initial lifesaving surgeries, total body surface area burns of greater than 40%, and sepsis (75,76). The hypermetabolic response is mediated by significant elevations of plasma catecholamines, cortisol, and circulating inflammatory cells that are associated with catabolism, elevated resting body energy consumption, and the potential for dysfunction of multiple organ systems and malnutrition (73). The hypermetabolic response also often leads to secondary hypoparathyroidism and significant bone loss and is discussed in detail in the following section (77–80). Pharmacologic and nonpharmacologic treatments that ameliorate postburn hypermetabolism/catabolism are critical in both acute and postacute care including inpatient rehabilitation (75). Pharmacologic treatments include anabolic and anticatabolic agents that may include low-dose insulin, beta-blockade with propranolol and the use of synthetic testosterone analogues such as oxandrolone (73–75). Nonpharmacologic treatments should include early excision and closure/grafting of burn wounds, sepsis prevention, aggressive sepsis treatment, maintenance of ambient room temperatures at thermal neutrality (31.5 ± 0.7°C), high carbohydrate/protein diets, and graded resistance exercises to build strength and endurance (73–75). Control of pain and anxiety is also very important in severe burn patients as these symptoms are associated with a secondary increase in metabolic rates (75). A nutritionist/dietician should be included in the care of severe burn patients during inpatient rehabilitation to ensure an adequate anabolic diet.
Secondary Hypoparathyroidism/Bone Loss

The stress and inflammatory pathophysiologic mechanisms of the hypermetabolic/catabolic response in severe burn patients, including excessive levels of circulating glucocorticoids and chemical mediators of inflammation, sometimes lead to the onset of secondary hypoparathyroidism (77–79). Secondary hypoparathyroidism is common in patients having greater than 40% total body surface area burns and it results in bone loss/osteoporosis and a high risk for fractures from falls (80–82). High levels of plasma cortisol cause bone resorption and osteoblast apoptosis, which results in an extreme loss of calcium from bone, at the same time inflammatory chemical mediators result in the upregulation of parathyroid gland calcium receptors that allows for urinary calcium wasting (77–79). In addition, patients with severe burns convert pre-vitamin D to active vitamin D at a rate that is 20% to 25% of the normal rate resulting in a vitamin D deficiency also impairing bone health (77). A magnesium deficit also often occurs in association with secondary hypoparathyroidism due to magnesium loss through burn wounds and an increased cellular uptake as a result of hypermetabolism (79). Magnesium deficits can impair parathyroid gland function further contributing to secondary hypoparathyroidism (79). In addition to these mechanisms, bone loss in severe burn patients is worsened by immobility. Treatments for secondary hypoparathyroidism/bone loss may include vitamin D supplementation, calcium, magnesium supplementation if deficient (79,82,83), anabolic agents (80), bone antiresorptive agents such as pamidronate (80,81), recombinant human growth hormone (82), and exercise (82). Any patient admitted to inpatient rehabilitation with 40% or more total body surface area burns is at risk for secondary hypoparathyroidism/bone loss and should be placed on treatment for this condition. The possible causes and treatments of secondary hypoparathyroidism and bone loss in burns are summarized in Table 3.5.

### TABLE 3.5 Secondary Hypoparathyroidism/Bone Loss

<table>
<thead>
<tr>
<th>Causes</th>
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<tbody>
<tr>
<td>– Hypermetabolism</td>
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<tr>
<td>– Excessive plasma glucocorticoids</td>
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<td>– Excessive chemical mediators of inflammation</td>
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<tr>
<td>– Vitamin D deficiency</td>
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<td>– Magnesium deficiency</td>
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<td>– Immobility</td>
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<tr>
<th>Treatments</th>
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<tbody>
<tr>
<td>– Vitamin D supplemenation</td>
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<td>– Calcium supplementation</td>
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<tr>
<td>– Magnesium supplementation (if deficient)</td>
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<tr>
<td>– Anabolic agents</td>
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<tr>
<td>– Bone antiresorptive agents</td>
</tr>
<tr>
<td>– Recombinant human growth hormone</td>
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<tr>
<td>– Exercise</td>
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</table>
Hypertrophic Scarring/Contractures

Burns can lead to hypertrophic scarring and contractures, which in turn may cause significant problems resulting from loss of function at various regions of the body, including the face, neck, hands, feet, joints, and genitalia, even when the total body surface of a burn may be small. The potential for hypertrophic scarring and contractures increases immensely with large total body surface area burns and deep burns of the limbs. Hypertrophic scarring and contractures occur reportedly in as many as 5% to 40% of all burn patients (84). During inpatient rehabilitation, burns involving the face, neck, hands, feet, joints, and/or genitalia require special attention and interventions to maintain the full range of motion of these areas while the wounds heal and reepithelialize. For example, burn wounds to the hands and feet that include the digits require a great deal of attention to prevent and/or decrease the formation of contractures in the web spaces and across the joints. Burns of the face require special attention as the development of contractures in the area of the eyes could pull on the eyelids and maintain them in an open position increasing the risk for eye exposure injury/corneal injury over time. Burn patients with eyelid contractures would require aggressive lubrication of the eyes to prevent ocular abrasions and infections, which can sometimes be severe enough to result in loss of the globe. Inpatient rehabilitation patients having burns on the face in the vicinity of the eyes should have an evaluation and periodic follow-up with an ophthalmologist for early diagnosis and treatment of a potential ocular injury. Contracture of the commissure of the mouth and/or the neck can result in problems that may include the inability to close the jaws to eat properly. Contractures at the neck may also result in loss of range of motion at the neck with permanent malpositioning of the head/neck posture. Burn wounds in the area of the genitalia may require interventions to allow the patient to void properly, and this situation may sometimes call for the assistance of an urologist.

Inpatient rehabilitation interventions to decrease hypertrophic scarring and for the prevention of contractures in burn patients include static splinting, pressure garments, scar massage, and aggressive range of motion exercises unless contraindicated by recent skin grafts, open wounds, or tendon or bone injuries (84–87). Static splinting, though still controversial (84), is widely used when burn patients are at rest because patients will naturally assume positions of comfort, which will usually result in a tendency toward limb flexion. Flexion contractures are more common than extension contractures in burns (85). Affected body regions must be splinted in positions of function to avoid contractures (87). Continuous immobilization of joints by static splinting is indicated only for burn patients having tendon or bone injuries or recent skin grafts (86). Aggressive range of motion exercises, including active, active assisted, and passive range of motion is critical in all burn patients for contracture prevention as immobility is a primary cause of contractures. Also, hypertrophic scarring which results from a buildup of excessive collagen in nonuniform whorled patterns
is another important factor that may lead to the development of a contracture (86). Pressure on healing burn wounds may reduce excessive scarring by facilitating collagen fibers into uniform parallel patterns, which may hasten scar maturation (86). Custom fitted pressure garments are used as a main intervention for the prevention of hypertrophic scars. These garments should be fitted within a week after skin grafting, so that they may be available as soon as possible (86). Face/neck burns will require special garments or acrylic masks that must be comfortable enough to wear at all times, including at bedtime (86). Moisturizing and massage are also useful in the prevention of hypertrophic scarring (61). Measures to decrease hypertrophic scarring are necessary until scar maturation is completed. Burn patients who develop contractures will require surgical release to restore functional use of the affected extremity (85). The causes and treatments of hypertrophic scarring and burn contractures are summarized in Table 3.6.

**Heterotopic Ossification**

Burn patients are at risk for heterotopic ossification, which involves the growth of lamellar bone in locations where bone would normally not exist such as the soft tissue around the joints (88,89). The limitation of joint range of motion that occurs in burn patients having heterotopic ossification results in further impairment of mobility in patients whose daily function is often already significantly compromised, leading to greater risks from the complications of immobility. Mean total body surface area burns of 39% to 54% may be associated with a greater risk of heterotopic ossification (90,91). Also patients having flame burns seem to be at the greatest risk as opposed to those having burns resulting from scald, contact, or high-voltage electrical injuries (91). The elbow seems to be the most commonly involved joint having heterotopic ossification in burns (91). Signs of the possible development of heterotopic ossification during inpatient rehabilitation would include a loss of joint range of motion that may be reported by a patient or by therapists, and the so called “locking sign” that

<table>
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<tr>
<th>TABLE 3.6 Hypertrophic Scarring/Contractures</th>
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<tbody>
<tr>
<td>• Etiologies</td>
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<tr>
<td>– Large total body surface area burns</td>
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<tr>
<td>– Deep burns of the extremities</td>
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<tr>
<td>– Immobility</td>
</tr>
<tr>
<td>• Treatments</td>
</tr>
<tr>
<td>– Static splinting in positions of function</td>
</tr>
<tr>
<td>– Custom fitted pressure garments</td>
</tr>
<tr>
<td>– Scar massage</td>
</tr>
<tr>
<td>– Aggressive range of motion exercises (unless contraindicated)</td>
</tr>
</tbody>
</table>


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would occur on passive range of motion examination of the affected joint to a point of locked-fixed resistance (91). A diagnosis of heterotopic ossification may be confirmed by an x-ray exam. Surgical excision is indicated when conservative therapeutic interventions fail to restore joint range of motion (89). The conservative approach would involve an orthopedic surgeon who would attempt to force the joint range of motion to normal by disrupting/fracturing the heterotopic bone. Reportedly up to 8% of burn patients may have a recurrence of heterotopic ossification following surgical excision (91), but the recurrence may be reduced by perioperative radiation (90). The risk factors, diagnosis, and treatment of heterotopic ossification in burns is summarized in Table 3.7.

### Wound Infections/Tissue Necrosis/Need for Secondary Amputations

Full-thickness burn injury, often referred to as eschar, results in a loss of skin elasticity. Therefore, any circumferential full-thickness burn of an extremity may act as a tourniquet. As the deep tissues and muscles of the affected extremity become edematous from fluid resuscitation, blood flow to the extremity can be lost leading to ischemia and permanent dysfunction, often requiring an amputation. Circumferential full-thickness burns of the upper torso may result in the inability of appropriate chest wall expansion resulting in inadequate ventilation. Escharotomy is the process of making full thickness skin incisions into the eschar to allow the underlying edematous tissues to expand and is often necessary to prevent limb ischemia and hypercarbia, which may lead to arrhythmia and death if untreated. Burn patients who have had escharotomies will present to inpatient rehabilitation units with open wounds that will require special attention to prevent and monitor for wound infections. Also, open partial thickness wounds that have not been grafted will also require special attention during inpatient rehabilitation.

<table>
<thead>
<tr>
<th>TABLE 3.7 Heterotopic Ossification in Burns</th>
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<tbody>
<tr>
<td>• Risk factors</td>
</tr>
<tr>
<td>– Total body surface area burns &gt;39%</td>
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<tr>
<td>– Flame burns</td>
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<tr>
<td>– Immobility</td>
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<tr>
<td>• Diagnosis</td>
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<tr>
<td>– “Locking sign”</td>
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<tr>
<td>– Loss of range of motion</td>
</tr>
<tr>
<td>– X-ray studies</td>
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<tr>
<td>• Possible treatments</td>
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<tr>
<td>– Forced range of motion</td>
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<td>– Surgical excision</td>
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Prior to the development of effective antimicrobial agents in the mid-1960s, the wound was the most common site of infection resulting in devastating morbidity and virtually universal mortality in burn patients (92). The development of sophisticated antimicrobial therapy and improved techniques for burn patient wound care management has significantly ameliorated this problem, but early detection and treatment are essential (93). The main signs of a burn wound infection are dark brown, black, or violaceous discoloration of a wound which can be focal, multifocal, or generalized, as well as conversion of partial thickness injury to full-thickness necrosis with hemorrhagic discoloration of sub-eschar tissue (93). Edema and/or violaceous discoloration of unburned skin at wound margins, which is most commonly seen with pseudomonas infections, and unexpectedly rapid slough of eschar, which is most commonly a result of fungal infections, are other well-known signs. Inpatient rehabilitation physicians and nurses should be mindful of these signs of infection when inspecting burn wounds each day.

There are three usual forms of burn wound infections: (a) cellulitis which is most commonly caused by *Staphylococcus aureus*; (b) invasive wound infections within unexcised eschar, necrotizing fasciitis, which are most commonly caused by *Pseudomonas aeruginosa* that is often associated with other anaerobic organisms such as Clostridium and/or facultative anaerobes (eg, *Aeromonas*) causing invasive burn wound sepsis; and (c) burn wound impetigo, which occurs in wounds where there is loss of a reepithelialized surface such as a previously grafted wound or a healed donor site; this is most commonly caused by gram positive skin flora such as coagulase negative *Staphylococci* and *Staphylococcus aureus* including methicillin-resistant *S. aureus* (93–95). Early appropriate debridement and the use of topical and intravenous systemic broad-spectrum antibiotics are often necessary for successful treatment of these infections. Silver sulfadiazine and other silver containing topical agents are commonly used for a broad spectrum of coverage against gram negative, gram positive, and fungal organisms. A patient should be transferred back to the acute care hospital burn unit if any of these three types of burn wound infections is suspected during inpatient rehabilitation. Early diagnosis and treatment of burn wound infections are critical in the prevention of life-threatening sepsis and the possible need for a secondary amputation of a limb. The signs, types, and treatment options for burn wound infections are summarized in Table 3.8.

Importantly, blood-borne and urinary tract infections are more commonly seen than invasive wound infections in severely burned patients (93,96). Approximately 73% of all deaths within the first five days postburn have been shown to be directly or indirectly caused by septic processes (97), but sepsis can still develop during inpatient rehabilitation. The burn patient is at high risk for nosocomial infection as a result of the nature of the burn injury itself, the immune-compromising effects of burns, prolonged hospital stays, and intensive therapeutic and diagnostic procedures (98). Reports from burn centers vary as to the most commonly seen infections, with the cause varying from wound infection to pneumonia to blood stream infections. Systemic antibiotics should not be used prophylactically in burn patients as these promote the development
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of secondary infections and are a risk factor for the acquisition of antibiotic resistant organisms. Broad spectrum antibiotics do have a role for short term use in perioperative prophylaxis and in the treatment of known or suspected infections in burn patients. When available, infectious disease specialists should be consulted to follow burn patients who are receiving antibiotics in inpatient rehabilitation to avoid complications.

Psychological Sequelae

Psychological sequelae including anxiety, depression, and posttraumatic stress disorder may result from memories of the incident that caused the burn injury and the pain associated with the burning process, and subsequent pain, itching, disfigurement, and physical/functional and social limitations that occur afterward. Anxiety, depression, and posttraumatic stress disorder, including nightmares, flashbacks, fear of going back into a similar place or situation in which the burn occurred, and worries about integrating back into society may negatively impact a burn patient’s functional progress during inpatient rehabilitation. Depression is reportedly prevalent in 13% to 23% of all burn patients (99), while posttraumatic stress disorder occurs with a prevalence of 13% to 45% of all cases (99,100), and the two psychological disorders may coexist in the same patients. At two months postburn trauma, approximately 50% of in-hospital patients have symptoms of depression (101). In general, uncontrolled burn pain and itching are associated with a high risk for anxiety, depression, and related insomnia (60,62,68). Specific risk factors related to depression in burns include a previous history of depression and/or facial disfigurement, particularly in female patients (99). Risk factors for posttraumatic stress disorder include preburn affective disorders including depression, history of delirium or severe pain during acute care, and poor perceived social support (99,100). Insomnia is highly prevalent in patients having posttraumatic stress disorder and uncontrolled pain (102).

TABLE 3.8 Burn Wound Infections

- Types of infections
  - Cellulitis
  - Invasive wound infections/necrotizing fasciitis
  - Impetigo
- Signs
  - New wound discoloration (dark brown, black, or violaceous)
  - Hemorrhagic discoloration of sub-eschar tissue
  - Edema and/or discoloration at unburned wound margins
  - Rapid slough of eschar tissue
- Treatment options
  - Debridement
  - Topical and/or IV antibiotics
  - Silver coating topical agents or dressings
  - Urgent follow-up with treating burn surgeon
Acute stress disorder that occurs in the first month of trauma and posttraumatic stress disorder, which occurs after one month, are seen more often after burns than with any other form of injury (103). Recent studies have shown that greater levels of acute pain are associated with negative long-term psychological effects such as depression, suicidal ideation, and posttraumatic stress disorder for as long as 2 years after the initial burn injury (104). Delayed wound healing resulting from psychological stress has been documented (105). Some evidence suggests that the stress associated with unmanaged acute pain can result in delayed wound healing, which may lead to further medical complications (104). Inpatient rehabilitation burn patients face significant stressors that are direct effects of the burn injuries that include the problems associated with managing and compensating for physical impairments, limited endurance, severe itching, and continued pain (103,106). These patients must also deal with the indirect effects of the burn injuries that include social stressors such as family strains, worries regarding economic issues and the need to return to work, concerns regarding sexual function, change in body image, and disruption of daily life (103,106). Studies suggest that burn disfigurement in general leads to decreased self-esteem in women and social withdrawal in men (103). There is evidence that adjustment to burn injuries improves over time, independent of the extent of burn injury in patients having good psychosocial support (103,106). Good social support can play an important mediating role in decreasing stress, reducing pain, and promoting wound healing (99,100,107). It is important for the inpatient rehabilitation team to include a qualified burn psychologist as well as therapists and nursing staff who understand the special needs of burn patients. Support groups and peer counseling by burn survivors who are willing to talk to patients is an important service that should be included, if possible, during inpatient rehabilitation. Interdisciplinary rehabilitation professionals are more likely to be trusted with important information about emotional distress than friends or family and should therefore respond proactively when burn patients describe psychological difficulties (108). The ways in which burn patients cope with physical and psychosocial problems is influenced by the types of problems faced, personality characteristics, and cultural preferences and, therefore, the multidisciplinary rehabilitation team should be sensitive to these various issues (109). A program of support that involves interventions to help burn patients cope with new bodily sensations and new body image is necessary during inpatient rehabilitation (109).

In general, the treatment of anxiety, depression, and/or posttraumatic stress disorder during inpatient rehabilitation should involve both pharmacologic and nonpharmacologic interventions. Various anxiolytic and antidepressant medications may be helpful. In addition there must be aggressive treatment of pain and itching. Massage may be helpful in reducing pain, itching, and anxiety (60,62,68). A psychologist should be involved to assist burn patients with the various psychodynamic issues such as body image. A psychiatrist should be consulted in cases in which there are prominent symptoms of anxiety, depression, or suicidal ideation. The common psychological sequelae of burns, including risk factors and treatment options, are summarized in Table 3.9.
TABLE 3.9 Psychological Sequelae of Burns

- **Common manifestations**
  - Anxiety
  - Depression
  - Posttraumatic stress disorder

- **Risk factors**
  - Uncontrolled pain
  - Uncontrolled itching
  - Facial disfigurement
  - History of depression
  - Perception of poor social support

- **Treatments**
  - Aggressive interventions to control pain and itching
  - Anxiolytics
  - Antidepressants
  - Massage
  - Psychological therapies/treatments
  - Support groups/peer guidance

**SUMMARY**

Trauma patients, including those with multiple trauma and/or burns, are at risk for multiple medical, physical, and psychological complications that may occur during inpatient rehabilitation, which are given in Table 3.1. Rehabilitation professionals, including all the members of the interdisciplinary treatment team, must be vigilant for early symptoms and signs of any of these potential complications. Most of these complications may lead to significant morbidity and/or mortality if not prevented or treated early.

**Timeline for Potential Inpatient Rehabilitation Complications in Trauma Patients**

<table>
<thead>
<tr>
<th>Complication</th>
<th>Onset of Complication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complication Timeline for Multiple Trauma</td>
<td>Early/Acute</td>
</tr>
<tr>
<td>Missed injuries</td>
<td>X</td>
</tr>
<tr>
<td>Posttraumatic cholecystitis</td>
<td>X</td>
</tr>
<tr>
<td>Paralytic ileus/bowel obstruction</td>
<td>X</td>
</tr>
<tr>
<td>Complications of immobility</td>
<td>X</td>
</tr>
<tr>
<td>Falls</td>
<td>X</td>
</tr>
<tr>
<td>Inadequate pain management</td>
<td>X</td>
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</tbody>
</table>

(continued)
Timeline for Potential Inpatient Rehabilitation Complications in Trauma Patients (continued)

Complication Timeline for Burns

<table>
<thead>
<tr>
<th>Complication</th>
<th>Onset of Complication</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Early/Acute</td>
</tr>
<tr>
<td>Pruritus/special pain concerns</td>
<td>X</td>
</tr>
<tr>
<td>Hypermetabolism/catabolism</td>
<td>X</td>
</tr>
<tr>
<td>Secondary hypoparathyroidism/bone loss</td>
<td>X</td>
</tr>
<tr>
<td>Wound infections/tissue necrosis</td>
<td>X</td>
</tr>
<tr>
<td>Need for secondary amputations</td>
<td>X</td>
</tr>
<tr>
<td>Complications of immobility</td>
<td>X</td>
</tr>
<tr>
<td>Psychological sequelae</td>
<td>X</td>
</tr>
<tr>
<td>Hypertrophic scarring/contractures</td>
<td></td>
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<tr>
<td>Heterotopic ossification</td>
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</tbody>
</table>

REFERENCES


3. MULTIPLE TRAUMA AND BURNS

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60. Parlak GA, Polat S, Akcay MN. Itching, pain and anxiety levels are reduced with massage therapy in burned adolescents. *J Burn Care Res.* 2010;31(3):429–432.


Approximately 800,000 strokes occur annually in the United States making stroke, a cerebrovascular brain injury, a leading cause of long-term disability among adults (1). The current prevalence of stroke in the United States ranges from 500 to 800 per 100,000 people (1,2). It is estimated that currently more than 4 million Americans have survived a stroke and that the total number of Americans living with stroke is expected to increase further as the United States elderly population expands (1,2). Direct and indirect costs to society resulting from stroke in the United States were estimated at >$73 billion in 2010 (2). These statistics highlight the increasing importance of the role of stroke rehabilitation interventions in limiting the direct and indirect costs to society by maximizing the recovery of functional independence of each individual stroke survivor. Most functional recovery occurs in the first 3 months following a stroke (3,4), though some further improvement may occur at up to 6 months (5). The greatest degree of functional recovery may occur in the first poststroke month underscoring the importance of initial inpatient rehabilitation (4). Inpatient rehabilitation efforts during this time frame help to potentiate the extent of long-term functional recovery while also limiting the risk for poststroke medical complications. Approximately 65% of individuals having motor and/or sensory deficits poststroke will regain full functional independence, whereas only 10% of those having a combination of motor, sensory, and cognitive impairments will recover the ability to live independently (6); however, rehabilitation can enhance the degree of functional recovery. Cognitive deficits after a stroke may include aphasia and/or hemineglect. Aphasia occurs in more than 20% of patients following a stroke (7), whereas hemineglect is present in up to one-third of cases (8). Hemineglect can resolve in some patients by 3 months poststroke (8); however, its persistence can be a limiting factor to functional recovery. Early rehabilitation efforts help to enhance a stroke patient’s potential for recovery by limiting the negative role that motor, sensory, cognitive, and psychological impairments could have on functional independence. One of the key roles of early rehabilitation efforts is the prevention of the multiple possible medical complications of stroke, which would be barriers to long-term recovery.
Rehabilitation interventions should begin as early as possible in medically stable patients following an acute stroke to maximize the potential for functional recovery and to prevent complications. Rehabilitation encompasses medical, physical, psychological, social, educational, and vocational interventions that can be provided in a variety of institutional and community settings (9). Optimally stroke rehabilitation begins during acute care and involves a comprehensive multidisciplinary team that provides intensive coordinated rehabilitation efforts (10,11); then this approach continues in a postacute inpatient rehabilitation unit (12). Rehabilitation may also continue in a nursing home, in the patient’s home, or in an outpatient facility/program. Third-party payers often influence the setting and the duration of rehabilitation in an effort to control costs (13). However, regardless of the setting, rehabilitation goals should always include the prevention of secondary complications, restorative treatments to reduce neurologic impairments, compensatory strategies for residual disabilities, patient/care-taker education, and maintenance of function (9).

This chapter focuses on the prevention and management of the most common potential medical complications that occur during inpatient stroke rehabilitation (Table 4.1). Routine continuous monitoring of health status and physical function is essential throughout the continuum of a poststroke patient’s rehabilitation process to minimize the risk for complications and to maximize the potential for recovery.

### TABLE 4.1 Possible Complications of Inpatient Poststroke Rehabilitation

- Disorders of homeostasis
  - Dehydration and malnutrition
  - Bladder and bowel dysfunction
  - Insomnia/impaired sleep
- Complications of immobility
  - Aspiration pneumonia
  - Venous thromboembolism
  - Skin breakdown/ulceration
  - Spasticity and joint contractures
- Falls and associated fractures/trauma
- Seizures and epilepsy
- Poststroke pain syndromes
  - Shoulder pain
  - Central poststroke pain
  - Affective disorder related pain
- Poststroke affective disorders
  - Depression
  - Pseudobulbar affective disorder
- Secondary stroke
of function. Included in this endeavor should be efforts to ensure the maintenance of homeostasis, including proper nutrition and hydration, normal bladder and bowel function, and adequacy of sleep. In addition, there must be prevention of the complications of immobility, including venous thromboembolism, aspiration pneumonia, skin ulcerations, and development of joint contracture. Poststroke patients having cognitive impairments are at a high risk for falls and associated fractures and injuries, which must also be prevented. There should also be management of poststroke depression and emotional dysfunction as well as chronic pain, which will otherwise interfere with recovery. Stroke is the leading cause of seizures and new onset epilepsy in adults, which is another complication that must be managed accordingly for those at risk. In addition, stroke patients have a high risk for a secondary stroke, which is potentially one of the most devastating complications that may occur during rehabilitation, and which must be prevented. Poststroke medical complications impede rehabilitation resulting in poor functional outcomes and increased costs of care. The prevention and management of potential medical complications of inpatient stroke rehabilitation are discussed in detail in the following sections of this chapter.

MAINTENANCE OF HOMEOSTASIS

Dehydration and Malnutrition

Dehydration and malnutrition may occur in stroke patients secondary to dysphagia, inability to self-feed, confusion, or inability to communicate hunger or thirst. A patient’s risk for malnutrition and dehydration may be reduced by efforts that may include the monitoring of daily intake of calories and liquids, weekly measurement of body weights, supervision and assistance with meals, nutritional supplements, and tube feedings if necessary. 45% to 70% of stroke patients initially have dysphagia (1,14–16). The prevalence of dysphagia may approach 90% in brainstem strokes (17,18). Bilateral representation of the cortical swallowing centers in the brainstem and the motor cortex may account for the greater prevalence of dysphagia in brainstem strokes than unilateral hemisphere strokes (17). Signs and symptoms associated with dysphagia may include frequent coughing, choking on liquids or solids, nasal regurgitation, confusion, dysarthria, and pneumonia. Dysphagia may be diagnosed clinically or by a standard modified barium swallow study (19). Traditional dysphagia treatments include oral-motor exercises to target strengthening of muscles in disuse atrophy (20), biofeedback techniques, and sensory stimulation to target the swallowing center in the brainstem for plasticity (17,21–23), and compensatory swallowing strategies, including various modifications of head, neck, and body postures (20,24). Adjustment of food/liquid temperature, viscosity, and volume (24,25), and the use of tube feedings for severe dysphagia are also included.
Bladder and Bowel Dysfunction

Bladder and bowel dysfunction frequently occur following a stroke and may complicate the rehabilitation process. Bladder dysfunction after a stroke may result from hypertonicity, hypotonicity with areflexia, and incoordination of internal or external sphincter control. The most common cause after a stroke is detrusor hyperreflexia, which results in urinary incontinence (26). Incidence of urinary incontinence ranges from approximately 40% to 60% in the early recovery period following a stroke (27,28). In many cases a patient’s inability to communicate the need to void will also result in incontinence (26). A regular toileting program, where nursing staff frequently check on a patient’s toileting needs, should resolve this source of incontinence. Though less common, a hypotonic bladder with urinary retention and overflow incontinence may also occur after a stroke. Patients having large postvoid residual urine volumes because of hypotonic bladders may require a course of intermittent straight catheterizations. Individuals having persistent difficulties with poststroke bladder dysfunction may require a urologic consultation and urodynamic testing to diagnose the etiology. In some cases the etiology may be unrelated to the stroke. Treatment may involve certain medications and bladder training with toileting at regular intervals. Use of indwelling Foley catheters should be avoided except in the case of patients with urinary retention that cannot be otherwise controlled, extensive skin ulcerations, or incontinence that temporarily interferes with fluid or electrolyte-balance monitoring. In most cases urinary incontinence improves/resolves over time spontaneously or with treatment.

Bowel dysfunction, and particularly constipation or fecal impaction, may occur following a stroke as a result of immobility, inadequate nutrition (solid or liquid), cognitive impairment, neurogenic bowel, medications (ie, narcotic analgesics), and depression. Treatment measures may include adequate intake of fluids and fiber, use of a regular toileting schedule, judicious use of stool softeners, laxatives, and therapeutic enemas, and the discontinuation of certain medications when possible. Most causes will gradually resolve over time with treatment. In extreme cases a gastroenterology evaluation may be helpful.

Insomnia

Insomnia may occur as a direct result of the stroke, or it may result indirectly from comorbidities, including depression, agitation, anxiety, and the side effect of medications, muscle spasms/spasticity, untreated pain, and inability to move in bed, urinary frequency/incontinence, or interruptions of sleep as a result of the hospital environment. Inadequate sleep can result in daytime drowsiness and the inability to fully benefit from rehabilitation therapies. Goals of management include the determination and treatment of the specific cause for the insomnia. Patients may respond to an alteration
of the sleep environment to reduce disturbances of sleep, other sleep hygiene measures such as avoidance of caffeine or stimulant medications prior to sleep, and a limited course of a mild sedative/hypnotic sleep medication may be helpful. Polysomnography may be indicated in severe cases of insomnia refractive to these treatments as there may be an underlying sleep disorder such as sleep apnea.

COMPLICATIONS OF IMMOBILITY

Aspiration Pneumonia

Aspiration pneumonia is the most common cause of death in individuals having untreated dysphagia following stroke (29), accounting for at least 10% of deaths occurring within 30 days of the initial hospital admission (30). Dysphagia is the primary risk factor for aspiration pneumonia in stroke patients. Other risk factors include depressed cognition and impaired mobility. Risk reduction for pneumonia in patients who have had a stroke includes efforts at early mobilization as well as prevention of aspiration through modification of diet, proper positioning during feedings, maintaining the head of bed elevated at more than 30°, and temporary tube feedings if necessary. Prolonged bed rest can result in poor aeration of the lungs, atelectasis, and a greater likelihood for the development of pneumonia. Early patient mobilization can minimize this risk.

Venous Thromboembolism

Immobility, particularly the paralysis of a lower extremity, places individuals poststroke at risk for deep venous thrombosis and pulmonary embolism. Approximately 10% to 30% of patients having an acute stroke are at risk for venous thromboembolism (31). Risk increases in stroke patients with comorbid diseases, including cancer, pulmonary disease, cardiovascular disease, diabetes mellitus, and inflammatory bowel disease, as well as other rheumatologic and infectious diseases. Predisposing risk factors also include a history of prior deep venous thrombosis or pulmonary embolism, obesity, thrombophilia, or advanced age. Randomized trials have shown effective risk reduction with the use of unfractionated heparin, low molecular weight heparins and other anticoagulation medications in the prevention of venous thromboembolism (31,32). However, a reduction in mortality rates with the use of these agents has not yet been demonstrated (31). There may be a higher rate of bleeding complications in patients receiving unfractionated heparin than those receiving low molecular weight heparins (31,33). There is currently no definitive research data supporting the use of aspirin, warfarin, or mechanical methods for the prevention of thromboembolism in acute stroke patients (31). However, the use of mechanical methods, including long compression stockings and sequential compression may still be helpful to reduce risk in patients having hemorrhagic strokes where anticoagulation is contraindicated (34–36). These mechanical methods may also
be useful in cases of large ischemic strokes and embolic strokes where hemorrhagic conversion involving the area of infarction is a possibility. Emerging evidence may eventually support the use of low-molecular weight heparin in some cases of intracerebral hemorrhage for thromboembolism prophylaxis (35).

**Skin Breakdown/Ulceration**

Pressure sores may occur in patients during poststroke rehabilitation care in comprehensive rehabilitation units or in subacute rehabilitation/skilled nursing centers. Risk factors for skin breakdown include immobility, incontinence, poor nutritional status, impaired cognition, obesity, and altered pain perception (37). The risk may be greatest in patients having stroke and comorbid renal failure (38), or cardiovascular disease with impaired circulation (39). The most frequent sites of pressure ulceration are the areas of skin overlying the bony prominences, including the coccyx/sacrum, heels, ankles, and ischial tuberosities (39). Steps to maintain skin integrity in poststroke patients include daily skin inspection, gentle routine cleansing, protection from moisture, maintenance of hydration and nutrition, efforts to improve mobility, frequent turning and repositioning of immobile patients, and avoidance of skin pressure, friction, and shearing. Proper pressure relief mattresses and wheelchair cushions are also essential for immobile stroke patients to prevent skin breakdown.

**Spasticity and Joint Contractures**

More than one third of stroke patients develop spasticity in their paretic limbs (40). Young patients and those having severe hemiparesis are most at risk for the development of spasticity poststroke (41). Spasticity is manifested as an abnormal increase in muscle tone (hypertonicity), hyperactive reflexes, Babinski sign, clonus, and rigidity that results from the impairment of upper motor neuron inhibitory pathways because of the stroke. The loss of normal cortical inhibition in poststroke spasticity also results in abnormal cocontraction of flexor and extensor muscle groups during attempts at voluntary movement in paretic extremities, which can interfere with functional progress during rehabilitation. In addition, spasticity at rest presents as hypertonic predominance of flexion muscle synergy in the paretic upper extremity and extensor muscle synergy at the lower extremity. On examination at rest, the hemiparetic upper extremity in a stroke patient with spasticity will have flexion at the wrist and elbow with exaggeration of adduction, flexion, and internal rotation at the shoulder (42); whereas there will be a tendency for adduction/extension at the hip, with extension of the knee and plantar flexion (ankle extension) and inversion at the foot (43,44). The combination of poststroke hemiparetic muscle weakness and hypertonicity results in prolonged shortening of muscles and soft tissues around the joints contributing to
the development of fixed contractures over time (45,46). The treatment of established contractures is difficult and involves surgical interventions, including tendon transfers, tendon lengthening, tenotomies, and arthrodesis, all of which may be unsuccessful (44,46). Rehabilitation interventions to limit the effects of poststroke spasticity and to prevent the development of contractures include passive/active stretching/joint mobilization (42,44,46,47), splinting/bracing (42,48–50), strengthening of antagonist muscles (42,44,50), use of orthoses (44), oral muscle relaxant medications (42,44), botulinum toxin injections (40,42,51–54), and sensorimotor robotic assisted training (55,56). There are some controversies involving the use of splinting and bracing in the prevention and treatment of spasticity and contractures in stroke patients (42,48–50). Botulinum toxin injections may be most effective if administered early in acute and subacute stroke patients while the spasticity is still evolving (40). However, in chronic stroke patients admitted to inpatient rehabilitation for treatment of late effects of stroke, botulinum toxin injections may still be helpful in those stroke patients with upper limb spasticity particularly when it is administered in conjunction with constraint-induced movement therapy (51), or when it is administered once every 3 months for a course of 5 treatments over 15 months (52). It is very important that clinicians administering botulinum toxin properly identify the muscles contributing to problematic tone by eliciting resistance to movement at rest and by observing patterns of hypertonicity or cocontraction during active movement (42). Botulinum toxin has an advantage over the use of oral muscle relaxant medications in that the effect is local rather than systemic, thus reducing the risk for side-effects. It is also important that chronic pain be controlled in poststroke patients as pain can exacerbate spasticity. Early mobilization and the encouragement of early participation in self-care activities is a primary objective of rehabilitation in acute stroke patients, which will also be helpful in minimizing the likelihood of the development of contractures.

FALLS AND FRACTURES/TRAUMA

Stroke patients are at a high risk for falls during inpatient rehabilitation with approximately 37% to 40% of patients having one fall (57–59) and about 20% having two or more falls (58,60). Falls may result in physical or psychosocial injury in poststroke patients. Minor physical injuries occur in 20% to 25% of these falls, including contusions, abrasions, and skin tears (57–61), whereas fractures and other serious injuries occur in about 1% to 5% of all poststroke falls (57–62). Psychosocial injury resulting from one or more falls may manifest as a fear of falling, which may lead to decreased physical activity/immobility, loss of independence, and social deprivation/isolation (63,64). The risk of intracerebral hemorrhage is low in anticoagulated stroke patients having falls without evidence of head trauma (60) but the risk increases if there is loss of consciousness (65), change in mental status or external signs of head trauma. Those stroke patients on antiplatelet medications or on warfarin anticoagulation with signs
or symptoms of head trauma are at higher risk for intracranial bleeding (65–67), especially if the INR at the time of the fall is 2.43 or more (66); and these patients should be referred for an emergency brain CT scan. Factors associated with an increased risk of falls in stroke patients include: impaired balance (58,63,68), Berg Balance Scale scores less than 30 (58), visual–spatial impairments/hemineglect (68,69), impaired performance of activities of daily living (68), apraxia (58), cognitive deficits (9,58,70), urinary incontinence (70), hypotonia/hypoesthesia/paralysis (hemiplegia having more risk than complete hemiparesis) (69), communication impairment (9,69), and tranquilizing/sedative/neuroleptic medications (69). Most falls occur during the daytime (69,70), with more than 60% occurring close to the patient’s bed (69). Falls during transfers or from sitting in wheelchairs is also most common (57,61). Rehabilitation interventions to reduce risk of falls in stroke patients may include task-specific exercise programs targeting balance and gait impairments such as reduced propulsion at gait push-off, decreased hip and knee flexion during the swing phase, and reduced stability during the stance phase (63). Nursing/medical interventions to reduce risk of falls and associated injuries may include a low bed, bed alarm, pelvic belt for wheelchairs, frequent toileting/bladder training program, frequently checking on the needs of patients with communication impairments, strict supervision of all transfers/ambulation, and patient/family education. Pharmacologic interventions may include psychotropic drugs in restless or agitated stroke patients (70), and vitamin D supplementation in patients having a documented vitamin D deficiency (59). Clinicians should identify risk factors for falls in stroke patients on admission to inpatient rehabilitation and then formulate a prevention plan accordingly. Any stroke patient having a reported fall while in the inpatient rehabilitation unit needs to be evaluated for signs of serious injury, therapies should be temporarily suspended, and appropriate imaging studies should be ordered as necessary.

Seizures and Epilepsy

Seizures are one of the most common complications of both ischemic and hemorrhagic stroke, and stroke is the leading cause of new onset seizures and epilepsy in adults and particularly the elderly (68–73). The incidence of seizures following a stroke ranges from 3% to 15% (62,68,71–73). Poststroke seizures are classified as early or late, with early seizures occurring within the first 1 to 2 weeks of a stroke (68,70,71,72,74). Metabolic and physiologic abnormalities associated with an acute ischemic or hemorrhagic stroke likely contribute to the onset of early seizures, which peak within the first 24 hours of a stroke (68,69,71,72). A single early poststroke seizure may be followed by further seizures (71). Early seizures are an independent risk factor for the occurrence of unprovoked late seizures (68,72,75–77). Late-onset seizures peak within 6 to 12 months of a stroke (72), and likely result from permanent poststroke changes in neural networks and pathways resulting in hyperexcitability, which contributes to
epileptogenesis (68). Late-onset seizures occur in 3% to 5% of all stroke patients (73). Epilepsy, a recurrent seizure disorder, develops in one-third of patients having early-onset seizures (72) and one-half of patients having late-onset seizures (72,73). The risk for seizures after a stroke is greatest in those having a large area of cortical infarction and/or an intracerebral hemorrhage (68–70,72,74,78). There is almost a 2-fold greater risk for seizures with a hemorrhagic stroke than with an ischemic stroke (78). The risk for late-onset seizures may be highest in those patients having a large disabling cortical infarction involving the middle cerebral artery vascular territory (74).

The decision regarding the use of prophylactic anticonvulsant medications after an acute stroke is controversial. Physicians caring for acute stroke patients during inpatient rehabilitation may face this dilemma especially after a single early seizure. Concerns affecting this decision include the possible adverse effects of anticonvulsant medications, the risk of further seizures, and the effects of further seizures on mortality and/or long-term functional outcomes. The effects of seizures on mortality and long-term functional outcomes after a stroke remain controversial (68–70,72,73). In addition, first-generation anticonvulsants such as phenytoin, carbamazepine, and valproic acid may have harmful impacts on functional recovery, bone health, and/or suboptimal pharmacokinetic profiles that allow for potentially dangerous drug interactions with anticoagulants, salicylates, and other medications especially in the elderly (73,79). Gabapentin, lamotrigine, and levetiracetam are newer generation anticonvulsants effective in reducing poststroke seizures, with more favorable pharmacokinetic profiles that should not result in any adverse interactions with anticoagulant antiplatelet agents nor involve any negative impacts to bone health (73,80). Low-dose extended release carbamazepine may be considered as an option in young patients with good bone health who do not require anticoagulant medications (73). Physicians must make the final decision regarding the use of anticonvulsant prophylaxis during inpatient rehabilitation based on the clinical impact of the first seizure, patient/family preference, and the likelihood of further seizures, which is greatest in those patients having intracerebral hemorrhages and/or large cortical strokes, in particular, in those involving the middle cerebral artery vascular territory.

**POSTSTROKE PAIN SYNDROMES**

Poststroke pain is common and may be multifactorial in origin. Etiologies of poststroke pain may include neurological, musculoskeletal, and affective factors. Neurological causes of pain include the impairment of central afferent/sensory pathways that contribute to abnormal sensations such as hypersensitivity and hyperpathia and the impairment of efferent/motor pathways, which contribute to weakness and spasticity. Musculoskeletal causes of pain include injury to joints, muscles, and/or tendons that are secondary to weakness or impaired sensation. Untreated depression is the main affective factor contributing to chronic poststroke pain in some patients. Conversely,
improperly treated pain can result in the development of anxiety and depression in stroke patients. The two most common poststroke pain syndromes involve shoulder pain and/or central neurogenic pain.

**Shoulder Pain**

Shoulder pain occurs in up to 70% to 80% of patients after a stroke (81–83). Shoulder pain impacts progress during stroke rehabilitation by directly limiting a patient’s potential for recovery of passive or active range of motion at the affected arm, as well as by indirectly limiting progress in mobility and activities of daily living. Weakness in the shoulder-stabilizing rotator cuff muscles makes this joint vulnerable to injury following a stroke. Subluxation of the humerus from the glenoid fossa is a physical sign of shoulder instability because of rotator cuff weakness. The role of shoulder subluxation as a direct cause of shoulder pain remains controversial (82–85). Impaired sensation, spasticity, and restricted rotation are also factors that make a shoulder vulnerable to injury and to the development of poststroke pain (84,85). Repetitive microtrauma of pain sensitive structures within and around the shoulder joint results in somatosensory sensitization leading to the onset and maintenance of pain (85). The most common causes of shoulder pain in stroke patients are adhesive capsulitis in 50% of cases and rotator cuff tears in 20% (86). Other possible causes of poststroke shoulder pain are given in Table 4.2. A subset of stroke patients with shoulder pain may develop a complex regional pain syndrome known as the *shoulder-hand syndrome*, which presents as a reflex sympathetic dystrophy with autonomic nervous system related abnormalities in the affected arm and hand, including discoloration, swelling, and significant pain (87). Specific causes of shoulder pain may be diagnosed by clinical examination

<table>
<thead>
<tr>
<th>TABLE 4.2 Possible Causes of Poststroke Shoulder Pain</th>
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<tbody>
<tr>
<td>• Adhesive capsulitis</td>
</tr>
<tr>
<td>• Rotator cuff tears</td>
</tr>
<tr>
<td>• Traction/compression neuropathy</td>
</tr>
<tr>
<td>• Shoulder trauma</td>
</tr>
<tr>
<td>• Bursitis/tendonitis</td>
</tr>
<tr>
<td>• Heterotopic ossification</td>
</tr>
<tr>
<td>• Complex regional pain syndrome/reflex sympathetic dystrophy</td>
</tr>
<tr>
<td>• Shoulder subluxation</td>
</tr>
<tr>
<td>• Repetitive micro-trauma</td>
</tr>
<tr>
<td>• Central poststroke pain syndrome</td>
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</tbody>
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and/or by sonography, arthrography, or radiography. Prevention involves the avoidance of shoulder traction or torsion by rehabilitation staff during range of motion therapies, transfers, positioning, and wheelchair seating. Careful passive range of motion is important to improve joint volume to prevent the development of adhesive capsulitis (86). Electrical stimulation also has a role in both the prevention and treatment of this condition by reducing shoulder subluxation, improving passive range of motion, and decreasing pain (82,87,88,89). Shoulder pain may also respond to treatments that include intra-articular corticosteroid injection (82,90), anti-inflammatory medications, modalities including ice, heat, and soft tissue massage and/or the use of topical analgesics such as a lidocaine patch. A summary of prevention and management recommendations for poststroke shoulder pain during inpatient rehabilitation are given in Table 4.3.

Central Poststroke Pain

Central poststroke pain (CPSP) occurs in as many as 8% to 14% of patients following a stroke as the direct result of a brain lesion involving the spinal-thalamic-cortical tract at any point in its course from the brainstem through the thalamus to the sensory cortex (81,91,92). This type of chronic poststroke pain is often described as a burning, shooting, or lancinating sensation, which occurs spontaneously or may be triggered by light touch or cold sensations in the body region affected by hemisensory loss. The CPSP syndrome can occur in both ischemic and hemorrhagic strokes (91) and is hypothesized to result from hyperexcitation in the damaged sensory pathway and/or from dysfunction of central pain inhibition (81). The treatment of CPSP includes use of anticonvulsant medications such as pregabalin, lamotrigine, and gabapentin, which target neuronal hyperexcitability (93–95). Amitriptyline is another medication that has been shown to be useful in CPSP treatment (95). Transcranial magnetic stimulation may also be useful in CPSP pain control (96).
Affective Disorders and Chronic Poststroke Pain

Untreated or improperly treated chronic pain in stroke patients could have a negative impact on functional recovery by contributing to the onset and exacerbation of affective disorders, including anxiety and depression. The relationship between pain, anxiety, and depression is well established in head trauma patients and, in particular, those having poor functional recoveries after a concussion (97). Similarly it is known that poststroke patients who are depressed will also have greater cognitive impairments than those who are not depressed (98). In poststroke patients having chronic pain the reduced capacity to perform complex cognitive tasks may be because of the direct distraction of pain, and/or related to associated fatigue, sleep deprivation, depression, anxiety, poor motivation as well as the sedative side effects of certain analgesic medications. Analgesic medications, which may have sedative side effects, should be used with caution in stroke patients. A correlation has been documented between positive affect, including the absence of anxiety or depression, and less subjective complaints of pain in poststroke patients (99). It is important for chronic pain to be fully evaluated and properly treated in any patient following a stroke to maximize the potential for recovery while minimizing the risk for the development of affective disorders, including anxiety and depression, which will hinder recovery.

DEPRESSION AND PSEUDOBULBAR AFFECT

Depression

Depression and pseudobulbar affect are the most common emotional disorders following a stroke (100,101). Depression develops in approximately 40% of patients after a stroke (102). The overall prognosis for functional recovery is worsened by depression in poststroke patients as there is an associated increased risk for mortality, as well as worsened impairments of cognition and physical function (98,102). The diagnosis of depression is made based on the usual symptoms and signs such as tearfulness, depressed affect, changes in appetite and sleep patterns, apathy, fatigue, and suicidal ideation. Fatigue and apathy may also sometimes occur as isolated symptoms after a stroke in the absence of depression (103–106). Acute basal ganglia infarcts may be an independent predictor of poststroke fatigue (104), whereas bilateral basal ganglia strokes may be more associated with the development of depression in which apathy is a prominent symptom, which is known as apathetic depression (106). Affective depression, in which overt symptoms and signs of sadness are apparent, is more associated with left frontal lobe strokes (106). The treatment of poststroke depression should include interventions to reduce depressive symptoms while improving mood, energy, and quality of life through a multi-disciplinary approach. Chronic pain in depressed patients should be evaluated and
treated since pain is known to contribute to the onset and maintenance of depression (97,99). Improvements in trunk stability, mobility, and activities of daily living may also reduce symptoms of depression and apathy (103). Randomized controlled studies have demonstrated the efficacy of sertraline, citalopram, and nortriptyline in the treatment of poststroke depression (102). However, mild depression in elderly patients may not warrant treatment with these antidepressant medications because of the risk of drug interactions and other potential side effects from these agents (107). The selective serotonin reuptake inhibitors are the first choice drugs in the elderly because they have a lesser potential for adverse reactions than the tricyclic antidepressants (107).

**Pseudobulbar Affect**

Pseudobulbar affect, also known as emotional incontinence, emotional lability, or emotionalism, is manifested by bouts of uncontrollable laughter or crying incongruent with a patient’s mood. Interestingly most patients having pseudobulbar affect do not have depression (100,101). The etiology of this poststroke emotional disorder is thought to be related to infarct injury involving serotonergic neurons in predominantly subcortical brain regions, including the basal ganglia, pons, and the internal capsule (100,101). Thalamic bleeds have also been implicated as a possible cause for this disorder (108). Pharmacologic treatment may include dextromethorphan and quinidine combined therapy, which received FDA approval in 2010 (109), or the use of selective serotonin reuptake inhibitors such as sertraline (109,110). Psychosocial behavioral interventions may also help to reduce the frequency and intensity of pseudobulbar affective symptoms (100).

**SECONDARY STROKE PREVENTION**

Any individual who has had a stroke is at a high risk for the occurrence of further strokes. Nearly 200,000 of the estimated 800,000 strokes that occur annually in the United States are recurrent events (111). Secondary stroke is one of the most devastating of the potential poststroke medical complications. Physicians who treat patients after a stroke, including those physicians involved during inpatient rehabilitation, share in the responsibility to ensure that adequate measures are taken for the prevention of further strokes. Stroke subtypes may be divided into those that result from ischemia, which account for approximately 85% of all strokes, and those that are a result of hemorrhage, which account for the remaining 15% (Table 4.4). Risk factors for ischemic stroke may be divided into both modifiable and nonmodifiable categories (Table 4.5). There is overlap between the risk factors for ischemic stroke and the risk factors for hemorrhagic stroke (Table 4.6). This section focuses on the strategies
I. MEDICAL COMPLICATIONS

TABLE 4.4 Stroke Subtypes

<table>
<thead>
<tr>
<th>Ischemic (85%)</th>
<th>Hemorrhagic (15%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Atherosclerotic/large vessel</td>
<td>• Subarachnoid hemorrhage</td>
</tr>
<tr>
<td>• Cardioembolic</td>
<td>– Aneurysm</td>
</tr>
<tr>
<td>• Lacunar/small vessel</td>
<td>– Vascular malformation</td>
</tr>
<tr>
<td>• Cryptogenic</td>
<td>• Lobar/intracerebral hemorrhage</td>
</tr>
<tr>
<td>• Other</td>
<td>• Other</td>
</tr>
</tbody>
</table>

TABLE 4.5 Ischemic Stroke Risk Factors

- Nonmodifiable factors
  - Age
  - Gender
  - Race
  - Heredity

- Modifiable factors
  - Medical conditions
    - Hypertension
    - Diabetes mellitus
    - Atrial fibrillation
    - Cardiac disease
    - Hyperlipidemia
    - Carotid artery stenosis
    - Prior stroke or transient ischemic attack
  - Behaviors
    - Cigarette smoking
    - Alcohol overuse
    - Physical inactivity

TABLE 4.6 Risk Factors for Hemorrhagic Stroke

- Medical conditions
  - Hypertension
  - Vascular malformation
  - Aneurysm
  - Bleeding disorders
  - Amyloid angiopathy
  - Drugs
  - Tumors
  - Trauma
  - Other

- Behaviors
  - Cigarette smoking
  - Alcohol overuse
  - Physical inactivity
and interventions that should be used during inpatient rehabilitation for the secondary prevention of the most common subtypes of ischemic and hemorrhagic strokes.

**General Medical Risk Factor Management**

**Hypertension**, which is defined as a systolic blood pressure (BP) greater than or equal to 140 mmHg or diastolic BP greater than or equal to 90 mmHg affects approximately 72 million Americans (112) and is the most important cause of both ischemic and hemorrhagic stroke (113). There is a 30% to 40% reduction in the risk for stroke with adequate BP reduction in hypertensive patients (111). Hypertension may be controlled by both pharmacologic and behavioral interventions. BP should be lowered to less than 140/90 mmHg in all patients with stroke and to less than 130/80 mmHg if anti-hypertensive treatment is well tolerated (114). An average BP reduction of 10 mmHg in the systolic BP and 5 mmHg in the diastolic BP has been associated with less recurrent strokes and other cardiovascular events (111). The optimal drug regimen to achieve the recommended level of BP reduction may vary, but diuretics or the combination of diuretics and angiotensin converting enzyme inhibitors have been shown to be useful (111). Behavioral interventions may include the encouragement of weight loss, salt restriction, a diet rich in fruits, vegetables, and low fat dairy products, regular aerobic exercise, and limited alcohol use (115). Inpatient rehabilitation recommendations for BP management in stroke patients for the secondary prevention of stroke or other cardiovascular events are summarized in Table 4.7.

**Diabetes** is a risk factor for stroke and recurrent stroke (111). The prevalence of diabetes in ischemic stroke patients is 15% to 33% (111,116). Type 2 diabetes is almost always associated with insulin resistance. Insulin resistance, a subnormal

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**TABLE 4.7 Inpatient Rehabilitation Blood Pressure (BP) Management Summary**

- BP reduction benefits extend to stroke patients with and without a documented history of hypertension
- Benefits have been associated with an average BP reduction of 10/5 mmHg
- BP should be lowered to <140/90 mmHg in all stroke patients
- Behavioral modifications may include patient education regarding:
  - salt restriction
  - weight loss to achieve ideal body weight
  - diet rich in fruit, vegetables, and low fat dairy products
  - regular aerobic exercise
  - limited, if any, alcohol consumption
- Diuretics or the combination of diuretics and angiotensin converting enzyme inhibitors are useful in BP control; other drugs for optimal BP reduction should be individualized

Adapted from Refs. (111,114).
metabolic response to insulin, often occurs in association with dyslipidemia, hypertension, and abdominal obesity, all of which are risk factors for atherosclerosis, stroke, and cardiovascular disease. The metabolic syndrome is a name given to a prediabetic condition in which there is insulin resistance, hypertriglyceridemia, low HDL-C, hypertension, hyperglycemia with fasting glucose >100 mg/dL, and abdominal obesity; and this condition is present in 40% to 50% ischemic stroke patients (111). Diet, exercise, weight loss, and oral hypoglycemic drugs that enhance insulin sensitivity are useful treatments for the metabolic syndrome; and these treatments in addition to insulin are recommended for diabetes (111,117). A hemoglobin A1c >7% is defined as inadequate control of hyperglycemia. Table 4.8 summarizes inpatient rehabilitation recommendations for the management of diabetes to minimize the risks for a recurrent stroke.

Hyperlipidemia, including elevated total cholesterol or low-density lipoprotein cholesterol (LDL-C), is associated with increased risk for ischemic stroke and particularly large vessel atherosclerotic stroke (111). Risk for stroke and other cardiovascular diseases is reduced by strategies that lower LDL-C blood levels (111,118). These strategies should include lifestyle modifications such as a reduction in saturated fat and cholesterol intake, exercise, weight loss to an ideal body weight, and medications. Medications to lower total cholesterol and LDL-C may include statins, niacin, fibrates, and cholesterol absorption inhibitors. Statin therapy is associated with a significant reduction in recurrent strokes (119). Table 4.8 summarizes the inpatient rehabilitation recommendations for the management of hyperlipidemia to prevent a secondary stroke.

Physical inactivity, obesity, alcohol overuse/abuse, and cigarette smoking are all risk factors for both ischemic and hemorrhagic strokes. Stroke patients need to be educated regarding these risk factors during inpatient rehabilitation to prevent further strokes. Exercise tends to lower BP and body weight, improve glucose tolerance, and promote cardiovascular health (111). Moderate exercise, which is defined as 30 minutes of physical activity sufficient to raise heart rate and cause sweating 1 to 3 times a week may reduce the risk for stroke by 20% (111). Since stroke predisposes patients to physical inactivity because of the neurologic impairments and disabilities, the challenge during inpatient rehabilitation is for the clinicians (physician and therapists) to devise an exercise program sufficient for secondary stroke prevention. Obesity, which is defined as a body mass index >30 kg/m², is associated with physical inactivity and is an independent risk factor for cardiovascular disease, and an indirect risk factor for stroke. Patients with a history of alcohol overuse or alcoholism should be advised that there is clear evidence that it is associated with an increased risk for further strokes of all types both ischemic and hemorrhagic (111,113). Similarly cigarette smoking is also associated with a risk for both ischemic and hemorrhagic strokes (111,120,121). Smoking may also have a synergistic effect with hypertension in increasing the risk for subarachnoid hemorrhage in persons with cerebrovascular
TABLE 4.8 Inpatient Rehabilitation Management for Diabetes, Hyperlipidemia, and Modifiable Behaviors

- Diabetic management with goal of normoglycemia and hemoglobin A1c of 7 or less
- Low-density lipoprotein cholesterol target level <70 mg/dL, if possible
- Total cholesterol management per existing guidelines
- Low levels of high-density lipoprotein cholesterol may be managed with niacin or gemfibrozole
- Educate on importance of exercise; develop appropriate exercise program for each stroke patient
- Educate regarding cigarette smoking cessation; consider use of smoking cessation medications
- Educate on dangers of heavy alcohol consumption
- Educate on appropriate dietary modifications based on patient’s clinical history; target weight loss to ideal body weight

aneurysms (122). Table 4.8 summarizes patient lifestyle modification interventions, including education that should be undertaken during inpatient rehabilitation for secondary stroke prevention.

Prevention of Cardio-Embolic Secondary Stroke

Approximately 20% of ischemic strokes are because of cardiogenic cerebral embolism resulting from nonvalvular atrial fibrillation (AF) in one-half the cases, valvular heart disease in one-fourth, and a left ventricle mural thrombus in one-third (111). Persistent and paroxysmal AF are associated with a 4.5% annual rate of new and recurrent strokes resulting in approximately 75,000 cases of stroke in the United States each year (111,123,124). Multiple clinical trials have shown the superiority of vitamin-K antagonists, such as warfarin, when compared to aspirin or the combination of aspirin and clopidogrel for the prevention of stroke in AF (111,124,125). Recent studies suggest that the direct thrombin inhibitor dabigatran may be superior to warfarin for stroke prevention in AF and causes no increase in major bleeding (123–125). All stroke patients having AF, unless otherwise contraindicated, should be on anticoagulation treatment throughout inpatient rehabilitation to prevent further strokes. Similarly, anticoagulation is recommended throughout inpatient rehabilitation for the secondary prevention of stroke in patients with a recent history of anterior myocardial infarction or infarct involving the left ventricle apex as there is a 10% risk for cardioembolic stroke in these patients from left ventricle thrombus formation (111). Approximately 10% of patients having cardiomyopathy or congestive heart failure with a left ventricle...
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TABLE 4.9 Medical Conditions for Which Anticoagulation Is Indicated for Secondary Stroke Prevention

- Nonvalvular persistent or paroxysmal atrial fibrillation
- Recent myocardial infarction and known left ventricle mural thrombus
- Rheumatic mitral valve disease
- Mechanical or bio-prosthetic heart valves

Prevention of Ischemic Noncardioembolic Stroke

Antiplatelet treatment is more effective than anticoagulation for the prevention of first and secondary ischemic noncardioembolic strokes, including atherosclerotic, lacunar, and cryptogenic infarctions (111,126,127). Aspirin, combination aspirin with dipyridamole, clopidogrel, and ticlopidine on average reduce cardiovascular events, including stroke by about 22%, and all have been approved by the FDA for this purpose for use in patients with transient ischemic attacks or stroke (111,126,127). A number of issues should be considered in the selection of an antiplatelet agent. There is clear evidence from clinical trials that aspirin, ticlopidine, and the combination of aspirin with dipyridamole are each significantly more effective than placebo for secondary stroke prevention (111,126,127). Currently there are no studies comparing the efficacy of clopidogrel with a placebo; and studies comparing it to other antiplatelet agents have not established superiority or clear equivalency (111,126,127). The combination of
aspirin with dipyridamole may be more effective than aspirin alone for secondary prevention of stroke with less risk for bleeding complications (111,126,127). Ticlopidine may also be more effective than aspirin for secondary stroke prevention, but its usefulness is limited by safety concerns regarding the potential for neutropenia and thrombotic thrombocytopenia purpura (111). Clopidogrel therapy may involve less risk for gastrointestinal bleeding and other major bleeding complications than aspirin or the aspirin with dipyridamole combination (111,126,127). Clopidogrel is also useful as stroke prophylaxis in patients allergic to aspirin. The addition of aspirin to clopidogrel increases the risk for major hemorrhages, including life-threatening intracerebral and gastrointestinal bleeds and, therefore, should be avoided (111,126). In patients who have an ischemic stroke while already on aspirin prophylaxis, there is no evidence that increasing the dose provides additional benefit.

**SUMMARY**

There are multiple potential poststroke medical complications that may occur during inpatient rehabilitation as discussed in this chapter. These complications may all have a negative impact on a patient’s long-term functional outcome. Proper prevention and management of these possible problems during inpatient rehabilitation is critical because the greatest degree of poststroke functional recovery may occur in the first poststroke month (4) and any medical complications during this time frame will limit a patient’s overall recovery.

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**TABLE 4.10 Antithrombotic Therapy Recommendations for Noncardioembolic Ischemic Stroke**

- Antiplatelet agents rather than oral anticoagulation is advised
- Initial monotherapy using aspirin, combination of aspirin with dipyridamole or clopidogrel advised
- The addition of aspirin to clopidogrel is not advised because of increased risk for bleeding
- In patients allergic to aspirin clopidogrel is an alternative therapeutic option
- In patients having ischemic stroke while on aspirin there is no evidence that increasing the dose provides additional benefit

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## Complication Timeline for Stroke

<table>
<thead>
<tr>
<th>Complication</th>
<th>Onset of Complication</th>
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<tbody>
<tr>
<td></td>
<td>Early/Acute</td>
</tr>
<tr>
<td>Dehydration/malnutrition</td>
<td>X</td>
</tr>
<tr>
<td>Bladder/bowel dysfunction</td>
<td>X</td>
</tr>
<tr>
<td>Insomnia/impaired sleep</td>
<td>X</td>
</tr>
<tr>
<td>Aspiration pneumonia</td>
<td>X</td>
</tr>
<tr>
<td>Venous thromboembolism</td>
<td>X</td>
</tr>
<tr>
<td>Joint contractures</td>
<td>X</td>
</tr>
<tr>
<td>Poststroke pain syndromes</td>
<td>X</td>
</tr>
<tr>
<td>Poststroke affective disorders</td>
<td>X</td>
</tr>
<tr>
<td>Secondary stroke</td>
<td>X</td>
</tr>
</tbody>
</table>

## REFERENCES


I. MEDICAL COMPLICATIONS


EPIDEMIOLOGY OF TRAUMATIC BRAIN INJURY

Although the definition of traumatic brain injury (TBI), and its specific inclusion criteria, may vary from specialty to specialty, the definition agreed upon by a working group of the International and Interagency Initiative for Research on Traumatic Brain Injury is “an alteration in brain function, or other evidence of brain pathology, caused by an external force” (1). According to this expert panel, diagnosis of TBI must include at least one of the following: (a) loss of memory for events just before or after the injury; (b) loss or decreased level of consciousness, and/or (c) the presence of neurologic deficits (e.g., loss of balance, sensory alterations, paralysis) (1). The severity of TBI is typically assessed using the Glasgow Coma Scale (2), which includes assessments of eye opening, verbal response, and motor response, and uses a graded scale with defined ranges for mild, moderate, and severe brain injury.

According to TBI data from the Centers for Disease Control from 2002 to 2006, more than 1.7 million people sustain a TBI each year in the United States, which leads to approximately 1.4 million emergency room visits and 275,000 hospitalizations annually (3). Young children (0–4 years), adolescents (15–19 years), and older adults (75+ years) are the most likely groups to sustain a TBI, with males sustaining more TBIs across all age groups and an overall prevalence that is approximately 1.4 times that of females. Rates of hospitalization and death for adults over 65 (34% and 6%, respectively) are almost double that for average rates across all other age groups (approximately 16% for hospitalization, and 3% for death) (3). The TBI Model Systems National Database Statistical Center reported in 2011 that, among their sample of 7749 patients who visited an emergency department due to TBI, 38% sustained a mild injury, 16% a moderate injury, and 46% a severe injury, according to Glasgow Coma Scale scores at admission (4).

Although TBI is often thought of as an injury “event,” the consequences of the event frequently result in life-long treatment and rehabilitation efforts. It is estimated that 43% of people who are discharged with TBI from acute hospitalization will have
long-term disability because of their injury (5). Some have proposed that TBI be considered a “chronic disease process,” with ongoing consequences to multiple organ systems that can ultimately contribute to death years after the initial injury (6).

ETIOLOGY OF TBI

The most common external causes of TBI are falls, motor vehicle accidents (pedestrian and nonpedestrian), and assaults, which account for approximately 23%, 21%, and 6%, respectively, of hospitalizations due to TBI in the United States (3). Falls account for approximately 42% of TBI hospitalizations in children less than 4 years old, 37% of TBI hospitalizations for adults over 75 years old, while motor vehicle accidents are the most frequent cause of TBI hospitalizations in adolescents and young adults between the ages of 15 and 35 (approximately 35%) (3). Recently, TBIs due to blast injuries and other combat-related causes have become more common as a result of incidents involving U.S. troops serving in the Iraq and the Afghanistan conflicts.

Deficits resulting from a TBI can be caused both by the focal damage that occurs when the head collides with an object and the diffuse damage that can occur with either direct head collision or with acceleration and deceleration of the brain inside the skull (with or without physical contact). In addition to the damage that occurs at the time of the injury, progressive secondary damage is also thought to contribute to the long-term outcomes after a TBI (6).

Several mechanisms may contribute to the immediate brain damage that accompanies a head injury, including mechanical tissue destruction, cell death, release of excitotoxic molecules, and intracranial hemorrhages (7). Extensive, wide-spread damage to the white matter of the brain, referred to as diffuse axonal injury, is not only because of the immediate mechanical strains of acceleration and deceleration on brain tissue, but also because of secondary mechanisms, including changes in cerebral blood flow and cerebral hypoxia (7,8). The extent of white matter injury has been shown to continue to progress in the frontal and temporal lobes in research subjects whose brain imaging results were compared at 4.5 months and 29 months postinjury (9). This diffuse axonal injury is thought to be a major contributor to many of the chronic conditions that are prevalent after TBI (eg, cognitive decline, motor and sensory disorders, and psychiatric conditions) (10).

Centrally important to the care of a patient with TBI, both during the acute phase and during chronic follow-up, is the recognition that many interrelated systems may be affected by the injury. This chapter identifies the most common complications and comorbidities after TBI, and the most current recommended evaluations and treatments of these conditions. The evaluation of, and treatment decisions made for, each complication encountered in this patient population should include consideration of
the potential effects that procedures and treatments used for one condition may have on other conditions that are also present.

AGITATION

Agitation has been described as one or more repetitive, nonpurposeful and inappropriate verbal and/or motor behaviors, including some combination of aggression, akathisia, disinhibition, and emotional lability. It is the most frequently observed behavioral problem seen following TBI.

Epidemiology

Agitation has been reported in approximately 11% to 96% of patients in the acute phase following TBI and approximately 30% to 70% in the chronic stage (11,12). It has been suggested by many authors that the major period for the onset of agitation is from the first 24 hours to a week after emerging from a coma (13–15). It is often the first symptom exhibited at the posttraumatic amnesia (PTA) phase during acute rehabilitation. Agitation presents with multiple challenges during rehabilitation and is often one of the leading causes for increased length of stay, decreased return rate to previous home environment, and disruption/dissolution of family units.

Pathophysiology/Etiology

Damage to the temporal lobe of the brain often results in memory and attention deficits, while frontal lobe injury often results in loss of executive function. With such injuries, the individual’s decreased cognitive ability can lead to internal frustration. The individual may have difficulty recognizing environmental stimuli, which results in a lowered stress threshold, eventually leading to agitated behavior. This may also be seen because of internal stressors such as pain and fatigue.

Assessment and Treatment

The treatment of agitation requires a multidisciplinary and comprehensive approach. The first step should be to exclude any potential medical complications or issues that may be causing the behavior. The treatment should include thorough assessment and documentation of the behavior, which may be facilitated by using appropriate scales such as the Agitation Behavior Scale (13). Consideration should be given as to how best to maximize the patient’s ability to participate in rehabilitation with the least amount
of disruption. The first step should be to omit excessive external environmental stimuli. This would include creating a quiet environment, limiting the number of visitors, and maintaining a consistent treating team (therapists, nurses, and medical assistants). Research has demonstrated that cognitively-impaired TBI patients are less agitated in a more familiar environment than in a strange environment with new people (16).

Although behavioral therapy does not have firm evidence of efficacy in the treatment of agitation symptoms, it should still be considered, as detrimental side effects of pharmacological interventions may be more harmful than untreated agitation symptoms. Medication-induced drowsiness can interrupt patient participation in therapy (17,18). Potentially-useful behavioral therapies include environmental intervention, such as offering a private room and prohibiting TV watching, which has been documented to effectively reduce agitated behavior (19). Physical restraints are often used as a safety measure for the patient to prevent harm to themselves as well as others; however, their use has been discouraged for agitated patients because they might increase agitation and cause additional injuries (18,20).

Pharmacological treatment may be helpful in reducing agitated behavior, but such approaches must be monitored closely as many of these medications have cognitive side effects, including sedation. Table 5.1 includes a list of the most-commonly used pharmacological agents for agitation.

POSTTRAUMATIC SEIZURES

Posttraumatic seizures (PTS) are single or recurrent seizure episodes occurring after a TBI. They are classified into immediate, early, and late seizures, with immediate seizures occurring within 24 hours, early occurring within the first seven days, and late occurring after the first week following injury (21). PTS can have a negative effect on patient recovery following TBI and can increase morbidity and mortality. TBIs account for 20% of symptomatic epilepsy observed in the general population and 5% of all epilepsy (21). It is the leading cause of epilepsy in young adults.

Epidemiology

The onset of PTSs following TBI has been described as bimodal, with the highest incidence occurring during the first week postinjury, and a second peak occurring at about 6 months postinjury (22). The incidence of early PTS in nonpenetrating TBI has been reported to be approximately 5% (21). Penetrating trauma, severe injury, depressed skull fracture, and intracranial hematoma increase the risk of early seizure development. All types of seizures may occur as a result of trauma, but the most frequent are focal or partial complex seizures. Generalized complex seizures (what are commonly called “grand mal” seizures) occur in approximately 33% of people with TBI (23).
### TABLE 5.1 Medications for Agitation in TBI

<table>
<thead>
<tr>
<th>Medication</th>
<th>Mechanism of Action</th>
<th>Side Effects</th>
<th>Suggested Doses</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antipsychotic 1st Generation</strong></td>
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<td></td>
</tr>
<tr>
<td>Haldol</td>
<td>Affinity for blocking D2 dopamine receptor</td>
<td>EPS, galactorrhea, malignant epileptic syndrome</td>
<td>2 to 15 mg/day</td>
</tr>
<tr>
<td><strong>Atypical Antipsychotics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clozapine</td>
<td>5-Ht2 receptor antagonist, selectively antagonizes dopamine D1 and D4 receptors</td>
<td>May increase seizure incidence</td>
<td>12.5 to 600 mg/day</td>
</tr>
<tr>
<td>Risperidone</td>
<td>5-Ht2 receptor antagonist, selectively antagonizes dopamine D2 receptors</td>
<td>High D2 and alpha 1 affinity—may increase risk of orthostatic hypotension</td>
<td>2 to 6 mg/day</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>5-Ht2 receptor antagonist, selectively antagonizes dopamine D2 receptors</td>
<td>Highly sedative</td>
<td>25 mg bid up to 750 mg/day</td>
</tr>
<tr>
<td>Ziprasidone</td>
<td>5-Ht2 receptor antagonist, selectively antagonizes dopamine D2 receptors</td>
<td>Potential to cause QT prolongation, more favorable side effect profile</td>
<td>20 mg bid up to 80 mg bid</td>
</tr>
<tr>
<td>Aripiprazole</td>
<td>Partially agonizes dopamine D2 and serotonin 5-Ht1A receptors, antagonizes serotonin 5-Ht2A receptors</td>
<td>Low incidence of weight gain, EPS, and diabetes</td>
<td>10 mg daily up to 30 mg/day</td>
</tr>
<tr>
<td>Olanzapine</td>
<td>5-Ht2 receptor antagonist, selectively antagonizes dopamine D2 receptors</td>
<td>Severe weight gain, hyperlipidemia and diabetes</td>
<td>5 mg/day up to 10 mg/day</td>
</tr>
<tr>
<td><strong>Antiepileptics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Valproic acid</td>
<td>Inhibit glutamate/NMDA</td>
<td>Hepatotoxicity, thrombocytopenia, medicine toxicity</td>
<td>750 to 1000 mg/day</td>
</tr>
<tr>
<td>Carbamezepine</td>
<td>Exact mechanism unknown</td>
<td>Hyponatremia, renal failure, aplastic anemia</td>
<td>200 mg/day increased to a maximum dose of 400 to 800 mg/day</td>
</tr>
</tbody>
</table>

(continued)
TABLE 5.1 Medications for Agitation in TBI (continued)

<table>
<thead>
<tr>
<th>Medication</th>
<th>Mechanism of Action</th>
<th>Side Effects</th>
<th>Suggested Doses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Divalproex sodium</td>
<td>Increases GABA effects, may inhibit glutamate/NMDA mediated neuronal excitation</td>
<td>May interfere with cognitive function, excessive sedation</td>
<td>250 mg tid up to 500 mg tid</td>
</tr>
<tr>
<td>Antidepressants</td>
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<tr>
<td>Tricyclics (Amitriptyline)</td>
<td>Greater affinity for serotonergic receptors</td>
<td>Sedative, potential cardiac effects, potential reduction of seizure threshold</td>
<td>25 mg/day increased to maximum dose of 150 mg/day</td>
</tr>
<tr>
<td>Selective serotonin reuptake inhibitors (Sertraline)</td>
<td>Selectively inhibit seroton reuptake</td>
<td>Less effect on seizure threshold</td>
<td>25 to 200 mg/day</td>
</tr>
<tr>
<td>Beta Blockers</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Propranolol</td>
<td>Nonselectively antagonizes beta-1 and beta-2 adrenergic receptors</td>
<td>Bradycardia, hypotension, depression, fatigue</td>
<td>Up to 200 mg/day</td>
</tr>
<tr>
<td>Neurostimulants</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bromocriptine</td>
<td>Stimulates dopamine receptors, inhibits anterior pituitary prolaction secretion</td>
<td>Seizures, headache, fatigue, orthostatic hypotension</td>
<td>10 to 30 mg tid</td>
</tr>
<tr>
<td>Amantadine</td>
<td>Potentiates CNS dopaminergic responses</td>
<td>Somnolence, orthostatic hypotension</td>
<td>100 mg up to 100 mg qid</td>
</tr>
<tr>
<td>Methylphenidate</td>
<td>Blocks reuptake and increases release of norepinephrine and dopamine in extraneuronal space</td>
<td>Motor tics, insomnia, tachycardia, nausea</td>
<td>5 to 15 mg tid</td>
</tr>
</tbody>
</table>

EPS, extrapyramidal symptoms; GABA, gamma-aminobutyric acid; Ht, hydroxytryptophan; NMDA, N-methyl-D-aspartate.

Incidence of late seizures in hospitalized patients has been reported to be 5% to 18% (23). Associated risk factors that increase a patient’s susceptibility to late seizures include chronic alcoholism, older age, and a history of seizure disorder. Patients who suffer one late onset seizure are 50% more likely to suffer an additional seizure (24). About half the patients who develop late PTS have three or fewer seizures and go into spontaneous remission thereafter (24). The risk of PTS decreases with time and reaches normal incidence for the population at five years after the head injury.
Pathophysiology

The mechanism by which TBI leads to seizures is unknown. It is postulated that cortical lesions may be attributed to epileptic activity. The “kindling model” of epilepsy is the most recognizable animal model of epileptogenesis (25). It was first proposed in the late 1960s by Goddard and colleagues. The kindling model suggests that repeated stimulation “lowers the threshold” for more seizures to occur (26). The model refers to a phenomenon whereby the brain region can be rendered permanently epileptic when subjected to brief, repeated electrical stimulations that, alone, would not normally induce behavioral seizures (25). Although its applicability to human epilepsy remains controversial, it is used by scientists to study the effects of repeated seizures on the brain (25).

Treatment

Clinical trials and literature reviews provide current guidelines on seizure prevention. Although there is evidence that seizure prophylaxis reduces the incidence of early PTS (27), there is no evidence that the antiepileptic drug (AED) prophylaxis of early seizures can also reduce the occurrence of late seizures, death, or neurological disability (27).

Current practice parameters regarding AED prophylaxis have been published by groups, including the American Academy of Neurology (AAN) (28). For adult patients with severe TBI, treatment with phenytoin, beginning with an IV loading dose of 10 to 20 mg/kg divided into 3 doses 2 to 4 hours apart, should be initiated as soon as possible after injury to decrease the risk of posttraumatic seizures occurring within the first 7 days (28). The literature does not support the routine use of prophylactic treatment with phenytoin, carbamazepine, or valproate beyond the first 7 days after injury to decrease the risk of subsequent posttraumatic seizures (29).

POSTTRAUMATIC HYDROCEPHALUS

Posttraumatic hydrocephalus (PTH) is an active and progressive process of excessive cerebrospinal fluid (CSF) accumulation as a result of liquorodynamic disturbances following TBI (30). PTH commonly occurs in the first year post trauma and has been described as early as within 7 hours of injury (31).

Epidemiology

The reported incidence of PTH varies from 0.7% to 86% (30). This reported wide variability is in part to the result of the under diagnosis and atypical presentation of PTH, as well as the use of different sets of clinical criteria for diagnosis of PTH. Recognition
of PTH is often confounded by symptoms attributable to the primary or secondary traumatic injury inflicted upon the brain. In many cases, initial brain damage leading to cerebral atrophy with secondary ventriculomegaly (hydrocephalus ex-vacuo) can give a false impression of PTH.

PTH may present with various clinical symptoms, including obtundation, failure to improve, psychomotor retardation, memory loss, gait ataxia, and incontinence (31). In one study, patients presented with various combinations of clinical features after 65 ± 38 days (mean ± SD) of initial injury. Decrease in Glasgow Coma Scale, found in 58% of cases in this study, was the most common presentation (32). Longer duration of coma, increased age, decompressive craniectomy, and subarachnoid hemorrhage (SAH) have also been reported to increase the risk of developing PTH (30).

Pathophysiology

PTH results from an imbalance between CSF production and absorption, which may be because of a combination of pathophysiologic factors. These include excess production of CSF, obstruction of normal CSF outflow, and impaired absorption of CSF. It may present with or without an increase in intracranial pressure as is seen in normal pressure hydrocephalus. Increased intracranial pressure caused by obstruction leads to ventricular enlargement and hemispheric expansion. Conversely, in communicating hydrocephalus (also referred to as nonobstructive hydrocephalus), full communication between the ventricles and the subarachnoid space exists. Impaired CSF absorption and excess production may cause communicating hydrocephalus. The apparent mechanism is partial occlusion of the arachnoid villi, perhaps by blood and inflammatory mediators. Severe skull fractures, hemorrhage, and meningitis may predispose patients to this variant of PTH (33). SAH has been cited as the most important condition leading to PTH (34).

Decompressive craniectomy has been associated with development of PTH (30). Waziri et al (35), described the pathophysiology of PTH, related to the function of the arachnoid granulation, which function as pressure-dependent one-way valves from the subarachnoid space to draining venous sinuses. Following decompressive craniectomy, there is disruption of pulsatile intracranial pressure dynamics resulting in decreased CSF outflow.

Treatment

Clinical suspicion and evaluation are key to early diagnosis and management. Other conditions, such as infection, seizure disorder, encephalopathy, and metabolic disorders, must be ruled out. Initial diagnostic evaluation should include a CT scan, and, if there is suspicion, immediate neurosurgical consultation.
Shunting is the most common procedure performed for hydrocephalus. Many articles have attempted to describe predictive tests for selecting the most appropriate shunt candidates. Marmarou et al (36) showed that CSF dynamics may help formulate the diagnosis of PTH and identify patients who may benefit from shunt placement. These authors suggested that shunting procedures could improve outcome in the case of normal intracranial pressure and increased resistance to CSF outflow (36). The criteria for selecting patients for shunt surgery in the post acute phase are not defined and are a source of debate (37). At present, clinical investigation and neurosurgical guidance are recommended.

**AUTONOMIC STORMING**

Autonomic storming, also known as sympathetic storming, is a stress response that can occur after severe TBI. The precise mechanism for the increase of activity in the sympathetic nervous system is unknown (38). It has been described as an increase in activity in the sympathetic nervous system created by a disassociation or loss of balance between the sympathetic and parasympathetic nervous systems (39).

**Epidemiology**

Autonomic storming has been documented in the literature to occur in 15% to 33% of patients with severe TBI who are comatose. This increased sympathetic response is thought to be a stage of recovery from severe TBI (38). Autonomic storming can occur within the first 24 hours after injury and up to weeks later (40). This phenomenon has also been described as dysautonomia, paroxysmal autonomic instability, autonomic dysfunction syndrome, and diencephalic seizures (41).

**Pathophysiology**

The specific mechanisms that have been theorized to lead to autonomic storming include disruption of the relay mechanism, loss of cortical control, and dysregulation of autonomic balance. The autonomic system is comprised of both sympathetic and parasympathetic pathways. The sympathetic pathway conveys an excitatory or inhibitory response provoked by adrenergic receptor interaction. The parasympathetic nervous system normally works to dampen the effect of increased activity in the sympathetic nervous system, allowing homeostasis. In autonomic storming, however, this feedback mechanism does not occur and the body remains in a heightened response state.

Clinically, patients with autonomic storming may present with hyperthermia, tachycardia, tachypnea, diaphoresis, posturing, dystonia, hypertension, and signs of
agitation. Baguley et al (42) suggest that autonomic storming generally has three different phases. During phase 1, which lasts about one week, patients are symptomatic while sedated or receiving paralytic agents. In phase 2, the period of episodes of autonomic storming continue after sedation is discontinued, with a mean duration of 74 days after injury. The end of phase 2 is defined by the cessation of diaphoresis. In phase 3, no further episodes of persistent dystonia or spasms occur, though hyperthermia, tachycardia, tachypnea, hypertension, or signs of agitation continue.

Autonomic storming may also occur after a trigger or noxious stimulus. Examples include suctioning, environmental sensory stimulation, and repositioning. If one is able to clinically identify such responses then pretreatment may be initiated to help reduce that response.

Autonomic storming has been thought by many to be a diagnosis of exclusion. Blackman et al (43) required that signs and symptoms occur at a minimum of one cycle per day for three consecutive days in a patient with severe brain injury. The diagnosis is generally made through clinical evaluation, although elevated serum levels of epinephrine and catecholamines can be used to confirm suspicions.

Treatment

Autonomic storming left untreated can result in secondary brain injury and have a negative impact on brain recovery. Prolonged excitation of the sympathetic system can lead to an elevated metabolic rate and increase demand on vital organs, including the brain. This can ultimately lead to decreased cerebral perfusion. Hypertension and arrhythmias are sequelae associated with storming episodes. Prolonged hypertension increases the risk of secondary injury of the brain because of increased blood flow leading to edema, risk of rebleeding, and potential cardiac dysfunction related to prolonged stress on the heart (39).

Treatment should initially focus on finding the cause of autonomic storming, including identifying and removing any potentially noxious stimulus. By treating the cause, sympathetic excitation ceases. If no causal factors are found, treatment should consist of regulating the sympathetic response. This can be accomplished with antihypertensives such as beta blockers, alpha blockers, and calcium channel blockers. Recent evidence suggests that GABAergic medications such as gabapentin may be beneficial in the management of autonomic storming (42).

METABOLIC AND ENDOCRINE DISRUPTION FOLLOWING TBI

Endocrine complications have been of great concern following TBI. A number of metabolic complications have been shown to result from TBI. With moderate and
severe TBI, the pituitary stalk, which is connected to the anterior pituitary and hypothalamus, is vulnerable to the effects of TBI, especially in patients with associated facial fractures, cranial nerve injuries, and autonomic storming. Endocrine complications can produce significant impact on the progress and outcome of TBI rehabilitation. Prompt diagnosis and treatment of endocrine complications following TBI facilitate the rehabilitation process of patients with TBI (44).

Epidemiology

Endocrine complications have been reported in the United States in approximately 30% to 50% of patients who survive TBI (45). In general, the frequency of occurrence of pituitary hormone abnormalities has not been found to be related to the severity of the trauma (46–48), although there have been reports of a positive relationship (49). The largest systematic review on hypothalamopituitary dysfunction following TBI and aneurysmal SAH summarizes 19 studies comprising 1,137 patients. This metaanalysis showed that the pooled prevalences of hypopituitarism in the chronic phase after TBI and SAH were 27% and 47%, respectively. However, there was a large variation in the prevalence of hormone deficiencies in the different studies, perhaps because of the different methods used for patient selection, study designs, and tests (50).

Pathophysiology

The most common endocrine complication after a TBI is the syndrome of inappropriate antidiuretic hormone (SIADH) that is often clinically detected during acute TBI. SIADH causes a dilutional hyponatremia secondary to inappropriate renal water conservation. The incidence of SIADH following TBI is reportedly as high as 33% (51). The most common endocrinopathies associated with hypopituitarism include hypogonadism, hypothyroidism, adrenal insufficiency, hyperprolactinemia, diabetes insipidus, and growth hormone (GH) deficiency.

Recently, more emphasis has been placed on neuroendocrine complications resulting from hypopituitarism. One such complication is deficiency in GH or gonadotropin-releasing hormone (GnRH), which is more prevalent than deficiencies of the thyroid stimulating hormone or adrenocorticotropic (52–54). Low GH secretion has been associated with behavioral symptoms and deficits in several cognitive domains (55). Low GH may also have a deleterious effect on the cardiovascular system and predispose patients to hyperlipidemia. Five retrospective studies have shown that the risk of premature death from cardiovascular disease is elevated in patients with GH deficiency (56).
Diagnosis and Treatment

Measurement of basal circulating hormone concentrations is generally considered an appropriate screening tool for identification of deficient thyroid function, hypogonadism, and prolactin and oxytocin deficiencies. Diagnosis of significant abnormalities of vasopressin secretion normally require confirmation by measures of plasma and/or urine osmolality, urine specific gravity, and/or the administration of a water deprivation test. Although provocative testing is generally considered necessary for diagnosis of SIADH and GHD, measurement of basal cortisol and insulin-like growth factor 1 (IGF-1) concentrations remains a valuable screening tool to identify individuals most likely to benefit from additional testing and clinical referral (50). Evaluation of clinical signs and symptoms, along with laboratory testing, are essential for definitive diagnoses in all cases.

Treatment of any metabolic derangement should first explore potential iatrogenic causes such as medications, including antipsychotics, antiepileptics, serotonergic, and dopaminergic medications that may be contributing to findings. Consultation with an endocrine specialist is extremely important to determine appropriate treatment. The consequences of undiagnosed and untreated pituitary hormone deficiencies are significant and include diminished quality of life, cognitive deficiencies, fatigue, sleep disturbance, sexual dysfunction, deleterious changes in metabolism and body composition, behavioral and psychiatric problems, and increased cardiovascular mortality. Because the sequelae of brain injury may mask the signs of hypopituitarism, the threshold for endocrine assessment should be low, and in cases of uncertainty, endocrine assessment should be performed at least once. Also, in patients with basal skull fractures, diffuse axonal injury, increased intracranial pressure, or prolonged intensive care unit stay, pituitary assessment should be considered (57). Many of the symptoms of pituitary hormone deficiency can be reversed or ameliorated with correct diagnosis and appropriate hormone replacement therapy.

UPPER MOTOR NEURON SYNDROME

Upper motor neuron syndrome (UMNS) is a term used to describe the motor control changes that occur in skeletal muscle after an upper motor neuron lesion. Spasticity is characterized by a velocity-dependent increase in tonic stretch reflexes (muscle tone) with exaggerated tendon jerks, resulting from hyperexcitability of the stretch reflex (58). Spasticity causes increased tightness of muscles of the body. This can include both upper and lower limb musculature. Common patterns seen include increased upper limb flexor tone and lower limb extensor tone.

There are a number of indirect and direct consequences of spasticity, which make assessment and treatment essential. Some of the direct consequences of spasticity include increased tone, decreased range of motion, involuntary movements, increased autonomic reflexes, muscle fatigue, increased caloric needs, and abnormal
bone stress. Some of the indirect consequences include mobility dysfunction, contracture, pain, abnormal bone growth, weight loss, bowel and bladder dysfunction, respiratory dysfunction, skin breakdown, and impaired social, psychological, and vocational development.

**Epidemiology**

There are a limited number of studies on the incidence and prevalence of spasticity. The actual incidence of spasticity depends on the cause of the upper motor neuron lesion. Of the available reports in the literature, the studied populations have been limited to spinal cord injury, multiple sclerosis, stroke, and cerebral palsy. Unfortunately, there are insufficient data on patients with TBI to provide an accurate estimate of the incidence and prevalence of spasticity among TBI survivors (59).

**Pathophysiology**

The complete pathophysiological mechanism of spasticity is not fully understood. It is thought that alterations in the balance inputs from reticulospinal and other descending pathways to the motor and interneuronal circuits of the spinal cord in the absence of an intact corticospinal system may produce the changes seen in muscle tone. Physiologic evidence suggests that interruption of reticulospinal projections is important in the genesis of spasticity (60). Damage to these higher cortical centers may result in UMNS. Such damage causes immediate consequences, such as paralysis, and delayed consequences may be responsible for both rearrangement of spinal activity and altered supraspinal activity, thus causing positive signs such as muscle overactivity.

**Diagnosis and Treatment**

The evaluation of spasticity involves identifying the clinical pattern of motor dysfunction and its source, assessing the patient’s ability to control muscles involved in the clinical problem, and identifying the role of muscle stiffness and contracture as it relates to the functional problem. The assessment of spasticity typically involves the assessment of volitional motor control and manual muscle testing. Along with this, scales specifically designed to describe increase in tone have been developed, which include the Ashworth Scale, The Modified Ashworth Scale (61), the Tardieu Scale (62), the Adductor Tone Rating Scale, and the Spasm Frequency Scale (63).

Treatment of spasticity requires a multidisciplinary approach and can be looked at in a stepwise fashion. The initial assessment should include what the objective of such treatment would be and how would it impact the patient’s function. Spasticity
may be treated for improvement of function, hygiene, caregiver support, cosmesis, or pain. Determining whether the spasticity is generalized or localized may help in treatment decisions as well. If generalized, oral agents may be used if tolerated; intrathecal methods may also be used if oral agents fail and are intolerable. If the spasticity is more localized, chemodenervation techniques applied to select muscles or nerves may be more advantageous to prevent some of the systemic adverse effects of oral or intrathecal agents. Incorporating physical therapeutic techniques may be useful as an adjuvant therapy to allow improved muscle relaxation.

**ACUTE AND CHRONIC PAIN**

Although the co-occurrence of acute and/or chronic pain and TBI is high, and the potential impact of persistent pain on rehabilitation efforts is great, there is relatively limited research regarding pain in persons with TBI. This is likely due to a number of factors, including the diversity of types of acute pain that are present after a TBI and the inability to obtain accurate self-report from many patients with TBI. Indeed, it has been recognized that certain types of pain may be obscured, and, therefore, go undiagnosed in patients with TBI, and that there is a clear need for research examining the special considerations necessary to identify and measure pain in the TBI population (64).

**Epidemiology**

Estimates of the prevalence of pain symptoms in the TBI population vary from 30% to 90% (65–69). This large range is likely due to differences in data collection methods, severity of TBIs, and types of pain studied. A recent study examining data from structured interviews of TBI patients at discharge and at 3-, 6-, and 12-months post injury reported that 44% of patients experienced headache before discharge, 71% of patients experienced headaches during the first year after injury, and 30% of those with headaches during the first year experienced them daily or several times a week (70). Although the head is the most commonly-reported area for pain in persons with TBI, other locations of pain occur in high frequency as well (neck/shoulder: 25%–27%; back: 17%–25%), and many postacute TBI patients have persistent pain in more than one body region (65,66).

It has been difficult to establish who may be most at risk for pain after a TBI. The prevalence of headache pain in TBI has been reported to be significantly higher in women than in men in two studies (70,71), but another study found no such difference (72). Reports regarding the incidence of chronic pain for persons with mild TBIs and those with moderate-to-severe TBIs also present conflicting findings (65,66,70).
Pathophysiology

A number of different types and locations of pain may be present in the acute time period after a TBI, which may be because of the brain injury itself affecting central pain processing mechanisms, and/or because of injuries to other areas of the body that also occurred during the traumatic event. Peripheral mechanisms of pain include the activation of high-threshold receptors (nociceptors) in the skin or viscera, which convey information about the noxious stimulus to the brain. In the typical scenario, this activation serves as a protective mechanism, but prolonged activation of these nociceptive pathways can lead to central sensitization and, potentially, a chronic pain condition. Central sensitization can account for reduced threshold for pain, increased responsiveness to noxious stimuli, and expanded receptive fields of neurons in the affected area (73).

In addition to the pain initiated by an external, peripheral stimulus, patients with TBI are susceptible to neuropathic pain conditions, which are a result of injury to the somatosensory nervous system (74). Damage to particular brain areas in the patient with TBI may directly result in central neuropathic pain, as is often seen in stroke patients (75), whereas damage to the trigeminal nerves from the head injury may result in peripheral neuropathic pain. A multitude of both peripheral and central pathophysiological changes can result after nerve injury, including changes in transmitter synthesis and signaling, changes in expression and kinetics of ion channels, peripheral and central axon growth, ectopic discharge, degeneration of inhibitory interneurons, and reorganization within cortical and sub-cortical structures (73,76–78).

Assessment

The Joint Commission on the Accreditation of Healthcare Organizations (JCAHO) requires that pain be assessed as the “fifth” vital sign (79). However, establishing whether a patient with TBI has pain and to what extent he or she is suffering due to pain is particularly difficult in those who have a limited capacity to communicate. Nevertheless, efforts must be made to minimize pain. It has been suggested that conditions known to normally induce pain (eg, surgical pain) be treated with analgesics as standard procedure, and that observed behaviors indicative of patient discomfort be used as surrogate assessments when the patient cannot communicate effectively (80). An analgesic trial may be used to assess whether the observed pain-like behavior is because of physical pain or to some other source of discomfort (eg, aggravation, anxiety).

For most patients undergoing rehabilitation after TBI, communication is possible. Caution must be exercised, however, when assessing the severity of self-reported pain in this population, as the value of these reports depends on the
ability of the patient to understand the pain assessment scale and use it accurately and reliably. Although published studies examining the validity of pain reports in persons with TBI are not currently available, research in elderly and demented patients have shown that cognitive impairment can significantly impact the utility of such self-report scales for assessing analgesic efficacy (81–83). Although assessing the severity of pain may not always be accurate in this group, given their potential cognitive difficulties, reports of pain should not be ignored and should be treated appropriately.

Evaluating the type of pain present is just as important as evaluating the severity of the pain. Because different types of pain are often due to different underlying mechanisms, it is imperative to determine the type(s) of pain (eg, neuropathic or nociceptive, central or peripheral) an individual has in order to make effective treatment decisions. This is just as true for persons with TBI as it is for the general population. However, evidence regarding the prevalence of different pain types is lacking in the TBI population. For example, until a relatively recent study by Ofek and Defrin (84), which examined the sensory abnormalities present in a case series of 15 TBI patients with central neuropathic pain, there were only three case reports documenting the existence of neuropathic pain in patients with TBIs (85–87), despite the common occurrence of this type of pain in the clinic (88).

Treatment

A review of the treatment protocols for all of the pain types that may be present in patients with TBI is beyond the scope of this chapter, but sufficient reviews are available in the literature (89,90). It is particularly important in this patient population that the selection of analgesic treatments be balanced with information regarding side effect profiles that may affect other comorbidities and potential interactions with other pharmacologic agents being administered.

Headache is the most frequent cause of pain reported after TBI (88). Although the International Headache Society classifies headaches after TBI as “posttraumatic headache,” there is a large variety of the types and etiologies of headache associated with TBI. Proper assessment of posttraumatic headache often yields diagnoses of tension-type, migraine, cervicogenic, or mixed migraine and tension-type headache, with the most common being tension-type (91). Depending on diagnosis, pharmacological treatments can range from nonsteroidal anti-inflammatory drugs (NSAIDs) or acetaminophen for mild-to-moderate tension-type headaches to opioids for severe headaches. Use of opioid medications should be limited and carefully monitored for potential side-effects (eg, constipation, decreased cognitive function, respiratory dysfunction) and possible interactions with other medications. Nonpharmacologic therapies (eg, cognitive-behavioral therapy, exercise) have also been shown to be
moderately effective for headache relief (92,93). More detailed reviews of treatment for TBI-related headaches are available in the literature (88,90,94).

Treatment of nonheadache pains, including nociceptive/musculoskeletal and neuropathic pain in other parts of the body, may include both pharmacologic and nonpharmacologic therapies. Ice, heat, and other topical treatments, as well as physical therapies may be particularly effective for nociceptive pains, while avoiding potential interactions with other treatment modalities. For the patient with TBI, these therapies should be introduced slowly, keeping in mind the cognitive and physical limitations that may be present (90). Spasticity, including hypertonia and dystonia, may also be a common source of pain after TBI. Treatment of spasticity often includes baclofen, which has been shown to reduce pain reports in some patient groups (95,96). However, baclofen lowers the seizure threshold and should be used with caution in those TBI patients at increased risk. Neuropathic pain, usually characterized as “burning” or “shocking” pain, which may have allodynic or hyperalgesic characteristics, has been treated somewhat effectively with anticonvulsants and antidepressants in other patient groups (97–99), and opioid therapy may also be considered (76,100). Given the effect that these agents can have on a variety of systems, dosage should be carefully titrated and side-effects should be closely monitored in patients with TBI.

RESPIRATORY COMPLICATIONS

Pulmonary complications are common after severe head injury. Incidences of sepsis and pneumonia have been reported to occur in 60% to 75% of TBI patients (101). There are a variety of different lung dysfunctions that may occur as a result of a head injury and are dependent on areas of the brain that have been affected (102). Neurogenic pulmonary edema (NPE) is a potential complication of a central nervous system (CNS) insult, such as intracranial hemorrhage, uncontrolled generalized seizures, head trauma, tumors, and neurosurgical procedures, and is believed to occur because of massive sympathetic discharge following a CNS event. Rincon et al (102) looked at national trends of Acute Respiratory Distress Syndrome/Acute Lung Injury (ARDS/ALI) in the United States after admission for TBI, with specific examination of its prevalence, risk factors, and effect on outcome by a retrospective cohort study of the Nationwide Inpatient Sample (NIS). Results from their study revealed that the prevalence of ARDS/ALI after TBI increased from 2% in 1988 to 22% in 2008. In-hospital complications such as sepsis, cardiovascular dysfunction, renal dysfunction, and hematological dysfunction, were found to be associated with ARDS/ALI after admission for TBI. Male sex, increased age, injury severity score greater than 25, and Glasgow Coma Scale score less than 8 have been reported as independent risk factors for the development of pneumonia (100).
I. MEDICAL COMPLICATIONS

DYSPHAGIA

The incidence of dysphagia has been reported as high as 61% in acute level 1 trauma centers (103). Dysphagia in TBI can be attributed to a combination of factors, including physiologic deficits of the swallowing mechanism, which may have been injured during the TBI event itself, and behavioral and cognitive deficits occurring as a result of the TBI. For many TBI patients, the severity of the cognitive-communicative deficits will determine the type of management program and its functional outcomes rather than the integrity of the physiological swallowing mechanism (104).

Complication Timeline for Traumatic Brain Injury

<table>
<thead>
<tr>
<th>Complication</th>
<th>Onset of Complication</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Early/Acute</td>
</tr>
<tr>
<td>Agitation</td>
<td>X</td>
</tr>
<tr>
<td>Seizures</td>
<td>X</td>
</tr>
<tr>
<td>Hydrocephalus</td>
<td>X</td>
</tr>
<tr>
<td>Autonomic storming</td>
<td>X</td>
</tr>
<tr>
<td>Metabolic and endocrine disruption</td>
<td>X</td>
</tr>
<tr>
<td>Upper motor neuron syndrome</td>
<td>X</td>
</tr>
<tr>
<td>Pain</td>
<td>X</td>
</tr>
<tr>
<td>Dysphagia</td>
<td>X</td>
</tr>
<tr>
<td>Respiratory complications</td>
<td>X</td>
</tr>
</tbody>
</table>

REFERENCES

1. MEDICAL COMPLICATIONS


Rehabilitation medicine deals with several common neurological entities in the acute inpatient setting, and in general, the purpose of the rehabilitation program should aim to restore or improve performance in activities of daily living, motor function, and gait. Other areas, such as cognition and mood, should also be addressed based on the initial interdisciplinary evaluation (1).

In this chapter, we divide the most common nontraumatic neurological disorders that the physiatrist manages in acute inpatient rehabilitation facilities into:

1. Central nervous system: Demyelinating diseases, movement disorders, encephalopathies, and anterior horn cell diseases.
2. Peripheral nervous system: Peripheral nerve disorders, neuromuscular junction syndromes, and myopathies.

Other entities such as traumatic brain injury and stroke will be discussed in different chapters.

CENTRAL NERVOUS SYSTEM: DEMYELINATING DISEASES

Multiple Sclerosis

Among entities affecting the white matter, multiple sclerosis (MS) is most frequently encountered in acute inpatient rehabilitation settings, and for all these pathologies, the evaluation and treatment goals would remain the same.

MS is the most common cause of nontraumatic disability affecting young adults in the northern hemisphere (1).

There are approximately 400,000 persons in the United States with MS, with the highest prevalence in the highest latitudes (2). Approximately 85% of patients have
either the relapsing-remitting form, the most common form, or one of the secondary progressive forms (2).

With respect to prognosis, it has been estimated that the median time until a cane is required to aid movement is 20 years from the time of symptom onset and 30 years until wheelchair use. Also, about two-thirds of persons with MS are unemployed mostly due to disability caused by the disease.

Medical management has affected tremendous advances in the past 10 years with modifying agents that either decrease the number and frequency of exacerbations or the severity of the disease.

Symptomatic treatment and rehabilitative strategies still continue to give significant benefit to patients with MS.

The evaluation of patients with MS admitted to a rehabilitation floor should be focused on deficits that can be addressed by the interdisciplinary team during the hospital stay (2).

Special consideration should be given to evidence of:

- fatigue
- balance and gait
- weakness, sensory deficits
- spasticity
- bladder/bowel problems
- depression and cognition
- pain
- speech and vision difficulties

The rehabilitation approach to a patient with MS should have clear goals agreed upon by the patient and family from the beginning of the program as this disease carries progressive difficulties to achieve satisfactory long-term rehabilitation outcomes.

Several studies have found that inpatient rehabilitation benefits function, mobility, and several aspects of quality of life (2). However, these benefits tend to be short term—thus, periodic admissions for rehabilitation could be needed—as well as continued outpatient and home-based exercise programs to optimize achievement of benefits and ensure a more sustained recovery.

Patients with MS should have an inpatient rehabilitation program with combined physical, occupational, and speech therapy to evaluate and manage major impairments such as spasticity, pain, fatigue, balance, abnormal gait, and dysarthria.

Neuropsychology is also important for patients with cognitive decline, as is advanced rehabilitative nursing to provide bladder and bowel training if needed (1).

Complications of MS patients in the acute rehabilitation setting are few and not different from those encountered in a general medicine ward. These complications can extend from deep vein thrombosis (DVT) in nonambulatory patients to fractures...
as a result of falls related to balance and weakness, and should be addressed and managed appropriately along with medical teams.

**Parkinson’s Disease**

Degenerative central nervous system movement disorders that are commonly encountered in the rehabilitation service include Parkinson’s disease, Huntington’s disease, hereditary ataxias, dystonias, and Tourette’s syndrome. Parkinson’s disease is, by far, the most common, affecting 1% to 2% of the population over 65 years of age (2).

Parkinson’s disease can manifest itself in multiple ways that can lead to disability (2). These patients have high prevalence of both obstructive and restricted pulmonary diseases, which can impact the performance of activities of daily living. The speech in patients with Parkinson’s disease is monotonous with low volume and poor articulation.

Other areas to be evaluated by the rehabilitation team to formulate a comprehensive inpatient program are: handwriting, gait, balance, mood, and autonomic function.

Specific exercises have not proven to be effective and are not agreed upon. Careful attention to safety is needed when prescribing aerobic exercises because Parkinson’s disease patients are at high risk for falls (2).

With respect to psychosocial and cognitive aspects, depression is common in Parkinson’s disease and has an impact on cognitive performance. Depression can be related to a deficit in serotonergic transmission or diminished levels of noradrenaline and dopamine.

Different techniques have been tested to improve mood and cognition, but individual necessities have to be considered when planning a psychological approach.

The ideal treatment team includes first a consultation with neurology to optimize pharmaceutical therapies while rehabilitation is ongoing.

A rehabilitation plan should address specific impairments, once an initial assessment has been done by the inpatient rehabilitation team.

Assistive devices can be utilized to improve the patient’s independence and safety. Wheeled walkers might have added benefit over standard walkers.

Education regarding the disease is always important to patients and families.

**Gait.** Patients with Parkinson’s disease tend to walk with a rigid pattern, reduced arm swing, and festination phenomenon in which the short steps become more rapid accompanied by additional trunk flexion. This stereotypic pattern of gait is because the pelvis and thorax rotate together in a block rather than in a normal reciprocal way (3).

The most commonly employed technique to improve this gait is the addition of external sensory cues that are timed with step initiation (3). Cues may be tactile, auditory, or visual modalities, and both single and multiple cues can be used.
Tremor is usually at rest and reduced by voluntary movement. Severe tremor can be addressed with medication as well as rehabilitative techniques, including both biofeedback and relaxation techniques.

Orthostatic hypotension may be the result of autonomic dysfunction, and a tilt table may be necessary in some patients with severe orthostasis. Pressure garment stockings and abdominal binders can also be used to mechanically control the drop of blood pressure. Use of medications such as salt tablets might be required.

Speech and swallowing. Speech deficits in these patients include hypophonia, stuttering, and palilalia (rapid and involuntary word repetition). The strategy most commonly used to treat dysarthria in PD is the phonatory-respiratory effort model or Lee Silverman voice treatment. This technique uses the “think loud, think shout” (1). For swallowing deficits, the videofluoroscopy swallowing study remains the gold standard for diagnosis of dysphagia. The three phases of swallowing: oral, pharyngeal, and postpharyngeal seem to be altered.

Techniques typically include: food of different consistency, chin-down positioning, oral-motor exercises, electromyography, biofeedback, and verbal prompting.

Encephalopathies

Few patients, after an encephalopathy insult, come to acute inpatient rehabilitation floors, most often due to their altered mental status that usually is a barrier to performance in therapy.

The main common etiologies are: viral, anoxic, metabolic, and toxic.

Given the prognosis, especially in those caused by virus or anoxic events, these patients often require a prolonged stay in the acute medical floors and should be periodically evaluated by the rehabilitation physicians to guide preventive strategies and facilitate their transfer to the acute rehabilitation floor, provided patients can participate actively with the therapy team (4).

Once such patients are on the rehabilitation floor, focusing on mental status is mandatory to optimize progress in therapy. Sometimes the use of psycho-stimulants such as methylphenidate or modafinil (Table 6.1) is warranted to help with attention and concentration (4).

Treatment should continue to focus on improving range of motion (ROM), strengthening, transfers, and gait if applicable.

<table>
<thead>
<tr>
<th>TABLE 6.1 Medications Used to Improve Attention and Concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amantadine</td>
</tr>
<tr>
<td>Methylphenidate</td>
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<tr>
<td>Modafinil</td>
</tr>
</tbody>
</table>
Cognitive rehabilitation provided by the team psychologist needs to be maintained.

Family training and recommendations on daily and constant supervision should also be provided as part of the program, especially in the case of patients who will be going home with family after discharge.

The most common medical complications that occur in the rehabilitation unit are: congestive heart failure, hypertension, and urinary tract infections (4), which usually do not impair the rehabilitation course if appropriately treated (4).

Motor Neuron Diseases

Polio and amyotrophic lateral sclerosis (ALS) are the main entities in this group that we should consider in inpatient rehabilitation (2).

The use of exercise in patients with neuromuscular disease is controversial because of the possible deleterious effect of exercise on muscle fibers, but data are inconclusive.

On the other hand, the goal of the rehabilitation treatment in these patients is to maximize functional independence through a carefully developed plan of exercises.

Sinaki and Mulder (2) describe six stages of ALS as a guide in formulating therapies and treatment.

During stage I, the patient is independent with respect to mobility and ADLs, therapy focuses on education to patient and caregiver as well as home safety and energy conservation techniques (2).

In stage II, the patient will present with moderate weakness and slightly decreased independence in mobility and ADLs. Usually, patients in this stage might benefit from bracing such as ankle-foot-orthoses and wrist supports (2).

Patient should continue with ROM and stretching techniques in all of the stages.

Patients in stage III of ALS are still ambulatory, but can present weakness in certain groups. Patients should be assessed for a wheelchair prescription (2).

Neck extensor weakness often starts to occur in this stage. A cervical collar should be considered for this situation.

Stage IV is characterized by severe lower extremity and mild upper extremity weakness. Patients will be exclusive wheelchair users (2).

Stages V and VI refer to patients that are dependent for all ADLs and require assistance at all times and will need cardiopulmonary techniques to maximize ventilatory perfusion (2).

Speech, swallowing, and respiratory therapies should be implemented as needed as well as bracing and psychological support.

Constant education to patients and caregivers on safety strategies and the use of equipment at home after discharge is also important.
PERIPHERAL NERVOUS SYSTEM

There are two main groups that potentially could be admitted in acute inpatient rehabilitation as a result of severe disabilities.

Neuropathies

Only a few neuropathies require inpatient rehabilitation. Guillain-Barré syndrome, an acquired demyelinating neuropathy is a good example.

Often these patients need respiratory support and may arrive at the rehabilitation floor on a ventilator.

Patients on ventilators in the rehabilitation services can be challenging and demand high level of medical care, but that should not interfere with a comprehensive rehabilitation program (2).

The main goal in treating this patient is to improve quality of life by the use of different techniques based on specific motor and sensory deficits.

The major medical complications are the same as for patients with prolonged immobility if their motor deficits are severe. They can present with DVT and develop skin infections due to minor trauma, if they have sensory abnormalities.

Patients with Guillain-Barré Syndrome who develop dysautonomia can have orthostatic hypotension and respiratory distress.

Neuropathic pain can present in some of the neuropathies and demands accurate pharmacological treatment as pain may interfere with progress in therapy.

Myopathies

A multidisciplinary approach is the best way to deliver effective care to these patients.

Physiatrists on the rehabilitation floor frequently admit patients with inflammatory myopathies such as polymyositis or dermatomyositis.

In childhood, Duchene muscular dystrophy can be the most common and devastating muscle disease and offers a variety of challenges in terms of treatment.

Muscular diseases often cause proximal weakness involving the pelvic girdle muscles leading to the so-called “myopathic” gait pattern. Improving gait is one of the main goals when working with patients with Duchene muscular dystrophy as well as adult onset myopathies.

Limb contractures and scoliosis: the occurrence of contractures appears to be related to the prolonged static positioning of the limb.

Gentle stretching and splinting might slow the progression of contractures and should be added in the rehabilitation program offered for inpatient stay.

On the other hand, many children with DMD develop scoliosis before they become wheelchair dependent. Appropriate and timely spinal instrumentation and
fusion should be done before the primary curve becomes greater than 25°. It is also
critical that the vital capacity has not fallen below 40% of its predicted value to prevent
surgical complications.

Some patients might benefit from bracing, depending on the distribution of the
weakness with the goal of improving function and stability.

Exercise should be prescribed for these patients cautiously so as to prevent
exhaustion due to the risk of muscle damage.

Low impact aerobic exercises such as walking, swimming, and stationary bicycling
improve cardiovascular performance, increase muscle efficiency, and lessen fatigue.

Equipment should be provided upon discharge, and patients and caregivers need
to be trained.

This equipment will improve quality of life and includes items for daily activities such as grab bars, shower chair, commode chair, hospital bed ramps, light wheelchair, or scooters for long distances.

Complications for the above entity are the same as for patients with prolonged immobility, if their motor deficits are severe; they can present with DVT.

Also, patients with swallowing dysfunction such as in ALS or certain myopathies can suffer from aspiration pneumonia.

### Complication Timeline for Neurological Disorders

<table>
<thead>
<tr>
<th>Disease</th>
<th>Complication</th>
<th>Onset of Complication</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Early/Acute</td>
</tr>
<tr>
<td>Multiple sclerosis</td>
<td>DVT</td>
<td>X</td>
</tr>
<tr>
<td></td>
<td>Fractures</td>
<td>X</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Parkinson’s disease</td>
<td>DVT</td>
<td>X</td>
</tr>
<tr>
<td></td>
<td>Fractures</td>
<td>X</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amyotrophic lateral sclerosis</td>
<td>DVT</td>
<td>X</td>
</tr>
<tr>
<td></td>
<td>Fractures</td>
<td>X</td>
</tr>
<tr>
<td></td>
<td>Aspiration pneumonia</td>
<td>X</td>
</tr>
<tr>
<td>Peripheral neuropathy—</td>
<td>DVT</td>
<td>X</td>
</tr>
<tr>
<td>Guillain-Barré Syndrome</td>
<td>Fractures</td>
<td>X</td>
</tr>
<tr>
<td></td>
<td>Respiratory distress</td>
<td>X</td>
</tr>
<tr>
<td></td>
<td>Orthostatic hypotension/</td>
<td>X</td>
</tr>
<tr>
<td></td>
<td>dysautonomia</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Aspiration pneumonia</td>
<td>X</td>
</tr>
<tr>
<td></td>
<td>Neuropathic pain</td>
<td>X</td>
</tr>
<tr>
<td>Myopathy</td>
<td>DVT</td>
<td>X</td>
</tr>
<tr>
<td></td>
<td>Fractures</td>
<td>X</td>
</tr>
<tr>
<td></td>
<td>Aspiration pneumonia</td>
<td>X</td>
</tr>
</tbody>
</table>

DVT, deep vein thrombosis.
RHEUMATOLOGIC DISORDERS

Rheumatologic disease is a chronic prevalent condition that involves joint structures and surrounding soft tissues. Effects of this process will be swelling, cartilage erosions, bone erosions, tendon ruptures, ligament and capsule ruptures, joint space destruction, muscle atrophy, and osteoporosis. Moreover, joint instability, decreased endurance, psychosocial impairment, and reduction in the work capacity may occur. These late effects could result in the loss of adherence to treatment and rehabilitation regimens.

Based on all these effects, the rehabilitation of rheumatologic patients require a multidisciplinary approach: pharmacotherapy, physical and occupational therapy, optimal rest, use of orthoses and functional aids, psychological evaluation and management, surgery, patient education, and home and work environment evaluation and modification.

The benefits of exercise in patients with rheumatologic disorders go farther than physical and functional improvement, affecting mental health and psychosocial spheres with equal or better results than medications. The initial step for appropriate rehabilitation of the rheumatologic patient is to have a comprehensive evaluation of the patient to understand all the factors that could end in complications and disability.

There are several rheumatologic disorders that can be observed in acute inpatient rehabilitation: rheumatoid arthritis (RA), spondyloarthropathies, connective tissue diseases, nonarticular rheumatism, and metabolic disorders.

RHEUMATOID ARTHRITIS

RA is a chronic systemic inflammatory disease, with persistent symmetric polyarthritis that involves any joint lined by a synovial membrane; extra-articular involvement is also seen. The cause of RA is unknown; however, multiple factors can play a role: genetic, environmental, immunologic, hormonal, and/or infectious.

The prevalence of RA ranges from 0.5% to 1%, affecting nearly 2.5 million Americans and 165 million people worldwide. Age of onset is typically between 25 and 50 years. Female-to-male ratio is approximately 3:1. Annual incidence ranges from 14.3 cases per 100,000 in men to 35.9 cases per 100,000 in women. First-degree relatives of individuals with RA are at an increased risk (2- to 3-fold) for the disease (5).

Patients with RA have an increased morbidity: twice as likely to develop a myocardial infarction (MI), 70% more likely to suffer a stroke, 70% more likely to develop an infection, and up to 26-fold higher risk of lymphoma depending on severity of disease and exposure to immunosuppressive drugs, including methotrexate (5–7).
Clinical manifestations of RA are: symmetrical polyarthritis, morning stiffness, fatigue, malaise, ROM limitation, predilection for wrists and hands (metacarpophalangeal joints, proximal interphalangeal joints), hips, knees, and the cervical spine; however, any synovial joint may be involved. Extra-articular manifestations include: pericarditis, cardiomyopathy, valvular incompetence, scleritis, mononeuritis multiplex, peripheral compression syndrome (eg, carpal tunnel syndrome), vasculitis, keratoconjunctivitis, and xerostomia.

Findings in the physical exam are: tenosynovitis, ulnar deviation of the metacarpophalangeal joints, boutonniere deformity of the fingers, swan-neck deformity of the fingers, arthritis mutilans, disruption of the radioulnar joint, dorsal subluxation of the ulna, rheumatoid nodules, hallux valgus, hammer toe deformities, knee effusions, atrophy of the quadriceps, decreased range or motion of the affected joints, neck stiffness, radicular symptoms, spinal cord lesions, neck pain, and cervical myelopathy.

The main goals of the treatment in this pathology are to: ameliorate the pain, control the inflammation, prevent complications (atrophy, contractures and other deformities), improve functionality, and patient education. To ameliorate the pain we need to provide appropriate positioning of the patient, the use of orthoses, application of modalities, physical and occupational therapies, and medications to control the inflammation and the pain. There are a variety of medications to control the inflammation and disease progression: nonsteroidal anti-inflammatory drugs (NSAIDs), corticosteroids, tumor necrosis factor inhibitors, methotrexate, antimalarials, and leflunomide. To prevent complications, physical and occupational therapy have an important role initially with modalities to control pain and inflammation, then in applying orthoses to rest the joint and to prevent deformities, then in starting isometric exercises (to prevent atrophy), and finally, in progressing to ROM exercises/stretching, advancing to strengthening, all of this to improve functionality and endurance. Once the deformities have been established, the evaluation and prescription of special devices and instruments for activities of daily living will play a role in the treatment of the patient with RA. Patient education for the use of these instruments, for a home exercise program, and a continuous follow up to evaluate the disease progression should be the next step.

METABOLIC DISORDERS

Gout

Gout is a metabolic disorder where monosodium urate crystals deposit in tissues. These crystals are the end product of purine degradation in humans, and their increase is due to overproduction and/or underexcretion. Sources of purines are: diet, tissues
(nucleic acids), and endogenous purine synthesis. The most common cause is underexcretion (90% of patients), however, 10% of the patients can have overproduction causes (Table 6.2).

The cumulative incidence of gout is 10.9% among black men and 5.8% among white men in the United States (8). The prevalence is 6% for men and 2% for women over 45 years of age (9).

Certain conditions have been associated or predisposed to crystal deposition: decreased solubility of urate due to low temperatures or low pH, disturbances of the soft tissues or the joint as a result of trauma or tissue injury, increased reabsorption of water as seen during sleep, binges of alcohol, overeating, fasting, concurrent acute medical or surgical illness, marked rise or fall in serum uric acid, seasonal factors, male gender, postmenopausal women, posttransplant patients, and high body mass index.

Once the crystals have been deposited, an inflammatory response begins. Different manifestations can be found throughout the body:

- Acute monoarticular arthritis
- Acute oligoarticular arthritis
- Chronic polyarticular arthritis
- Gouty nephropathy
- Uric acid nephrolithiasis

The duration of the disease is divided into different stages: asymptomatic hyperuricemic state, acute flares, interacute flares, and long-term gouty complications.

Any of these conditions can be seen in patients during their admission to the acute inpatient rehabilitation unit. We discuss each stage in the following section.

### TABLE 6.2 Sources of Purine Accumulation

<table>
<thead>
<tr>
<th>Underexcretion Causes</th>
<th>Overproduction Causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renal insufficiency</td>
<td>Excess dietary purine consumption</td>
</tr>
<tr>
<td>Drugs</td>
<td>Alcohol consumption</td>
</tr>
<tr>
<td>• Low dose ASA</td>
<td>Myeloproliferative and lymphoproliferative disorders</td>
</tr>
<tr>
<td>• Cyclosporine</td>
<td>Psoriasis</td>
</tr>
<tr>
<td>• Diuretics</td>
<td>Partial deficiency of HGPRT Superactive PRPP</td>
</tr>
<tr>
<td>• Pyrazinamide</td>
<td></td>
</tr>
<tr>
<td>• Ethambutol</td>
<td></td>
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<tr>
<td>• Lead</td>
<td></td>
</tr>
<tr>
<td>Thyroid disease</td>
<td></td>
</tr>
<tr>
<td>Alcohol</td>
<td></td>
</tr>
</tbody>
</table>

ASA, aspirin; HGPRT, hypoxantine-guanine phosphoribosyltransferase; PRPP, phosphoribosylpyrophosphate synthetase.
Asymptomatic hyperuricemic stage: This stage is an incidental finding because there are no clinical manifestations, only a positive history of hyperuricemia or gout, however, without any physical manifestation. Unless we order uric acid levels, we would not detect this stage.

Acute flare: This stage is characterized by an acute onset of warmth, swelling, erythema, pain, and occasional fever, chills, and malaise, often at night. The most common sites of presentation are: first metatarsophalangeal joint (affected in 90% of individuals with gout, 50% in acute flares), knee, elbow, olecranon bursa, wrist, fingers, ankle, subtalar joint, midfoot, as well as bursae and tendons.

Interacute flares stage: This stage is similar to the first stage. However, the difference is that the patient has had acute flares. It is a clinically inactive stage; however, if the disease is untreated, this stage will be shortened over time, and the body’s urate stores will continue to increase. During this stage, we can find crystals inside the joints.

Long-term gouty complications stage: With uncontrolled hyperuricemia tissue urate stores increase, as well as the deposition inside the soft tissue and joints with the concurrent chronic arthritis characterized by stiff, swollen, persistently uncomfortable, and painful joints (however, to a minor degree as in acute flares). Radiographic changes (destructive and hypertrophic erosions, with overhanging edges, with preservation of the joint space) are common at this point of the disease.

Once we have diagnosed or we are faced with any of these stages, the goals are to: manage the exacerbation, decrease the possibility of new flare ups, and control the hyperuricemia to prevent disease progression. The first step in this treatment plan is going to be patient education to modify lifestyle (weight reduction, decrease alcohol consumption, and diet modifications). The second step will be symptom control with medications (NSAIDs, colchicine, steroids, adrenocorticotropic hormone [ACTH], and allopurinol), proper positioning, modalities, and splints. The third step will be to prevent contractions and other deformities by using proper positioning, patient education, splinting, physical therapy, and occupational therapy. The fourth step is to improve function with therapy. The fifth step will be to decrease the frequency and/or the severity of the outbreaks (low-dose colchicine, NSAIDs). And the sixth step will be to prevent disease progression (controlling the metabolic disorder, and lowering the urate pool).

Pseudogout

Pseudogout is a rheumatologic disorder in which calcium crystals are deposited in the joint and may lead to acute symptoms of joint inflammation or synovitis. The exact cause is unknown. The most common calcium crystals are calcium pyrophosphate dehydrate (CPPD) crystals, however, calcium hydroxyapatite and calcium oxalate crystals can be seen too.
Many people can have the crystals deposited inside the joint, at the level of the cartilage, and do not present any symptoms. However, some people present an inflammatory response to the crystals. There are many clinical presentations:

- Asymptomatic radiographic disease (chondrocalcinosis)
- Acute monoarticular arthritis (Pseudogout)
- Pseudo-OA
- Chronic polyarticular arthritis (Pseudo-RA)
- Pseudo-Charcot arthritis

Certain conditions have been associated with or predispose to crystal deposition: older age, joint trauma, genetics (familial chondrocalcinosis), excess iron (hemochromatosis), metabolic, and endocrine disorders (hyperparathyroidism, hypophosphatasia, hypomagnesemia, Gitelman’s syndrome, thyroid disease, and familial hypocalciuriahypercalcemia).

In the acute presentation, the major complaints are: joint pain, swelling, warmth, and redness. Physical findings are: effusion, warmth, redness, tenderness, decreased and painful ROM. In 50% of the cases, the knee is affected, then the wrist; however, ankles, feet, shoulder, elbows or hands can be affected too.

The first step in this treatment plan is going to be patient education to modify lifestyle (weight reduction, physical activity) and to explain the possible progression to destruction of the cartilage (osteoarthritis), bone cysts, and/or spurs. The second step will be symptoms control with medications (NSAIDs, colchicine, and/or steroids), proper positioning, modalities, and splints. The third step will be to prevent contractions and other deformities by using proper positioning, patient education, splinting, physical therapy, and occupational therapy. The fourth step is to improve function with therapy. The fifth step will be to prevent or to decrease the frequency and/or the severity of the outbreaks (low-dose colchicine), however, this may not decrease the risk of developing chronic arthritis.

**SPONDYLOARTHROPATHIES**

This group of rheumatic diseases has an involvement of the axial skeleton, association with HLA-B27, negative rheumatoid factor, and in the affected areas, fibroblastic proliferation followed by bone formation are common. This group is also called seronegative arthritides. The entities included are: ankylosing spondylitis (AS), Reiter’s syndrome, psoriatic arthritis, and inflammatory bowel disease.

These entities have systemic manifestations like low-grade fever, malaise, weight loss, aortitis. Specific manifestations like iritis (redness, pain, photophobia due to an inflammatory process), enthesopathies (common before back symptoms, most common localization is the achilles tendon, plantar fascia, and the metatarsal heads).
Specific symptoms of AS are: insidious pain associated with stiffness at the level of the lower back and sacroiliac joints with progressive loss of mobility. These symptoms are worse in the middle of the night or in the morning. Symptoms can progress to the thoracic and cervical spine. Hips, knees, ankles, and toes can be involved in early stages and before the back is compromised.

Reiter’s syndrome is characterized by peripheral arthritis (large joints, several joints at once), associated with urethritis and conjunctivitis. Occasionally, skin lesions can be seen. The spine and sacroiliac joints can be involved, as well as tendon and ligament insertions, and fingers (dactylitis).

AS and Reiter’s syndrome most often affect young adults and children between the ages 15 and 35 years. The male to female ratio is 9:1.

Rheumatoid factor, x-rays, HLA-B27 phenotype, CT scan, and MRI are used to confirm the diagnosis of these disorders. Rheumatoid factor is negative, and HLA-B27 is positive in 90% of the cases in AS, and 75% in Reiter’s syndrome.

The first step in the treatment plan is patient education. The patient must understand the nature of the disease, possible outcomes, and the treatment plan. The second step is the control of the inflammatory process (NSAIDs, tumor necrosis factor inhibitors, corticosteroids, and sulfasalazine). The third step is to maintain appropriate postures and rest, early in the course of the AS. A firm mattress and the prone position or the supine position are better, with small pillows to avoid cervical kyphosis; patient should maintain an erect position walking, standing or sitting; the use of chairs with straight backs can be helpful; occasionally, splints can help to prevent contractures. The fourth step is the maintenance of the ROM as much as possible with a daily exercise program by physical and occupational therapy; the program should emphasize extension of all segments of the spine, complete ROM of the neck, shoulders, and hips. Aquatic therapy can be an excellent option. The fifth step includes prevention of deformities and complications; however this step should be in effect from the beginning. The sixth step is the reintegration of the patient to daily living, a productive lifestyle and the evaluation by vocational therapy and psychology to help design a plan to achieve these goals.

POLYMYOSITIS

This is an immune-mediated inflammatory process of the skeletal muscle that occurs between the ages of 30 to 50, with a female to male ratio of 2:1. The annual incidence is 1 case per 100,000 persons per year. Its 5-year mortality is 20%, and the cause of death is related to malignancy or pulmonary complications. Polymyositis is most common in blacks (10).

The features of the clinical presentation are: insidious symmetric muscle involvement associated with weakness, usually painless, dysphagia, and aspiration may occur
in 30% of the cases (if pharyngeal muscles are involved). The patient complains of difficulty climbing/descending stairs, kneeling, weakness of neck extensors, and difficult upper extremity elevation. Occasionally, cardiac involvement may be seen (pericarditis and/or cardiomyopathy).

The physical findings are characterized by: muscle atrophy, tenderness, normal sensation and reflexes, arthralgias, and occasionally dysphagia, interstitial lung disease, pneumonia/aspiration, and congestive heart failure.

The first step in the treatment plan is patient education. The patient must understand the nature of the disease, possible outcomes, and the treatment plan. The second step is the control of the inflammatory process and clinical stabilization (corticosteroids, occasionally intravenous immunoglobulin, other immunosuppressive agents, and plasmapheresis). The third step is to maintain appropriate postures and rest; occasionally, splints can help to prevent contractures, swallowing evaluation, and chest physiotherapy. The fourth step is to avoid muscle atrophy and to maintain the ROM as much as possible with a daily exercise program by physical and occupational therapy; the program should start with gentle, supervised, and graded exercises. The fifth step includes prevention of deformities and complications; however, this step should be in effect from the beginning. The sixth step is the reintegration of the patient to daily living, productive lifestyle; the evaluation by vocational therapy and psychology will help in the plan design to achieve these goals.

COMPLICATIONS

One of the most common complications seen in patients with rheumatologic disorders are the contractures and deformities as a result of either pain, inflammation, and, therefore, decreased ROM or as a result of joint destruction. Sometimes, these complications are unstoppable; however, we can delay the progress or the damage through pain control, therapy, splints, counseling, teaching, and a home exercise program.

In patients with rheumatologic disorders, it is important to be aware of possible respiratory complications because of immunosuppression, immobility, or weak cough. To prevent these complications, it is important to consult with respiratory therapy.

Furthermore, immobility due to pain, joint involvement, or surgical procedures increases the risk of DVT and pulmonary embolism. These patients must be on prophylaxis with intermittent compression devices or fractioned heparin or low molecular weight heparin (LMWH).

Medications and immunosuppression are a cause of possible infections in these patients. In such cases, we must we aware and follow up any surgical incisions in detail, as well as any source of possible infection.
### Complication Timeline for Rheumatologic Disorders

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<tr>
<th>Complication</th>
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<tr>
<td></td>
<td>Early/Acute</td>
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<td>Contractures</td>
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<tr>
<td>Deformities</td>
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<td>Respiration complications</td>
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<tr>
<td>Atelectasis</td>
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<td>Pneumonia</td>
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<td>Deep venous thrombosis</td>
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<tr>
<td>Pulmonary embolism</td>
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<tr>
<td>Infection</td>
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### REFERENCES

In an era dominated by increased pressure to decrease length of stay on the acute medical ward, physiatrists are frequently consulted early in the course of medical management. They are often faced with admitting more acute patients to inpatient rehabilitation units. Although orthopedic, debility, and stroke patients represent the majority of conditions typically found on most general inpatient rehabilitation wards, there is an increasing number of medically complicated patients who have benefitted from inpatient rehabilitation programs (1). With more than 11 million people living with cancer, there is a large group of medically complicated patients who will likely be treated in inpatient rehabilitation units in the near future (2).

Despite such a large population of cancer patients in the community, admission to inpatient rehabilitation among this group is relatively low. This is likely due to a few reasons: the lack of awareness among health care providers of the functional deficits resulting from cancer and its treatment, the lack of awareness of the benefits of cancer rehabilitation programs, and the progressive nature of the disease. In addition, there may be reluctance on the part of some physiatrists to admit cancer patients to inpatient rehabilitation facilities because of the complexity of their medical condition.

In the literature, there are multiple studies that demonstrate the benefit of inpatient rehabilitation for cancer patients. Tay et al compared cancer patients with noncancer patients on inpatient rehabilitation units and found that both groups made significant improvements in functional independence measure (FIM) motor score gains (1). Marciniak et al grouped patients by tumor type and found that regardless of the tumor etiology, all groups showed FIM score improvements across several FIM categories (3). Additionally, Marciniak et al showed that the presence of metastatic disease and ongoing radiation treatments had no significant negative effects on functional gains in cancer patients in rehabilitation facilities (3). When comparing length of stay of cancer patients and noncancer patients, Tay et al reported no significant difference between the two groups (1). Although most of the studies listed are retrospective chart reviews, the evidence continues to support the efficacy of inpatient rehabilitation programs for cancer patients, regardless of the type of cancer or its severity.
Despite the evidence supporting inpatient cancer rehabilitation programs, there is also sufficient literature suggesting the complex and progressive nature of disease that commonly accompanies a cancer diagnosis. In a study published in 2008, Alam et al compared frequency of acute care transfers between cancer and noncancer patients. They found that 21% of patients in the cancer group required transfer back to the acute service versus 9.7% of those without cancer (4). In another retrospective chart review, Guo et al noted a 35% transfer rate back to acute services, with the most common reasons being respiratory distress, wound complications, and tumor progression (5). These studies by no means suggest that cancer patients should not be admitted to inpatient rehabilitation units; instead, they demonstrate the medical complexity of cancer patients and suggest that special attention should be paid to this population.

Although an in-depth review of each medically complicated condition seen on inpatient rehabilitation wards is outside the scope of this book, this chapter helps identify key issues facing cancer patients and provides strategies to help maximize each patient’s rehabilitation potential. On the basis of the increased prevalence of this condition, this chapter focuses primarily on cancer patients treated in the inpatient rehabilitation setting.

CANCER

Rehabilitation efforts focused on treating patients with a diagnosis of cancer have become more prevalent, and, in recent years, cancer rehabilitation has developed into a subspecialty within the field of rehabilitation medicine. Cancer is defined as the uncontrolled growth and spread of abnormal cells (2). Cancer is caused by both external and internal factors. External or environmental causes include toxin exposure, infectious agents, and radiation exposure. Internal causes include genetic or inherited mutations, immune-related factors, or metabolically derived mutations. Physical impairment may occur as a direct result of the tumor itself, systemic tumor effects, surgical efforts aimed at tumor resection, or medical treatments related to the tumor. Cancer can affect any tissue within the body; however, tissues that are exposed to the environment and tissues that are hormone sensitive have a higher incidence of cancer occurrence. Cancer also tends to affect older individuals; however, it can affect people of all ages. Thus, the tissue type involved, the severity of the cancer, the age and attitude of the patient, the treatments used, and access to health care can all play a role in mental and physical impairments suffered by those with cancer in the inpatient rehabilitation units.

With more than 1.5 million new cancers diagnosed in the United States in 2011, the prevalence of cancer continues to increase (2). Additionally, 5- and 10-year cancer survival rates have increased in large part because of the emphasis placed on early detection, improved detection modalities, and improved chemotherapeutic agents. The combination of increasing prevalence and increased survivorship has resulted in
a much larger population of those diagnosed with cancer. In the past, a cancer diagnosis was viewed almost always as a terminal diagnosis. In this day and age, many people live many years beyond their initial diagnosis of cancer, especially those diagnosed with breast and prostate cancers. As many of these individuals aspire to continue to live productive lives, the role of the physiatrist becomes increasingly important. Physiatric interventions are aimed at helping cancer patients deal with fatigue, pain, sleep disturbances, depression, and the physical decline that often accompanies a cancer diagnosis. Often, patients may require assistive devices to carry out activities of daily living or for ambulation, and the inpatient rehabilitation setting is the ideal place to identify those needs and to train patients in the proper use of assistive devices.

The specific abilities and rehabilitation needs can vary greatly from one patient to another even if they share the same medical diagnosis. When comparing the needs and treating patients with different medical conditions, these differences can be much greater. For example, the opiate requirements for postoperative total hip arthroplasty patients will be very different from those for cancer patients who may have been on chronic opiate therapy. In addition, the goals of treatment and the functional outcome goals often vary greatly between patients with differing medical conditions, and these differences are highlighted when treating medically complex patients. The physiatrist must also take current and ongoing treatments into account when devising therapeutic rehabilitation plans for this special group of rehabilitation patients. Often, patients undergoing active radiation/chemotherapy treatments may not be able to participate in physical and occupational therapy sessions. This can be especially challenging when considering the strict requirements for hours of therapy per day placed on accredited inpatient rehabilitation facilities by many insurance companies.

As mentioned previously, several studies have shown that cancer rehabilitation programs result in measurable benefits when individualized, specific, and realistic goals are set (6). Early physiatric consultation on the acute medical or surgical ward will allow for assessment of debility and initiation of therapy services, which may in turn lead to earlier discharge from the acute inpatient wards. On the inpatient rehabilitation unit, an individualized plan aimed at maximizing skills required for activities of daily living and promoting independent mobility with or without assistive devices is paramount (7). This plan should be established early and revisited on a weekly basis, allowing for efficient use of resources and time of both the patient and the rehabilitation team.

When transferring a cancer patient to the inpatient rehabilitation unit, information regarding the most recent radiation/chemotherapy treatments and the plan for future interventions must be obtained. Patients undergoing active radiation treatments require therapy sessions to be scheduled around radiation sessions. Radiation has a cumulative systemic effect and the rehabilitation team must be aware that therapy sessions may be less fruitful immediately following radiation treatments, although a study by Marciniak et al reported no significant detrimental effects in functional gains for patients receiving
radiation therapy (3). Nonetheless, it is clearly important to discuss the treatment plan with the primary oncology team prior to transferring patients to inpatient rehabilitation wards to make use of the patients’ time in the rehabilitation unit.

In-depth knowledge pertaining to each chemo-therapeutic agent and its side effects is the responsibility of the primary oncology physician; however, the inpatient physiatrist should have some knowledge of the different classes of agents and their side effects. For example, knowledge pertaining to the newest antitumor drugs is not absolutely necessary, but knowing that groups such as the vinca alkaloids and taxanes cause peripheral neuropathy is essential. The specifics with regard to length of treatment and systemic effects, such as medically induced neutropenia, can be communicated via transfer documentation by the oncologist or through direct verbal communication. This will help ensure the appropriate laboratory studies are followed and necessary steps are taken to correct for any abnormalities. It is not uncommon for patients treated with chemotherapeutic agents to suffer from marrow suppression, which may affect all cellular blood lines. In general, patients with absolute neutrophil counts less than 500 per microliter of blood should not be transferred to inpatient rehabilitation units as their risk of infection is too great. Extra care must be taken when contacting patients with low white blood cell counts, especially when the inpatient unit has other patients with skin, respiratory, or gastrointestinal infections, as these are highly communicable infections. Goals to decrease nosocomial infections in these patients include strict hand washing, limiting the number of contacts with the patient, and dedicating separate therapists to work with cancer patients only.

SELECTIVE ISSUES IN CANCER REHABILITATION

Pain

Pain is a common complaint by patients with cancer, occurring in 30% to 50% of patients undergoing chronic treatment and in up to 70% of those with advanced disease (8). Not only can pain lead to a decline in function, but it can also be debilitating and often has a large effect on the quality of life. In the inpatient rehabilitation setting, pain often leads to decreased productivity and unwillingness or inability to participate in scheduled physical, occupational, and/or speech therapy sessions, rendering the overall rehabilitation efforts less effective.

Treating pain effectively should begin with an accurate diagnosis of the cause of pain, which can be especially challenging in the cancer population. The pain may be related to the disease itself, to the treatments, or unrelated to either. Additionally, cancer patients often experience multiple concurrent pain syndromes (9). To help elucidate the source, a thorough history should be obtained that includes the type of cancer diagnosed, the initial date of diagnosis, the treatments used, including specific radiation data (Gy and fractions), chemotherapeutic agents used, as well as an
in-depth history of the pain (onset, quality, radiation, severity, aggravating/alleviating factors) and all prior treatments.

The physical exam is commonly undervalued but often plays an integral role in providing information to the clinician. For example, Stubblefield differentiates pain into two categories: somatic and neuropathic. If a push on it hurts, it is somatic in nature. Conversely, if a push on it is not related to pain, it is neuropathic in nature (10). Although there are many caveats to this theory, it can be used as a general construct when deciding which analgesic regimen is more appropriate for a specific patient based on their pain. For example, somatic pain caused by lateral epicondylitis would be treated better with bracing, steroid injection at the site, and anti-inflammatory medications. Conversely, cervical radiculopathy causing elbow pain and forearm pain would respond better to nerve stabilizing medications, a physical therapy program aimed at cervical core strengthening, and a cervical epidural.

The field of cancer pain is broad and entire texts have been dedicated to the topic. Chronic pain management in cancer patients tends to be treated in the outpatient setting; however, it would not be uncommon to care for a cancer patient who is suffering from “acute-on-chronic” pain in the inpatient rehabilitation setting. As a general starting point, the WHO created a three-step ladder as a guide to treat cancer pain. As stated by WHO, “If pain occurs, there should be prompt oral administration of drugs in the following order: nonopioids (aspirin and paracetamol); then, as necessary, mild opioids (codeine); then strong opioids such as morphine, until the patient is free of pain. To calm fears and anxiety, additional drugs—‘adjuvants’—should be used. To maintain freedom from pain, drugs should be given ‘by the clock,’ that is, every 3 to 6 hours, rather than ‘on demand.’ This three-step approach of administering the right drug in the right dose at the right time is inexpensive and 80% to 90% effective” (Figure 7.1; 11).

Treating cancer pain can be quite challenging. As with treating any type of pain, it is important to remind patients that eliminating all pain is an unrealistic expectation. Explaining to the patient that the goal is to reduce the pain to a level that will allow for participation in physical/occupational therapy sessions will set more realistic expectations and will typically be met with better results. Following the WHO model, nonopioid medications are typically initiated prior to administration of opiates. Nonsteroidal anti-inflammatory drugs (NSAIDs) are a particularly good choice for patients who are experiencing bone pain related to metastatic lesions. Prostaglandins have been implicated as the pain generators associated with lytic bone metastases, and NSAIDs are considered first-line treatment for this type of pain (12). As with any medication, the risks and benefits must be weighed prior to initiation of any analgesic. Dosing of the particular NSAID would be the same as would be used to treat any other common musculoskeletal condition. Adjuvants, such as bisphosphonates, to treat bone pain have been supported by the literature (13). In a study by Conte et al, 44% of breast cancer patients, with metastatic bone lesions and treated with pamidronate, experienced two-point pain reduction, compared to 30% treated with saline only (13). Additionally, the literature supports the use of corticosteroids for bone pain in cancer patients (14).
I. MEDICAL COMPLICATIONS

For pain that is recalcitrant to treatment with nonopioid analgesics, opiate therapy can and should be initiated. Often, patients are already on chronic opiate therapy at the time of admission to inpatient rehabilitation facilities. In those cases, simple continuation of their previous opiate regimen can provide the best analgesia and avoid confusion relating to changing doses. Typically, a long-acting opiate is administered to provide a continuous baseline of analgesia, and a short-acting opiate is used for breakthrough pain. It is recommended to use the same drug for the long-acting and short-acting formulations, which will allow patients to benefit from opiate rotation should they become less responsive to a particular drug in the future (15).

The judicious use of opiates for cancer pain is strongly supported by the available literature (16–18). Opiates can be administered orally, parenterally, transdermally, intrathecally, or transmucosally. Opiate doses used in cancer patients typically exceed those given by physiatrists to noncancer patients, and consultation with a pain specialist is recommended prior to dose escalation or when changing from one opiate to another. Common side effects of opiates include constipation, nausea/vomiting, lethargy, headache, and pruritus while serious side effects include respiratory/circulatory depression and death. Opiate therapy should always be administered along with a bowel regimen, such as dulcolax, senna, or docusate, and patients should always be monitored for respiratory depression when changing doses, altering the method of administration, or when switching from one opiate to another. This is not to say that all patients should not be
monitored continuously while taking any opiate, rather it suggests that the physician should exercise extra caution in the aforementioned scenarios.

Other medications that can be used to treat neuropathic type pain include nerve stabilizers (gabapentin, pregabalin), tricyclic antidepressants (amitriptyline), and selective serotonin norepinephrine reuptake inhibitors (SSNRIs; duloxetine). Transcutaneous electrical nerve stimulation (TENS) units as well as heat and cold can be utilized as well. Other modalities, such as ultrasound, should not be used in cancer patients because of the risk of promoting metastasis. For patients with advanced cancer and intractable pain, anterolateral cordotomy and myelotomy have been shown to be very effective in treating pain and may be utilized when medications have failed to provide adequate pain relief (19–22).

Fatigue

Fatigue is the most common symptom experienced by cancer patients, affecting between 70% and 100% of patients based on recent data (23). The degree of fatigue is highly dependent on the type of cancer, the stage of the cancer, types of ongoing treatments, and comorbidities. The etiology of fatigue in cancer patients is often multifactorial and can be difficult to discern, making its treatment a challenge for the rehabilitation team. Fatigue not only diminishes the patient’s quality of life, but also inhibits his or her ability to participate in physical/occupational therapy, thereby limiting functional gains in the inpatient rehabilitation units. Literature supports this idea, concluding that fatigue reduces the energy, mental capacity, functional status, and psychologic resilience of cancer patients (20,23). Considering the prevalence of fatigue in cancer patients and its deleterious effects on the rehabilitation process, addressing and treating fatigue in the inpatient setting is exceedingly important.

Although an extensive differential diagnosis of the causes of fatigue in cancer patients is outside the scope of this chapter, a few of the common causes include anemia, tumor load, host responses, chemotherapy agents, medications, nutritional deficiencies, debility, and depression. In most cases, the proper treatment of fatigue is contingent upon the diagnosis of the cause of fatigue. Although identifying the cause of the fatigue is important, Dimeo et al showed that a 3-week endurance and resistance exercise program resulted in significant improvements in physical and mental fatigue in cancer patients, regardless of the cause of fatigue (24). For patients whose fatigue is thought to be related to anemia, the American Society of Clinical Oncology recommends initiating epoetins in patients with prechemotherapy baseline hemoglobin <10 g/dL, symptomatic baseline anemia, or a drop of 1 to 2 g/dL per chemotherapy cycle (25). The recommended dose of epoetin alfa is 150 U/kg three times a week, or 40,000 U weekly (26). An appropriate response is an increase in hemoglobin of 1 g/dL or resolution of symptoms. In many cases, the delayed response associated with epoetin administration may not be suitable for the inpatient setting. Additionally, treatment with epoetin can be quite costly and may
not be available to all patients. In these cases, red cell transfusions can be utilized with great success. This treatment option is much more cost effective, and the response time is almost immediate.

Medications are another common cause of fatigue in cancer patients. Centrally acting agents, benzodiazepines, antihistamines, and other medications are all probable and likely culprits; unfortunately, opiates are also a common cause of medication-related fatigue. This is particularly problematic given the fact that up to 90% of cancer patients experience pain related to the disease process at some point during their treatment (27). In inpatient rehabilitation units, patients are even more likely to require opiate therapy as they are typically being transferred from an acute medical or surgical service where they may have recently received chemotherapy, radiation, or undergone surgical intervention. A trial by eliminating or decreasing one of the suspected medications may reveal the medication that is causing the fatigue. If opiates are deemed the responsible agent, it is recommended to find the minimum dose that controls the pain with the goal of minimizing the sedating side effects.

As stated previously, fatigue in cancer patients is often multifactorial and can therefore be challenging to treat. If the reversible causes have been treated or ruled out, the goal then becomes to treat the symptoms of fatigue. Low-impact, directed aerobic exercise has been shown to decrease fatigue in up to 70% of patients (28). Common medications used to treat fatigue include methylphenidate and modafinil. Methylphenidate can be started at 5 mg taken twice daily, with the effects of increased energy level and mental alertness noticeable within 1 hour of administration. Evidence of its use in the cancer population remains controversial and it has not been shown to confer benefit when compared with placebo in the treatment of cancer-related fatigue (29). Multiple studies have justified the use of modafinil, started at 100 to 200 mg daily with a maximum dose of 400 mg daily (30,31). Common side effects with these medications include nervousness, anxiety, insomnia, and anorexia. As with almost all medications, the goal should be to find the dose that provides maximum benefit with minimal or tolerable side effects. Other than creating an improved sense of well-being, treating fatigue in cancer patients should facilitate more productive therapy sessions and a more fruitful inpatient rehabilitation course.

**Bone Metastases**

Metastatic disease accompanies solid tumor in 60% to 84% of cases (32). Prostate, breast, kidney, thyroid, and lung cancers are the most common cancers that metastasize to bone, and as these cancers comprise 50% of all cancers, the likelihood of treating a patient with bony metastasis is very likely (33). In inpatient rehabilitation units, bony metastases have particular importance relating to the risk of fracture and further disability. New onset of focal bone pain should be considered metastatic in any patient with a history of cancer or ongoing cancer treatments until proven otherwise.
In addition, pain that is worse at night, onset of new focal neurologic findings, including weakness, numbness, or bowel/bladder incontinence should raise concerns of brain or spinal metastasis. This section outlines the initial steps in the management, guidelines for physical activity, and a brief summary of the treatment of bony metastatic disease.

The most common site of osseous metastasis is the axial skeleton, followed by the appendicular long bones, skull, and ribs (34). Clinical features of osseous metastatic spread include night pain, loss of range of motion, pain during therapy sessions, and hypercalcemia. As always, start with a thorough history and physical examination. Information pertaining to the type of cancer, grade, stage, nodal involvement, previous treatments and dates, as well as previous history of metastatic disease is important. Initial laboratory studies should include complete blood count (CBC), basic metabolic panel (BMP; including serum Ca\(^{2+}\)), liver function tests (LFTs), and serum protein electrophoresis/urine protein electrophoresis (SPEP/UPEP) if multiple myeloma is suspected. Imaging should start with plain films of the entire bone that is suspect. For example, if the lumbar spine is suspected, plain films of the cervical, thoracic, and lumbar spine should be ordered. If the femur is suspected, images of the entire femur will provide a comprehensive evaluation of the extent of disease and useful information for bracing. It must be kept in mind, however, that 50% of the cortical bone mass is destroyed before becoming apparent on plain films (35) (Figure 7.2). Technetium-labeled bone scans are also useful in detecting bony metastasis, but can lead to false negatives in osteolytic lesions (35). This is because of the fact that bone scans identify metabolically hyperactive tissue sites, such as osteoblastic lesions, but not areas of necrosis, as seen in osteolytic lesions. CT scans are the imaging modality of choice when evaluating the integrity and quality of the bone affected by metastatic lesions. This is particularly important when determining the likelihood of impending fracture and the role of conservative versus surgical intervention. When spinal and leptomeningeal spread is of concern, MRI with and without gadolinium is the diagnostic test of

**FIGURE 7.2** Metastatic osteolytic lesions of the humeral head.

I. MEDICAL COMPLICATIONS

MRI with and without gadolinium is also useful to confirm a metastatic deposit in bone and to further describe the size and borders of the lesion (Figures 7.3 and 7.4).

Osseous metastatic spread is an important complication for a few reasons: (a) it may carry important prognostic information; (b) it may lead to severe pain that limits the

**FIGURE 7.3** MRI with and without gadolinium showing diffuse metastatic disease with gross epidural extension at T8.

**FIGURE 7.4** T2-weighted MRI showing abnormal marrow signal in the junction of the body and spine of the scapula with disruption of the cortex representing metastatic lung cancer of the scapula.
ability to participate in inpatient physical therapy sessions; (c) it may lead to increased fracture risk and inhibit the ability to participate in therapy; and (d) it often requires treatment, including possible surgical fixation. In the inpatient rehabilitation setting, it is the last three points listed here that the physiatrist must be concerned about. This is not to minimize the importance of the overall prognosis of the patient, but rather to focus on the goal of minimizing risk while optimizing participation in skilled therapy sessions that enable the patient to return home with the highest level of independence attainable.

Surgical versus nonsurgical management of osseous metastases that pose a fracture risk remains controversial. Although not validated by clinical practice, the most commonly used grading scale for fracture risk is one based on a retrospective study by Mirels (36). This scale incorporates the anatomic location, lesion type, size, and pain intensity. Each category is scored 1 to 3, with 3 representing more severe disease, and a total of 12 points possible. He proposes prophylactic surgical fixation for a score of 9 or above, but again, this scale has not been validated in clinical practice (Table 7.1).

Conservative treatment for bony metastasis aims at controlling pain, maintaining or restoring function, and preventing bone degradation/fracture occurrence. Several recent studies have shown evidence for the empiric use of bisphosphonates, which reduce the risk of vertebral fracture, time to first skeletal event, and pain associated with metastatic disease (37). Pain is initially treated with NSAIDs, nonopiate medications, and then with opiates as necessary. Pain that is not ameliorated by these measures can be treated with external beam radiation, which continues to be the cornerstone of symptomatic osseous metastatic treatment (38). More recently, efforts have been focused on stereotactic radiosurgical techniques, which are more selective of the tumor and spare healthy tissue in the surrounding vicinity. Those treated with external beam radiation typically undergo 10 fractions of 300 cGy, although many different regimens exist and studies show relative equivalent efficacy among them (38,39). Immediately following radiation therapy, long bones may be at an increased risk of fracture and protected weight-bearing for the first few days is recommended.

**TABLE 7.1 Mirels’ Criteria**

<table>
<thead>
<tr>
<th>Score</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Site</td>
<td>Upper limb</td>
<td>Lower limb</td>
<td>Peritrochanteric</td>
</tr>
<tr>
<td>Pain</td>
<td>Mild</td>
<td>Moderate</td>
<td>Functional</td>
</tr>
<tr>
<td>Lesion</td>
<td>Blastic</td>
<td>Mixed</td>
<td>Lytic</td>
</tr>
<tr>
<td>Size</td>
<td>&lt;1/3</td>
<td>1/3 to 2/3</td>
<td>&gt;2/3</td>
</tr>
</tbody>
</table>

Score > 8 suggests prophylactic fixation.

Pathologic fractures of the pelvis and vertebral bodies are typically treated conservatively, with bracing and protected weight-bearing. For vertebral fractures, bracing, restricted range of motion of the spine, and occasionally vertebroplasty are the treatment options of choice. Fractures of the acetabulum, femur, tibia, and humerus are typically treated surgically, with immediate weight-bearing postoperatively.

The physical therapist is expected to be knowledgeable regarding pathologic fracture risk. Unless otherwise directed, a limb with osseous metastatic lesions should be protected against weight-bearing, and passive and active range of motion exercises should be minimized. The rehabilitation goals from a therapy perspective are to train the patient in donning and doffing protective braces as well as in the use of assistive devices.

CONCLUSION

Caring for cancer patients in an acute inpatient rehabilitation unit can be a challenging yet rewarding experience. While rehabilitation aims at restoring function and independence in all patients, cancer patients tend to present with a more complicated medical picture that makes their inpatient rehabilitation course more precarious. However, through effective communication between medical/surgical oncologists and the rehabilitation team, accurate diagnosis and treatment plans, as well as goal-directed rehabilitation plans that are specifically tailored to each patient, rehabilitation inpatient units can provide an invaluable service to cancer patients. As our treatments for various cancers continue to improve and the quantity of life is extended, it is the goal of the oncologic rehabilitation team to ensure that quality of life is restored in our cancer patients.

Complication Timeline for Cancer

<table>
<thead>
<tr>
<th>Complication</th>
<th>Onset of Complication</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Altered mental status</td>
<td>Variable</td>
<td>Possibly because of primary brain tumor, new onset metastasis, whole brain radiation, infection, metabolic, medication. Other causes similar to general inpatients</td>
</tr>
<tr>
<td>Cancer treatment</td>
<td>Early and late</td>
<td>Fatigue, nausea, vomiting, diarrhea associated with chemotherapy Skin changes, pain, neurologic decline, fatigue associated with radiation</td>
</tr>
<tr>
<td>Cardiac complications</td>
<td>Early and late</td>
<td>Hormonal imbalances (antiestrogens in breast cancer, which inhibit the beneficial effects of estrogen on CAD), cardiac toxicity due to chemotherapeutic agents, radiation induced cardiac fibrosis, cardiomyopathy, primary or metastatic cardiac tumors (rare) Deconditioning due to prolonged bed rest</td>
</tr>
</tbody>
</table>

(continued)
## Complication Timeline for Cancer (continued)

<table>
<thead>
<tr>
<th>Complication</th>
<th>Onset of Complication</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrointestinal</td>
<td>Early and late</td>
<td>Chemotherapy-induced nausea and vomiting, bowel obstructions, ostomies, primary and metastatic tumors, diarrhea, stomatitis, radiation gastropathy, GVHD, infections (<em>Clostridium difficile</em>, etc.)</td>
</tr>
</tbody>
</table>
| Hematologic   | Early and late         | Anemia, neutropenia, thrombocytopenia  
Avoid exercise if Hb < 8  
Avoid exercise if Plt < 20,000  
Avoid activity with ANC < 2,000  
Hyperviscosity syndrome  
Primary hematologic cancers |
| Infections    | Early or late          | Cancer patients at increased risk due to chemotherapeutic agents  
UTI, PNA, cellulitis, GI infections increased in cancer population |
| Pain          | Early and late         | Acute/chronic pain from the tumor itself, invasion of healthy tissues/neural structures (brachial plexitis), associated pathologic fractures, chemotherapy-induced peripheral neuropathy, radiation fibrosis  
Cancer patients can have noncancer related pain (HNP causing radiculitis)  
Central pain syndromes, funicular pain, CRPS |
| Pulmonary     | Late                   | Radiation pneumonitis (with direct radiation insult to lungs), chemotherapy pneumonitis, primary or metastatic pulmonary cancer, pneumonia, pleural effusions, COPD |
| Renal         | Early and late         | Primary or metastatic kidney cancer, tumor lysis syndrome, multiple myeloma, lymphoma, long-term NSAID use, contrast-induced nephrotoxicity, chemotherapy-related renal disease |
| Thromboembolic | Early and late         | DVT is the most common thrombotic event in cancer patients. Due to inflammatory cytokines, immobility, and cancer treatments  
Virchow’s triad  
Tumor emboli  
Arterial thrombosis  
Increased risk for PE |

ANC, absolute neutrophil count; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; DVT, deep vein thrombosis; CRPS, complex regional pain syndrome; GI, gastrointestinal; GVHD, graft versus host disease; Hb, hemoglobin; HNP, herniated nucleus pulposus; PE, pulmonary embolism; Plt, platelet; PNA, pneumonia; UTI, urinary tract infection.
REFERENCES


Amputations

Tamar Ference and German Ojeda-Correal

A limb loss is a major event for the patient and his or her family. It represents changes in body image, confidence, perception of the environment, and relationships with others. Patients with an amputation require a multidisciplinary approach with holistic treatment to maximize function. Sometimes a return to full function is not possible; however, an effort must be made to restore as much function as we can. Sometimes this process has many obstacles that make it more difficult for the patient to return to his or her previous level of functionality.

Some of those obstacles include the medical complications surrounding the amputation. In this chapter, common complications of amputation are described, and the epidemiology and etiology of amputations, factors that influence the level of amputation, the general rehabilitation approach to the patient with an amputation, and the treatment of medical complications are also discussed.

Sometimes the physiatrist has to approach the amputee patient in different stages of the disease—sometimes before the surgical procedure, sometimes after. It is important to cover the following topics no matter when the patient is approached: education, emotional support, pain control, patient safety/falls, complication prevention, incentive spirometry, tobacco cessation, bowel/bladder management, deep vein thrombosis (DVT) prevention, physical therapy/conditioning, contracture prevention, pressure ulcer reduction, edema control, sequence of amputation care, prosthetic options, role of interdisciplinary team members, peer support, protection of contralateral limb, and nutritional support.

However, to have the best results for the amputee and lower the incidence of complications, this has to be done as a team effort. The team includes the patient and his or her family, the surgeon, physiatrist, prosthetist, therapist, psychologist, social worker, recreational therapist, and nurse.
MEDICAL COMPLICATIONS IN PATIENTS WITH AMPUTATIONS

Epidemiology

The annual estimate of limb amputations in the United States is around 185,000 persons. The ratio of transfemoral amputations to transtibial amputations is 30:70. There are 1.6 million people living with limb loss, and around 27.6% are transtibial amputations, 25.8% are transfemoral amputations, and 42.8% are numerous other levels. Of the patients who undergo a lower limb amputation as a result of peripheral vascular disease, 26% will be readmitted for a subsequent amputation (1,2). Trauma is the main cause of amputation in the upper extremity in around 90% of the cases; finger amputation is the most common (78%) followed by transradial.

Etiology

The most common etiology for lower limb amputation is peripheral vascular disease (82%), followed by trauma (16%), and cancer (2%). The incidence of amputations because of peripheral vascular disease has been increasing, while the incidence of amputation as a result of trauma has been decreasing (2).

The most common cause of amputation in the upper limb is trauma, followed by malignancies, congenital deformities, peripheral vascular disease, infections, neurological disorders, and other causes.

Risks for amputation due to peripheral vascular disease increase with age in both sexes and in all racial groups. Men are at higher risk than women for trauma-related amputations (2). The risk of traumatic amputations increases with age, for males and females. There are no differences in the risk of cancer-related amputations between males and females.

Infection, occurring directly or indirectly, is another cause of amputation. In direct infection, the compromise of soft tissues and bone is severe and the infection itself cannot be controlled. Indirect infection occurs when medications used during sepsis create vasoconstriction and ischemia.

A transtibial amputation is indicated when attempts at salvage and reconstruction have been exhausted and when function is severely impaired after multiple procedures. The physiologic advantages of a transtibial amputation are listed in Table 8.1.

The appropriate level of amputation depends on several factors:

- Patient’s general condition, comorbidities, risk for additional surgeries
- Potential for healing
  - Objective data: palpable pulses, angiographic findings, Doppler pressure measurement, pulse volume recordings, photoplethysmographic pressures, transcutaneous oxygen determinations, and other data
1. Medical Complications

- Subjective data: appearance of the tissues at the time of the surgery, bleeding, skin color, and temperature
- Probable functional outcome
- Patient’s goals and considerations
- Prosthetic options
- Cosmesis
- Biomechanics of the residual limb

Regarding upper limb amputations, every level has advantages and disadvantages:

- Transradial: very functional; the strength and rotation is proportional to the length of the residual limb; it is important to preserve the elbow joint; if the etiology is vascular, distal third amputations will have healing issues.
- Above the elbow amputations or transhumeral: the most important concept at this level is to preserve length; distal third amputations are preferred more than elbow disarticulation because of the better fitting of the prosthesis with the elbow joint.

**Approach and Management of the Amputee**

The amputee patient has to be addressed at different stages of the disease, sometimes before the surgical procedure, and sometimes after. However, it is important to cover different areas related to evaluation and education of the amputee.

1. Preoperative phase: During this phase it is important to cover the following topics: need for education, emotional support, pain control, patient safety/falls, complication prevention, incentive spirometry, tobacco cessation, bowel/bladder management, DVT prevention, physical therapy/conditioning, contracture prevention, pressure ulcer reduction, edema control, sequence of amputation care, prosthetic options, role of interdisciplinary team members, peer support, protection of contralateral limb, nutritional support.
2. Postoperative phase: During this phase the main goals of medical care are wound healing, prevention of contractures, prevention of decubiti ulcers, edema
control, prevention of pulmonary complications, DVT prophylaxis, evaluation and protection of the contralateral limb, nutritional support, skin hygiene, and prevention of infections.

3. Rehabilitation phase: The main goals of this phase are strengthening and improving activities of daily living, and reintegrating to the home environment. However, this phase overlaps with the two previous phases, thus the sooner all these activities are started with the patient, the better the results will be. The prevention of contractures, edema control, protection of the contralateral limb, skin hygiene and maintenance, emotional and nutritional support have to be continued.

4. Prosthetic training phase: Once the patient receives the prosthesis, gait training with the new prosthesis starts, as well as the care of the prosthesis. It is important to continue with emotional support, pain control, patient safety/falls, physical therapy, conditioning, contracture prevention, edema control, peer support, protection of contralateral limb, nutritional support, awareness of signs and symptoms of infection, skin hygiene, and help in donning/doffing prosthesis.

5. Long-term follow-up phase: During this phase the main goal will be a greater social reintegration, and maximizing functional independence. Continued assessments and evaluations will be required in order to maintain proper prosthetic fit and to prevent complications of the contralateral limb.

The above goals can only be achieved through team effort. The team consists of the patient and his or her family, the surgeon, physiatrist, prosthetist, physical and occupational therapist, psychologist, social worker, recreational therapist, and nurse.

Care of the residual limb
Appropriate care of the residual limb is important in order to speed up the recovery process. It has to be dressed, either with a soft compressive dressing (see Figures 8.1 and 8.2) or with a rigid dressing. The main goal is to reduce the swelling, to improve the healing process, to minimize the inflammatory reaction, and to decrease the possibility of residual pain or phantom pain (3).

![Figure 8.1](imageurl) The correct way to apply soft dressing in a transtibial amputation.
Once the wound is healed and sutures or staples have been removed, the next step is to continue with the reshaping of the residual limb, decreasing its volume with an elastic shrinker sock. The process can be continued with ace wraps; however, the shrinker sock provides even better pressure and is easier to apply. It needs to be worn day and night, and it can be removed only for skin care. Two or more shrinker socks should be available for the amputee to be interchanged. Once the shrinker sock has lost the compressive force, it should be replaced by a new one.

Prevention of contractures
During the postoperative phase and the rehabilitation phase it is really important to follow some recommendations to prevent contractures of the residual limb.

- If the patient is in a chair or a wheelchair, his knee should be straight. A board can be used under the patient’s thigh and knee. It is not advisable to place a pillow, sheet, or towel under the knee.
- If the patient is on the bed, lying down, the knee should be kept straight. It is not advisable to place a pillow, sheet, or towel under the knee.
- It is not advisable to put weight or pressure on the end of the residual limb.
- It is important to perform knee range of motion exercises several times a day.

Psychological trauma of limb loss
Losing a part of the body is a different experience for everyone. Feelings and reactions are different, and depend on internal (personality, beliefs, psychological status, and so on) and external factors (circumstances of the amputation, family support, medical support, psychological support, and so on).
The psychological support for the amputee begins in the preoperative phase. During this phase, the patient should be given as much information as possible about the surgical procedure, recovery process, rehabilitation, and prosthetic options. It is important to discuss expectations. Sometimes peer support will help to answer questions and clarify expectations.

It is important to approach the amputee’s family to discuss with them how to approach, how to help, and how to prepare the environment. The family will be an important factor in the rehabilitation process, and if the family is well informed, this process will be easier or less traumatic.

Complications

Early complications
As in any surgical patient, there must be awareness of complications not directly related to the amputation. Pulmonary, genitourinary, and vascular complications can accompany the recovery of these patients, and must be prevented or treated early in order to speed up the functional improvement of the patient.

- Atelectasis: It is the collapse of alveoli that reduces the gas exchange surface. The most common symptom is fever in the early postoperative state. It is diagnosed by x-ray. It can be prevented by using an incentive spirometer, ambulation, and respiratory therapy. If these measures do not improve the symptoms, the next step will be a fibrobronchoscopy.

- DVT/pulmonary embolism (PE): This is another possible complication, common in all these patients, caused by immobility, stasis, and hypercoagulable state. These patients have to be on prophylaxis for DVT with fractionated heparin (low molecular weight heparin [LMWH]) unless there is a contraindication.

- Wound-related complications: One of the most common wound-related complications is delayed healing. Multiple causes can contribute to delay in healing: poor perfusion, infection, inadequate surgical technique (excessive tension on muscles, fascia, subcutaneous tissue, or skin during the surgical procedure or because of the sutures), premature removal of the sutures, poor nutritional status, and trauma. Once a delayed healing happens, the most important thing is to recognize the cause and correct it; if it is not corrected, the scar will be susceptible to opening, easy excoriations, and other complications. Vascular and nutritional studies should be done or reevaluated. If the cause is an infection, the patient may need adequate debridement and lavage, and antibiotic coverage. Transcutaneous oxygen pressure can be determined to evaluate the possibility of using hyperbaric oxygen therapy (3).

- Skin adherence: It is important to provide adequate soft-tissue coverage for the distal bone to prevent adherence of the incisional scar. One of the consequences of skin adherence is the loss of mobility, and loss of resistance
to shear forces when wearing prosthetics. It is important to massage the incisional scar for skin release.

Shape issues: Suboptimal surgical techniques end in shape issues of the residual limb. Redundant skin and muscle will delay the shrinkage process and the prosthetic fitting. Failure in the proper application of the soft or rigid dressings will create an abnormal shape of the residual limb leading to delays in prosthetic fitting (3).

Contractures: Range of motion of the knee is important while the patient is seated on a chair or lying in bed. Prolonged sitting positions with a flexed knee, comfortable positions of the knee (flexed) with pillows, sheets, or towels under the knee will end up in flexion contractures. It is important to explain to the patient the importance of a full range of motion of the knee, and full knee extension. Flexion contractures will affect the prosthesis design, fitting, and gait pattern.

Phantom limb sensation: This could be called a normal situation where the patient continues to sense the amputated part of the limb after the surgical procedure; most of the amputees experience this phenomenon, and the length of time it lasts varies. For some it lasts a few months, while in others it can last for years. Hypnosis therapy, massages, biofeedback, or mirror therapy can help in the management.

Phantom limb pain: It is described as pain in the portion of the limb that was amputated. The incidence ranges from 47% to 79% (4–6). Its time of presentation is right after surgery until 2 weeks after. The real cause is unknown; however, the theory states that this pain is the result of nerve injury, associated with changes in the brain, spinal cord, or peripheral nerves; and it has been associated with the severity and chronicity of the pain before the amputation.

The distribution of pain can be localized or generalized to the entire extremity. The presentation varies from neuropathic type to nociceptive type. The severity as well as its duration and frequency are variable.

Its treatment includes medications such as antidepressants, anticonvulsants, sodium channel blockers. Treatments also include spinal cord stimulation, electrical stimulation, vibration therapy, acupuncture, hypnosis, biofeedback, mirror therapy, relaxation techniques, massage, injection therapy, surgical therapy, and other therapies. Depending on the target area, treatments can be:

Supraspinal
- Deep brain stimulation
- Mirror therapy
- Motor cortex stimulation
- Hypnosis, biofeedback, guided imagery
- Opioids, anticonvulsants
Spinal cord
- Spinal cord stimulation
- Sodium channel blockers
- N-methyl-D-aspartate (NMDA) antagonists, opioids

Peripheral
- Injections with local anesthetics, botulinum toxin, corticosteroids
- Pulsed radiofrequency
- Surgery: neuromodulatory techniques and reconstructive techniques
- Peripheral nerve stimulation

Depending on the medication, treatments can be:

- Antidepressants
  - Amitriptyline start 10 mg/day titrated to maximum 125 mg/day
- Anticonvulsants
  - Gabapentin titrated to 3,600 mg/day
  - Carbamazepine in doses of 300 to 600 mg/day
  - Pregabalin in doses of 25 to 300 mg/day
- Sodium channel blockers
  - Lidocaine
  - Bupivacaine
- Opioids
  - Extended-release oral morphine in doses of 70 to 300 mg/day

Specific treatment guidelines with evidence-based support have not been established; multidisciplinary approaches (pharmacological therapy combined with adjuvant or no pharmacological therapy) have shown better results.

Chronic complications
- Wound sinus: Healed surgical wounds with a small opening and chronic discharge should sound the alert for a possible osteomyelitis. It is important to perform ultrasound, x-rays, cultures, excision of the sinus, and, possibly treat with antibiotics.
- Chronic pain: Chronic pain in the residual limb can be secondary to different causes. These have to be differentiated through history, physical exam, and imaging studies to have a clear diagnosis. One common cause of pain is hypermobility of the fibula because of the disruption of the interosseous membrane. A tibiofibular synostosis procedure will resolve the issue. Another cause of pain is at the level of the distal anterior part of the tibia, due to inadequate contouring of the distal tibia. Sometimes an additional cause of pain is a neuroma formation, with a positive Tinel’s sign. Heterotopic ossification also is a common cause in traumatic amputations.
Multiple treatments have been proposed:

- Socket modifications
- Local injections: anesthetics, corticosteroids, botulinum toxin
- Surgical reconstruction
- Surgical excision
- Peripheral nerve reconstruction
- Peripheral nerve stimulation
- If there is no physical abnormality in the residual limb, then any of the other alternatives mentioned in phantom limb pain can be used

**Choke syndrome (verrucous hyperplasia):** This syndrome is most common in the transtibial amputee and in amputees due to vascular reasons. The number one cause is a tight proximal fitting of the socket on the residual limb; the second most common cause is the inappropriate use of socks inside the socket. This obstruction of the venous flow will produce vascular congestion, erythema, edema, and color changes. The chronicity of this external compression over the residual limb will result in verrucous hyperplasia. If the symptoms persist, crackling of the skin can occur and then infection.

The treatment consists in a modification of the socket, looking for a perfect fit, and within weeks or months the syndrome will be resolved. In addition, an adequate training of the amputee in how to use liners and socks should be provided.

### Complication Timeline for Amputation

<table>
<thead>
<tr>
<th>Complication</th>
<th>Onset of Complication</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Early/Acute</td>
</tr>
<tr>
<td>Atelectasis</td>
<td>X</td>
</tr>
<tr>
<td>Deep vein thrombosis</td>
<td>X</td>
</tr>
<tr>
<td>Wound infection</td>
<td>X</td>
</tr>
<tr>
<td>Skin adherence</td>
<td>X</td>
</tr>
<tr>
<td>Contractures</td>
<td>X</td>
</tr>
<tr>
<td>Phantom limb sensation</td>
<td>X</td>
</tr>
<tr>
<td>Phantom limb pain</td>
<td>X</td>
</tr>
<tr>
<td>Wound sinus</td>
<td>X</td>
</tr>
<tr>
<td>Chronic pain</td>
<td>X</td>
</tr>
<tr>
<td>Choke syndrome</td>
<td>X</td>
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</tbody>
</table>
REFERENCES

Rehabilitation inpatient facilities host a heterogeneous group of patients. The age of such patients varies widely as does the range of their conditions, which includes neuromuscular diseases, brain injuries, stroke, spinal cord injuries, burns, fractures, prosthetic joint replacement, organ transplants, and conditioning following long-term hospitalizations. Consequently, special considerations are required in the evaluation of fevers since different patient groups may exhibit atypical symptoms of infection.

Fever is a frequent complication in patients in long-term care facilities (LTCF) and rehabilitation units. Among patients with spinal cord injury (SCI), the incidence of fever during rehabilitation is reported to be between 50% and 86% in several studies (1). Infections are the most common cause of fever. Several studies have shown that urinary tract infection (UTI), particularly catheter-associated (CA) UTI, is the most common infection in an LTCF as well as a rehabilitation unit (1,2), followed by respiratory infections (3–5). Noninfectious conditions such as thromboembolic disease, drug fever, thermo-regulatory dysfunction, and in SCI heterotopic ossification must also be considered. Furthermore, the absence of fever does not rule out infection as typical signs and symptoms of infection may be absent, particularly in elderly patients (6).

Patients in rehabilitation facilities have a high prevalence of multidrug resistant (MDR) organisms as most patients are admitted after an acute hospital stay (7), and they often have been exposed to antimicrobials during this time. As a result, treatment considerations are often more challenging in these patients (8). This chapter focuses on the etiology, evaluation, and management of fever in the patient undergoing inpatient rehabilitation.

DEFINITIONS

Fever has been defined using different thresholds in different populations, but it is reasonable to define it as an oral temperature >38°C in a hospitalized patient. Lower
temperatures may represent fever in some patients, as in the patient who has a persistent increase in temperature above his or her baseline observed over previous days in the hospital. In an immunosuppressed/neutropenic patient, fever has been defined as a single oral temperature >38.3°C or a temperature of 38.0°C sustained over one hour (9). Fever of unknown origin (FUO) in adults has been defined as a persistent temperature >38.3°C over three or more weeks without an established cause and with at least 1 week of monitoring and investigation in the hospital (10). Hypothermia has been defined as a core temperature of 36°C or lower, and may signify severe infection or even sepsis (4).

TERMS USED TO DESCRIBE SEVERE INFECTIONS

Fever may be an indicator of severe infection. Definitions of terms used to describe severe infection are shown in Table 9.1. It is important to recognize the severity of illness early so that the patient can receive appropriate therapy and adequate monitoring as early as possible. Systemic inflammatory response syndrome (SIRS) is a nonspecific term used for inflammation that can be caused by infectious or noninfectious causes such as trauma, burns, pancreatitis. In the immunocompetent adult host, the presence of SIRS suggests the presence of bacteremia (11). When SIRS is caused

| TABLE 9.1 Definitions of Terms Used to Describe Severe Infection or Noninfectious Syndromes |
|---------------------------------------------------------------|---------------------------------------------------------------|
| SIRS—The diagnosis of systemic inflammatory response syndrome (SIRS) requires at least two of the conditions in the column to the right (4) | Temperature >38°C or <36°C |
| | Heart rate >90 beats/min |
| | Respiratory rate >20 breaths/min or arterial PCO₂ <32 mmHg |
| | WBC count >12,000/mm³ or <4000/mm³ or >10% immature (band) forms |
| Sepsis | When SIRS is the result of an infection, the condition is called sepsis. |
| Severe sepsis | When sepsis is accompanied by dysfunction in one or more vital organs, the condition is called severe sepsis. |
| Septic shock | When severe sepsis is accompanied by hypotension that is refractory to volume infusion, the condition is called septic shock. |
| Multiorgan dysfunction syndrome (MODS) and multiorgan failure (MOF) (12) | Abnormal function in more than one vital organ is called multiorgan dysfunction syndrome and failure of more than one organ system is called multiorgan failure. |
by infection, the term “sepsis” is often used. It is very important that patients with severe sepsis, septic shock, or multiorgan dysfunction be fluid resuscitated, started on broad-spectrum antimicrobial therapy, and transferred to an intensive care setting for appropriate therapy and monitoring as quickly as possible.

ETIOLOGY OF FEVER

The most common causes of fever in patients in a rehabilitation unit are shown in Table 9.2. The most common cause is infection, and the most common infection is UTI, primarily CA-UTI, followed by respiratory tract infection and soft tissue infection (1,4,13). Gastrointestinal infections, including Clostridium difficile colitis, bacteremia, and prosthetic device infections are also common (3). In a study of SCI patients in a rehabilitation unit, it was found that fever was caused by UTI in 70% of the cases, upper respiratory tract infection in 9.6%, pneumonia in 3.2%, and wound infection in 3.2% (1).

The National Healthcare Safety Network at the Centers for Disease Control and Prevention reported in their annual update 2006 to 2007 that the most common bacteria causing hospital-acquired infections (HAI) were coagulase negative staphylococci and Staphylococcus aureus, followed by Enterococcus species, Candida, Escherichia coli, Pseudomonas aeruginosa, and Klebsiella pneumoniae. As many as 16% of all HAIs were associated with MDR pathogens, including the following: methicillin-resistant S. aureus (MRSA) (8% of HAIs), vancomycin-resistant Enterococcus faecium (4%), carbapenem-resistant P. aeruginosa (2%), extended-spectrum cephalosporin-resistant K. pneumoniae (1%), and extended-spectrum cephalosporin-resistant E. coli (0.5%) (14). These bacteria can cause infections at almost any site and complicate the choice for empiric antimicrobials. Infected patients in whom MDR organisms

<table>
<thead>
<tr>
<th>Table 9.2 The Etiology of Fever in Patients in a Rehabilitation Unit</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Etiology of Fever</strong></td>
</tr>
<tr>
<td><strong>Infectious Causes</strong></td>
</tr>
<tr>
<td>Catheter-associated UTI</td>
</tr>
<tr>
<td>Pneumonia</td>
</tr>
<tr>
<td>Skin and soft tissue infection and osteomyelitis</td>
</tr>
<tr>
<td>Clostridium difficile colitis</td>
</tr>
<tr>
<td>Bacteremia and endocarditis</td>
</tr>
<tr>
<td>Abscess</td>
</tr>
<tr>
<td>Viral illness</td>
</tr>
<tr>
<td>Other bacterial infections, tuberculosis, etc.</td>
</tr>
<tr>
<td><strong>Noninfectious Causes</strong></td>
</tr>
<tr>
<td>Drug fever</td>
</tr>
<tr>
<td>Central dysregulation</td>
</tr>
<tr>
<td>Thromboembolic disease</td>
</tr>
<tr>
<td>Other</td>
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are suspected or in whom such organisms have been cultured previously warrant consultation with an infectious diseases specialist.

INFECTIOUS CAUSES OF FEVER

Urinary Tract Infection

UTI is the most common source of fever in the rehabilitating patient and the most common health care associated infection. UTIs account for up to 40% of nosocomial infections in U.S. hospitals each year (15), and almost all are CA (16). Nosocomial UTI is the most common source of bacteremia in LTCFs, accounting for 40% to 50% of bacteremias (17). Fever in a catheterized person with bacteriuria ($\geq 10^5$ cfu/mL) in the absence of other obvious causes of the symptoms should be treated as a nosocomial UTI. The absence of pyuria in a symptomatic patient suggests a diagnosis other than CA-UTI. In a catheterized patient, the presence or absence of malodorous cloudy urine alone should not be used as a diagnostic criterion for CA-UTI (18). Signs and symptoms suggestive of UTI include dysuria, urinary urgency, or frequency and suprapubic pain. In patients with indwelling urethral or suprapubic catheters or for those who are intermittently catheterized, symptoms and signs of UTI may include new onset of fever, rigors, altered mental status, malaise, lethargy with no other identified cause, flank pain, costovertebral angle tenderness, acute hematuria, or pelvic discomfort. In patients with SCI, symptoms may also include increased spasticity, autonomic dysreflexia, and sense of unease. See Chapter 12 for a detailed discussion of UTIs in inpatient rehabilitation patients.

Pneumonia

Pneumonia is a common cause of fever in the rehabilitating patient, and the incidence varies greatly depending on the underlying condition of the patient. Pneumonia should be suspected if the patient has respiratory symptoms such as new or increased cough with purulent sputum production, increased respiratory rate, and/or hypoxemia. A chest radiograph should be obtained if pneumonia is suspected in order to identify the presence of a new infiltrate compatible with acute pneumonia and to exclude other noninfectious conditions such as volume overload, pneumothorax, pleural effusions.

Skin and Soft Tissue Infection and Osteomyelitis

Skin and soft tissue infections (SSTIs) typically occur as a consequence of physical trauma, pressure, or use of devices resulting in breaks in the skin and mucosa. Most SSTIs are bacterial, but viral infections such as herpes zoster or herpes simplex also
occur. Primary SSTIs include erysipelas, cellulitis, and folliculitis. The most common organisms isolated are *S. aureus* and beta-hemolytic streptococcus. Diagnosis and treatment decisions are made clinically. Secondary SSTIs include secondarily infected pressure ulcers. Infection is diagnosed primarily by clinical symptoms and signs such as poor healing, erythema, warmth, tenderness, and purulent discharge. Systemic symptoms may be absent. Cultures from superficial swabs do not allow one to differentiate between colonization and infection. Deeper specimens are preferred for culture, but all positive cultures need to be correlated with the clinical evidence that infection is present. Most pressure ulcer infections are polymicrobial with gram-negative bacilli, gram-positive cocci, and anaerobic flora most commonly isolated (19). Secondary infection may also involve the bone. See Chapter 14 for a further discussion of osteomyelitis in rehabilitating patients.

**Clostridium difficile Colitis**

*C. difficile* is the main pathogen found in antibiotic-associated colitis and 15% to 25% of cases of nosocomial antibiotic-associated diarrhea (20). Major risk factors include increased severity of underlying illness, increased age, prior antimicrobial use, and gastric acid suppression (21). *C. difficile* should be considered in patients with high grade fever, abdominal cramps, and/or diarrhea. Diarrhea can be bloody or nonbloody but typically contains white blood cells. See Chapter 15 for a further discussion of *C. difficile* colitis in rehabilitating patients.

**Bacteremia and Endocarditis**

Fever may be a manifestation of bacteremia and, rarely, infective endocarditis. Bacteremia may result from systemic spread of a localized infection such as UTI or pneumonia or from a central line site infection. Central line infection is an infection that may require line removal in addition to intravenous antibiotics. Bacteremia can lead to or result from infective endocarditis, which may be manifested by abrupt onset of high-grade fevers with virulent organisms such as *S. aureus* or by a more indolent course with persistent low-grade fevers. Endocarditis should be considered when several serial blood cultures with the same species are positive (22), but in up to 5% of endocarditis cases blood cultures are negative. Organisms difficult to grow on traditional culture media or those that require longer incubation periods cause the majority of episodes of culture-negative endocarditis. A transesophageal echocardiogram is more sensitive than a transthoracic echocardiogram in detecting infective endocarditis, and should be considered in patients with multiple positive blood cultures. An infectious diseases consultation should be obtained for management and treatment of infective endocarditis.
Abscess

Abscess should be suspected in the setting of persistent or intermittent fevers and/or significant leukocytosis. Occult abscesses are usually located in the abdomen or pelvis and there may be complications following intra-abdominal infections or inflammation. Risk factors include liver cirrhosis, steroid or immunosuppressive therapy, and diabetes. Pyogenic liver abscesses are usually a complication from biliary tract disease. Perinephric or renal abscesses may complicate a UTI. The urine culture may be negative if the infection does not connect with the drainage system. Splenic abscesses are usually due to hematogeneous spread complicating bacteremia, especially when bacteremia is persistent as with infective endocarditis. The diagnosis of an abscess is usually made by appropriate imaging such as a CT of the abdomen/pelvis with contrast. Generally, abscesses should be drained in conjunction with antimicrobial treatment. Consultation with surgery or interventional radiology and infectious diseases should be obtained depending on the characteristics of the abscess.

Viral Illness

Influenza can be a severe disease leading to significant morbidity and death. The risk of complicated influenza is highest in the elderly and patients with underlying medical conditions, including pulmonary and cardiac disease, diabetes, chronic renal dysfunction, immune suppression, or debilitation. Multiple influenza outbreaks have been described in rehabilitation units. The diagnosis of influenza should be considered in patients with fever and acute onset respiratory signs and symptoms during influenza season (defined as the period when influenza viruses are circulating in the community). Other signs and symptoms suggestive of influenza include myalgias, arthralgias, headache, and weakness. Nasopharyngeal wash or swab samples from the throat and nasopharynx should be collected from acutely ill patients soon after illness onset, preferably within five days. Rapid influenza tests give fast results but have low-to-moderate sensitivity and high specificity, which needs to be considered in any interpretation of the results. Influenza RT-PCR is recommended in high-risk individuals due to its high sensitivity and specificity. Early treatment with anti-viral medication may reduce the severity and duration of symptoms. Vaccination is the best method of preventing influenza, but antivirals may be used in an outbreak situation (23).

NONINFECTIOUS CAUSES OF FEVER

Drug Fever

One third of hospitalized patients suffer from adverse drug reactions (24). Fever may be the sole manifestation in 3% to 5% of cases (25). The mechanisms of drug fever
include, but are not limited to, hypersensitivity reactions, altered thermoregulatory mechanisms and reactions directly related to administration of a drug (25). Drug fever may occur shortly after initiating a medication or several weeks, months, or even years into treatment. The risk of developing drug fever increases with the number of medications prescribed, particularly in elderly patients. Antimicrobials account for one-third of the episodes of drug fever: beta-lactams, sulfonamides, minocycline, and nitrofurantoin are particularly implicated (26). Other medications commonly associated with drug fever include anticonvulsants such as carbamazepine and phenytoin, H1 and H2 blocking antihistamines, allopurinol, heparin, hydralazine, NSAIDS, amphotericin, and iodides. However, it is important to note that virtually any drug can cause fever. The diagnosis of drug fever is made by a therapeutic trial of discontinuing the suspected drug. Most patients defervesce in 72 hours once the offending drug is discontinued whereas others may take weeks to respond, depending on the pharmacokinetics of the drug.

Central Thermal Dysregulation

Central thermal dysregulation causing fever or a blunted temperature response may follow hypothalamic dysfunction after brain injury such as that caused by massive stroke or anoxic brain injury. In patients with SCIs, disordered temperature regulation may occur in patients with higher level of injury and rarely accompanies autonomic dysreflexia (27). It is critical, however, to rule out infection before attributing fever to central thermal dysregulation.

Thromboembolic Disease

Thromboembolic disease can cause low-grade fever. Thus, the clinician should include deep vein thrombosis and pulmonary embolism in the differential diagnosis of a febrile patient. Septic thrombophlebitis may be associated with bacteremia and high-grade fevers. Diagnosis of thromboembolic disease is made by visualizing a clot in the appropriate clinical setting in the absence of other likely sources of infection.

Other Potential Causes

Other potential causes of fever include hematoma with subsequent inflammation, endocrine disorders such as pheochromocytoma and adrenal insufficiency, inflammatory conditions such as giant cell arteritis, Wegener’s granulomatosis, adult stills disease, and polyarteritis nodosa, and malignancies such as lymphoma, leukemia, renal
cell carcinoma, hepatocellular carcinoma, or liver metastasis. Some patients with underlying psychiatric illness fabricate or induce fever (factitious fever) by factors such as the intake of medications and/or injection of foreign material. This condition more commonly affects women and health care workers.

EVALUATION OF THE FEBRILE PATIENT

Given that the most common reason for fever in a rehabilitation unit is infection, the febrile patient should be evaluated systematically for the common causes of infections in this population. An appropriate evaluation includes a thorough physical examination, a chart review with special attention to past medical history, recent procedures, and medication list, and a careful history to elicit symptoms suggestive of a genitourinary, respiratory, abdominal, skin, or bone infection. A thorough physical examination should include assessment of vital signs, severity of illness, and cardiovascular, pulmonary, abdominal, skin, and mental status. All catheters, intravenous devices or drainage tubes should be visualized and the surrounding skin should be evaluated for warmth, erythema, or purulent discharge. Laboratory evaluation should include a complete blood count (CBC) to look for an abnormal white blood cell count, bandemia, and an abnormal platelet count; tests for kidney function, electrolytes, liver function, and lactate levels; urinalysis; and urine and blood cultures. Microbiologic cultures should be obtained prior to initiating empiric antimicrobial therapy in febrile patients. Additional investigation should be guided by signs and symptoms and may include stool studies, including *C. difficile* toxin, chest radiograph, lumbar puncture, and abdominal imaging (11).

If no clear etiology of a fever is identified, a high index of suspicion for infection should still be maintained. Line infections with associated bacteremia often do not exhibit any local signs of infection, and UTI may be present without the typical signs or symptoms of infection. Cultures should be performed in such patients, but results are typically not available for at least 24 hours; importantly, in severely ill patients, initiation of empiric antimicrobial therapy should not be delayed.

SPECIAL CONSIDERATIONS REGARDING MICROBIOLOGIC CULTURES

Regardless of site, diagnostic cultures should be obtained before the start of antimicrobials to identify the offending organism and to guide the tailoring of antimicrobials. Cultures should be obtained in a way that minimizes contamination and should be sent to the laboratory as soon as possible, or refrigerated if there is to be a delay of more than a couple of hours. Appropriate information should be provided to the microbiology laboratory to maximize the usefulness of the culture.
For example, the microbiology laboratory should be able to report to the clinician as to whether a blood culture was obtained from a peripheral venipuncture or from an intravascular catheter, and whether a urine culture was from a voided specimen or a catheter specimen. There are very few reasons to repeat cultures in patients on antimicrobials, but they may be appropriate, for example, if one is treating an intravascular infection in which case it is important to ensure that the antimicrobial is sterilizing the bloodstream or if new or worsening symptoms occur on treatment and one suspects another infection.

**Blood Cultures**

The volume of blood obtained is one of the most important factors affecting the sensitivity of blood culture systems. The preferred volume is 20 mL (28). Blood cultures should not be drawn from intravascular devices unless one is specifically looking for line infection, and even then the culture should be paired with another culture obtained by peripheral venipuncture (29). The presence of fever at the time of blood culture collection does not improve the sensitivity or specificity for detection of bacteremia.

Two blood cultures are usually sufficient to detect bacteremia in the majority of patients. The two blood cultures (each 20 mL) should be obtained from two separate venipuncture sites using antiseptic techniques to clean the skin. The aim of obtaining two blood cultures is to detect bacteremia caused by infections that originate outside the bloodstream (such as intra-abdominal infection, pneumonia, or UTI) that tend to be intermittent in nature or to diagnose line infection as noted above. A single blood culture is insufficiently sensitive to detect certain bacteremias and fungemias. In addition, a single blood culture positive for an organism that is a common contaminant (such as coagulase-negative staphylococcus) makes it difficult to distinguish between contamination and true infection. Therefore, a single blood culture is not recommended as part of a fever workup.

Continuous bacteremia is suggestive of an intravascular infection such as infective endocarditis, endovascular catheter infection, or suppurative thrombophlebitis. Continuous bacteremia can be confirmed in the presence of two positive blood cultures with the same organism drawn more than 12 hours apart or culture positivity in all of three or a majority of four or more separate blood cultures with the first and last drawn at least one hour apart (Duke criteria) (22).

**Urine Cultures**

The urine sample should be obtained from a freshly placed catheter if the catheter has been in place for a few days as the catheter biofilm may result in spurious culture results (30).
Moreover, there are clinical outcome benefits associated with replacing a catheter prior to antimicrobial treatment if the catheter has been in place for several days (31). Obtaining a urine sample from the drainage bag is not recommended as microbial flora may not accurately reflect the bacteria in the bladder and may lead to inappropriate antimicrobial use.

Respiratory Cultures

Sputum samples should be obtained on all patients with suspected pneumonia. The samples can be either expectorated or suctioned endotracheal secretions depending on whether the patient is intubated or has a tracheotomy in place. To improve the yield of the sample, the specimen should be collected from deep in the respiratory tract whenever possible, obtained prior to starting antimicrobials, and processed soon after collection, ideally within 2 hours. Microbiology in expectorated sputum samples is often difficult to assess due to contamination from the upper airways. Therefore, it is very important to assess the quality of the sample, as described below, to determine if it is adequate for use. If a submitted specimen is rejected as unsuitable for culture, the clinician should be notified, and a repeat specimen should be requested. Urinary antigen testing to detect *Streptococcus pneumoniae* or *Legionella pneumophila* (serogroup 1) can be considered if available. The sensitivity of the urinary antigen test for *S. pneumoniae* is about 75%, but the specificity is approximately 90%. The test characteristics for urinary antigen testing for legionella serogroup 1 are similar but less useful unless there is an outbreak of legionella pneumonia in the institution (32).

Wound Cultures

Superficial wound cultures of pressure ulcers cannot be used to differentiate between colonization and infection because their surfaces are always colonized with bacteria. Nevertheless, superficial cultures are frequently performed, and this often leads to inappropriate broad-spectrum therapy in an attempt to cover all the potential pathogens isolated. Thus, patients are often on antimicrobial treatment prior to subsequent attempts to obtain more appropriate deep cultures in cases of SSTIs and osteomyelitis. In the setting of a pressure ulcer with poor healing and/or persistent purulent discharge, it is optimal to obtain a deep specimen for culture of tissue and bone at the time of surgical debridement or biopsy.

INTERPRETATION OF MICROBIOLOGIC CULTURES

Blood Cultures

To appropriately interpret blood culture results, it is important to take into account the patient’s history, clinical presentation and condition, how and from where the blood
cultures were obtained, and how many bottles were drawn (see previous section). An organism is more likely to represent a true pathogen if more than one blood culture obtained at separate venipuncture sticks is positive for the same species or if the same species is present in a blood culture as well as in a culture from another normally sterile site. Blood cultures that turn positive after five days of incubation are often contaminants. Exceptions include certain microorganisms such as mycobacteria and dimorphic fungi that require longer incubations. The identity of the organism can also give clues as to whether it is likely in the bloodstream or a contaminant from the skin. Examples of microorganisms that almost always should be assumed to be true pathogens when isolated from the bloodstream include \textit{S. aureus}, \textit{E. coli} and other Enterobacteriaceae, \textit{P. aeruginosa}, \textit{S. pneumoniae}, \textit{Candida} spp. (28), Bacteroidaceae, and \textit{Hemophilus influenza}. On the other hand, isolates from the broth only that rarely represent true bloodstream infection include corynebacteria, \textit{Bacillus} spp., and propionibacteria, but these organisms may cause infections in certain patient groups (eg, patients with orthopedic devices or prosthetic heart valves). Coagulase negative staphylococci are often difficult to distinguish between pathogen and contaminant. Yeasts and other fungi are generally always considered true pathogens. In general, positive blood cultures should be repeated after treatment has been initiated to ensure clearance. If a patient with a central line in place has positive blood cultures, the line generally should be removed and ID consultation should be requested, particularly in the setting of MRSA or candida infections (33).

\textbf{Urine Culture}

Interpretation of urine cultures is discussed in the UTI chapter (see Chapter 12).

\textbf{Sputum Cultures}

For a sputum sample to be considered adequate, the gram-stain should have polymorphonuclear leukocytes (PMNs) but a low or absent number of squamous epithelial cells per low power field. Culture results are reported in a semiquantitative manner, and most true pathogens are present in at least moderate amounts. Given that organisms can colonize the respiratory tract, especially in patients with chronic illness or recent hospitalization, the diagnosis of pneumonia must be based on clinical rather than solely on laboratory criteria. Any positive sputum culture result must therefore be interpreted in the context of the clinical setting. Some organisms should virtually never be considered pulmonary pathogens, including \textit{Candida} spp., coagulase-negative staphylococci, enterococci, gram-positive bacilli other than nocardia and \textit{H. parainfluenzae}, and streptococci other than \textit{S. pneumoniae}, \textit{S. pyogenes}, \textit{S. agalactiae}, and \textit{S. anginosus}. 
Wound Cultures

Caution must be taken in the interpretation of wound/tissue cultures to ensure that the sample reflects pathogens rather than colonizers as described previously. The clinical presentation and method of obtaining the culture must be considered prior to initiating antimicrobial therapy.

MANAGEMENT

Infectious Etiologies

In order to determine the appropriate empiric antimicrobial treatment of a febrile patient suspected of having an infection, one should first consider the severity of illness. If unstable (with severe sepsis, septic shock, or multiorgan failure), the patient needs urgent evaluation and consultation with specialists, institution of empiric broad-spectrum antimicrobial therapy, and transfer to an intensive care unit. The risk of death from septic shock increases by over 7% with every hour that passes from the onset of shock until the start of targeted therapy (34). The choice of empiric antimicrobials should be guided by the likely source of infection, the patient’s microbiological history, and the local antibiogram. The likelihood of multidrug resistance is much greater in patients with health care associated infections, particularly in patients with prior exposure to an ICU or LTCF. Patients with severe disease should be treated empirically with an aggressive broad-spectrum antimicrobial regimen, including piperacillin-tazobactam or a carbapenem. Vancomycin should be added, as MRSA is a common cause for severe infection.

The antimicrobial regimen should be tailored when the infecting strain has been identified and susceptibilities are known. Further work up, often including computed tomography of the chest and abdomen, may be indicated to establish the source of the infection and appropriate definitive treatment. Consultation with infectious diseases should be sought for further guidance regarding the identification of the source of infection and appropriate management, including the choice and duration of antimicrobial treatment. Infectious diseases management of this patient population may be particularly challenging given the high prevalence of MDR organisms.

SUMMARY

Rehabilitation inpatient facilities host a heterogeneous group of patients with diverse underlying conditions. Special considerations are required in the evaluation of fevers since different patient groups may exhibit atypical symptoms of infection and the etiology of fever includes noninfectious causes. Nevertheless, infection is the most
II. SPECIFIC MEDICAL COMPLICATIONS

common cause of fever in a rehabilitation unit. Several studies have shown that UTI is the most frequently encountered infection in a rehabilitation unit, followed by respiratory tract infections and SSTIs. The underlying cause of fever needs to be determined, and the work up should include a careful physical examination, laboratory tests, appropriate imaging, and specimen collection. The prevalence of MDR organisms is very high among rehabilitation unit patients, and this must be taken into account when choosing an empiric antimicrobial regimen.

REFERENCES

Acute chest pain is a common reason for a patient to seek medical attention and accounts for approximately 7 million emergency department visits annually in the United States (1). Common causes of acute chest pain are listed in Table 10.1. The prevalence of chest pain etiologies varies according to the population studied. In the primary care setting, the most common cause is musculoskeletal pain. Even in the emergency department setting, only 15% to 25% of patients with acute chest pain are actually found to have acute coronary syndromes (ACS). The immediate challenge is to diagnose or exclude acute coronary syndromes and other potentially life-threatening conditions such as pulmonary embolism, aortic dissection, pericardial tamponade, and pneumothorax. A diagnosis of acute coronary syndrome is missed in approximately 2% of patients visiting the emergency department for acute chest pain (2). Among these patients, the short-term mortality is about 25% and is twofold higher compared to patients who are hospitalized and treated. Although the initial differential diagnosis of chest pain is extensive (Table 10.1), a good history, focused physical examination, electrocardiogram (ECG), chest radiograph, and commonly available blood tests for cardiac biomarkers usually lead to the correct diagnosis.

**HISTORY AND PHYSICAL EXAMINATION**

Despite the numerous technologies available to diagnose coronary artery disease, the most useful and reliable diagnostic tool in an acute situation is a good history. The examiner should elicit specific details such as the quality, location, and radiation of the pain, and precipitating, aggravating, and mitigating factors. In addition, it is important to be familiar with risk factors for potentially life-threatening conditions and question the patient specifically about their presence.
TABLE 10.1 Differential Diagnosis of Acute Chest Pain

- **Cardiac**
  - Acute coronary syndromes
  - Aortic dissection
  - Pericarditis

- **Pulmonary**
  - Pulmonary embolism
  - Pneumothorax
  - Pneumonia

- **Gastrointestinal**
  - Esophageal spasm
  - Gastro esophageal reflux
  - Peptic ulcer disease

- **Musculoskeletal**
  - Costochondritis
  - Chest wall pain
  - Degenerative disease of cervical and thoracic spine

- **Infectious**
  - Herpes zoster

- **Psychogenic**
  - Anxiety disorder
  - Panic attack

**ACUTE CORONARY SYNDROMES**

The most common serious conditions that cause acute chest pain is ACS which includes unstable angina, non-ST-segment elevation myocardial infarction (non-STEMI), and ST-segment elevation myocardial infarction (STEMI). Risk factors for ACS include cigarette smoking, diabetes, dyslipidemia, hypertension, family history of premature coronary artery disease, obesity, and age. Coronary spasm may cause myocardial ischemia in patients with normal coronary arteries. Cocaine abuse can lead to coronary artery spasm and myocardial infarction. Typical angina is described as chest pressure, squeezing, burning feeling, or difficulty in breathing. The chest discomfort often radiates to the left shoulder, neck, or arm. Many patients deny the presence of frank chest pain. ACS usually occurs spontaneously but may be precipitated by physical or emotional stress. Pain that is similar to a patient’s usual angina symptoms but now occurring at rest, occurring more frequently, or persisting more than 30 minutes is very suggestive of unstable angina or myocardial infarction.

Atypical presentations of ACS are more common among women, elderly, and patients with diabetes, and include heartburn, epigastric pain associated with nausea, unexplained weakness, anxiety, sweating, or syncope. Characteristics of chest pain that strongly suggests that the pain is not caused by myocardial ischemia include sharp pains that are brought on by respirations or coughing, pain localized with the tip of
one finger, pain reproduced by palpation of the chest wall or by the movement of neck or arms, pain that persists for many hours, or pain that lasts for only a few seconds.

Physical examination may not reveal any abnormalities. Tachycardia, hypotension, signs of left ventricular failure, and a murmur of ischemic mitral regurgitation indicate a poor prognosis. Absence of these signs does not exclude the diagnosis of ACS.

Pulmonary Embolism

Risk factors for pulmonary embolism include the presence of deep vein thrombosis, spinal cord injury, immobilization for 3 or more days, surgery in the previous 4 weeks, past history of deep vein thrombosis or pulmonary embolism, history of malignancy, hypercoagulable states, pregnancy, use of contraceptive pills, or the presence of indwelling central catheters and pacemaker leads. Most patients with pulmonary embolism have an identifiable risk factor at the time of presentation. The pain may be pleuritic and associated with anxiety, cough, and dyspnea. On physical examination, patients are frequently noted to be dyspneic and tachypneic. The presence of dyspnea, syncope, or cyanosis is more common with large pulmonary emboli. Symptoms may be mild or absent in smaller pulmonary emboli involving only the segmental pulmonary branches (3).

Pericarditis

In acute infectious pericarditis, there is inflammation of the surrounding pleura, and pleuritic pain is common. The pain is usually retrosternal radiating to the upper back, neck, and shoulders. It is worse when the patient is supine and improves when the patient leans forward. There may be associated fever. The classic physical finding is a pericardial friction rub caused by friction between the inflamed visceral and parietal pericardia. Classically the rub has three components related to ventricular systole and diastole and atrial systole. Rubs are best heard using the diaphragm of the stethoscope with the patient sitting up and leaning forward in expiration. Since the visceral surface of the pericardium does not have pain receptors, noninfectious causes of pericardial effusion usually do not cause chest pain. Tachycardia, hypotension, jugular vein distension, and pulsus paradoxus suggest pericardial tamponade, which is potentially life threatening. If pericarditis is suspected, an ECG must be obtained.

Aortic Dissection

Risk factors for aortic dissection include hypertension, bicuspid aortic valve with aortic root abnormality, coarctation of the aorta, and trauma, including placement of
intra-aortic devices. Connective tissue disorders that cause cystic medial necrosis such as Marfan Syndrome and Ehlers—Danlos Syndromes also increase the risk for aortic dissection. Most patients present with acute onset of chest pain. The pain is sudden and maximal at onset in comparison to acute myocardial infarction where the pain is more gradual in onset. The patients usually describe the pain as tearing or ripping. The pain may radiate from chest to the back. In some cases, the complications arising from dissection dominate the clinical scenario. For example, depending on the location of the dissection, coronary artery occlusion, acute aortic regurgitation, hemorrhagic pleural or pericardial effusion, or stroke may result. The absence of these findings does not exclude the diagnosis of dissection. Hypertension is present in 70% of the patients with acute dissection. Delayed pulse or lower systolic blood pressure in one limb in a patient with acute chest pain is highly suggestive of aortic dissection.

**Gastrointestinal Conditions**

Gastroesophageal reflux disease can produce chest pain. The pain is usually described as a burning sensation, and is exacerbated by alcohol and certain foods. Symptoms are worsened by the recumbent position and are relieved by sitting upright and by acid reducing therapies. Spasm of the esophagus may produce chest pain that is very difficult to distinguish from angina and may also be relieved by nitroglycerin.

**Musculoskeletal Conditions**

In the nonemergency department setting, musculoskeletal pain is a common cause of chest pain. The pain is often worsened by position or palpation and is associated with localized tenderness. Pain may be reproduced by movement of the patient’s neck or arms.

**Psychological Conditions**

Panic disorder is a common cause of chest pain. The chest pain is usually associated with dyspnea, tachycardia, and tachypnea, and a feeling of anxiety that generally lasts more than 30 minutes. The patient may have a history of anxiety disorder or other emotional disorders.

**ELECTROCARDIOGRAM (ECG)**

ECG is extremely helpful in the diagnosis and management of the patient with acute chest pain and should be obtained at the bedside as rapidly as possible (4). Most modern ECG machines can provide an immediate interpretation of the ECG using built-in standard software. In a good quality ECG tracing with no arrhythmias, there is excellent
correlation between the interpretations by the computer and cardiologists. These computer interpretations can be used as a screening tool by physicians who are not adept at ECG interpretation, and a cardiologist should be consulted if there is a question.

ST-segment elevation ≥1 mm in two consecutive leads or a new left bundle branch block is highly suggestive of a STEMI, and the institutional protocol for management of STEMI should be activated. If the patient is in an institution where acute coronary intervention is not available, the usual protocol is to immediately transfer the patient to the nearest hospital capable of treating STEMI by calling 911. If the ECG interpretation is inconclusive, urgent cardiology consultation is recommended. New ST-segment depression ≥0.5 mm that is persistent or transient during symptoms is highly suggestive of acute ischemia and severe coronary artery disease. Nonspecific ST-segment and T wave abnormalities, defined as lesser degrees of ST segment deviation or T inversion of 0.2 mm or less are less helpful in risk stratification. Patients with new ECG abnormalities should be transferred to a setting where continuous ECG monitoring is available for further observation and management. Availability of a prior ECG improves the diagnostic accuracy. ST-segment and T wave abnormalities or LBBB that are unchanged from a prior ECG reduces the diagnostic value. A completely normal ECG does not exclude the diagnosis of ACS in a patient with chest pain; the risk of myocardial infarction is about 4% in such patients with history of coronary artery disease and 2% in those without (5). Patients with chest pain and a normal ECG have a better prognosis compared with those with an abnormal ECG. Even if the ECG is not abnormal, patients with chest pain who are at risk for ACS should get serial ECGs and measurement of cardiac biomarkers while they are under continuous ECG monitoring for 8 to 12 hours.

Presence of diffuse ST-segment elevation in most leads except aVR with PR-segment depression indicates acute pericarditis. An echocardiogram should be obtained for confirmation. Sinus tachycardia, new right axis deviation and new right bundle branch block are highly suggestive of acute pulmonary embolism. ST-segment and T wave abnormalities in the right precordial leads and S1Q3T3 pattern may also be seen but are less specific for the diagnosis of pulmonary embolism.

CHEST RADIOGRAPHY

A chest radiograph should be obtained in all patients with new onset of acute chest pain. It is usually normal in patients with ACS. If the myocardial ischemia is severe and left ventricular failure develops, pulmonary congestion will be seen. A widened mediastinum may be seen in aortic dissection. In pulmonary embolism, the chest radiograph may be normal, but atelectasis, pleural effusion and elevated hemidiaphragm may be present. However, these radiographic signs are not diagnostic since they can be seen in many other conditions. Chest radiography is very helpful in diagnosing other conditions such as pneumonia and pneumothorax that cause chest pain.
LABORATORY TESTS

Various cardiac biomarkers are available for the diagnosis of myocardial injury. At present the preferred biomarker is troponin, either troponin I or troponin T. They are proteins in the myocardium that are released into the circulation following myocardial injury or infarction. Detection of the rise and/or fall of troponin (with at least one value above the 99th percentile of the upper reference limit) is used to diagnose myocardial infarction when associated with suggestive symptoms or ECG abnormalities or imaging evidence of myocardial ischemia. It should be noted that the troponin does not rise for 4 to 6 hours after the onset of myocardial injury. Thus, two consecutive measurements at least 6 hours apart should be obtained, and normal values make myocardial infarction very unlikely. Although the sensitivity of troponin is high for ruling out myocardial infarction, the specificity is low. Many cardiac conditions such as myocarditis, pericarditis, infiltrative cardiomyopathies, drugs toxic to the heart (ie, adriamycin), tachyarrhythmias, heart failure, cardioversion, and ablation can cause elevation of troponin. In addition, critically ill patients with sepsis and respiratory failure and patients with renal failure often have elevated troponins. Troponin elevation has prognostic value in ACS. Even among patients in whom troponin is elevated secondary to noncardiac causes, the mortality rates are higher. Thus, serial troponin measurements are very useful to rule out myocardial injury, but abnormal values need clinical correlation. Continuous ECG monitoring is recommended for patients in whom ACS is suspected and serial troponin measurements are being obtained.

D-dimer is a fibrin degradation product, present in the blood after a thrombus is degraded by fibrinolysis. It is not normally present in the plasma, and a negative test rules out pulmonary embolism. However, it is elevated in many conditions such as trauma, recent surgery, malignancy, and inflammation. Thus it is not recommended as a screening test in patients with such comorbidities (6). Patients with elevated d-dimer or those at high risk for pulmonary embolism need imaging studies such as CT angiography or ventilation/perfusion scanning.

A STEPWISE APPROACH TO EVALUATION OF ACUTE CHEST PAIN

- Potentially life-threatening conditions include ACS, pulmonary embolism, aortic dissection, pericardial tamponade, and pneumothorax.
- Check vital signs and assure hemodynamic stability and order a 12-lead ECG at bedside.
- Obtain immediate consultation from appropriate specialist for potentially life-threatening conditions or hemodynamic instability.
II. SPECIFIC MEDICAL COMPLICATIONS

- Obtain a good history, keeping in mind the presenting symptoms and risk factors for the serious conditions. The patient with clear evidence of musculoskeletal or gastrointestinal etiologies needs to be treated for symptom relief, but no further urgent interventions are needed.
- Obtain a bedside chest radiograph.
- If the ECG shows localized ST-elevation or new LBBB, activate the institutional STEMI protocol. If new ST-segment depressions are found, transfer patient to ward with continuous ECG monitoring (telemetry). If ECG is nonspecific or normal, patients at risk for ACS need serial ECGs and serum troponin measurements while under continuous ECG monitoring for 8 to 12 hours.
- ECG showing diffuse ST elevation (except in aVR) and PR-segment depression is suggestive of pericarditis—get an echocardiogram to confirm
- Chest radiograph will be diagnostic of pneumothorax and pneumonia. If widened mediastinum is found and clinical evaluation suggests aortic dissection, additional imaging (CT, MRI, or transesophageal ECG) will be needed urgently
- If pulmonary embolism is suspected, d-dimer measurement may help to exclude the diagnosis in low risk patients. Patients with elevated d-dimer or those at high risk for pulmonary embolism or comorbidities need imaging studies such as CT angiography or ventilation/perfusion scanning
- Patients who are at risk for ACS but have normal serial ECGs and troponins need a stress test done before or soon after discharge.

REFERENCES

Common Laboratory Abnormalities

Bridget S. Norwood

The rehabilitation patient population often includes patients recovering from stroke, spinal cord injury, neurologic disorders, sports injury, orthopedic surgery, amputation, and musculoskeletal syndromes. Laboratory abnormalities are commonly encountered in these patients during their stay in an inpatient rehabilitation unit. Recognizing and correcting these abnormalities are essential in reducing complications that may arise and interruptions to the rehabilitation process that can result in prolonged stays, impaired ability of the patient to fully participate in rehabilitation activities, and increased psychological stress. Some of the most common medical comorbidities seen in the inpatient rehabilitation population include peripheral vascular disease, diabetes mellitus, coronary artery disease, congestive heart failure, stroke, obstructive lung disease, and renal failure—all of which can be associated with various laboratory derangements. Impaired mobility, which is universal to most patients in inpatient rehabilitation, also lends itself to metabolic derangements. This chapter addresses some of the more commonly encountered laboratory abnormalities and how to approach them, once recognized.

HYPOGLYCEMIA AND HYPERGLYCEMIA

Diabetes mellitus is a common diagnosis shared by many rehabilitation patients, and derangements in blood glucose levels are seen frequently.

Hypoglycemia

Hypoglycemia (blood glucose <70 mg/dL) can result from poor oral intake related to mood disturbances or displeasure with institution food, nausea and vomiting related to gastroparesis, increased glucose utilization related to exercise, and fasting while awaiting procedures and diagnostic studies, particularly in patients treated with insulin or insulin secretagogues. Symptoms of hypoglycemia include weakness, confusion, nausea, vomiting, diaphoresis, palpitations, anxiety, and tremor; however,
some diabetic patients are unaware of hypoglycemic episodes. When hypoglycemia is recognized, it is imperative to quickly administer glucose in order to prevent severe neurologic complications such as seizure or coma. This can easily be accomplished by ingestion of sugar in the form of juice or hard candy or can be done intravenously with the administration of dextrose. If repeated bouts of hypoglycemia occur, endocrinology consultation is warranted.

**Hyperglycemia**

Hyperglycemia (fasting blood glucose >140 mg/dL or postprandial blood glucose >180 mg/dL) most commonly results from an inadequate insulin and/or oral hypoglycemic regimen, concurrent infection, side effect of medications such as glucocorticoids and some psychotropic agents, or nonadherence to a carbohydrate controlled diet. Symptoms of hyperglycemia may include polyuria, polydipsia, polyphagia, and blurry vision. In trying to achieve optimal glycemic control, one should avoid reducing blood sugar levels to <90 to 100 mg/dL in order to prevent symptoms and complications resulting from hypoglycemia as previously mentioned. In an established diabetic patient with adequate oral intake, his or her home medication regimen can usually be continued safely in the inpatient rehabilitation setting, with adjustments as needed, to achieve a blood glucose goal ranging between 90 and 180 mg/dL. Endocrinology consultation is indicated for persistent blood glucose elevations >300 mg/dL.

**HYPOKALEMIA AND HYPERKALEMIA**

**Hypokalemia**

Hypokalemia (serum potassium <3.5 mEq/L) can be observed in the rehabilitation population and is often the result of gastrointestinal (GI) potassium loss from diarrhea or vomiting, or the result of side effects from medications such as diuretics or beta-2 agonists. Mild hypokalemia (serum potassium 3.0–3.4 mEq/L) is usually asymptomatic. More severe hypokalemia (serum potassium <3.0 mEq/L) can cause muscle weakness that may involve the respiratory muscles resulting in respiratory failure, rhabdomyolysis, paralysis, and ileus with ensuing nausea, vomiting, and abdominal distention. However, muscle weakness does not usually occur until the serum potassium level is <2.5 mEq/L, unless the fall in potassium level is rapid. It is important to recognize and quickly correct severe hypokalemia to avoid serious consequences such as malignant cardiac arrhythmias. A 12-lead EKG should be obtained in patients with serum potassium levels <3.0 mEq/L to assess for cardiac disturbances, including but not limited to, sinus bradycardia, QT prolongation, atrioventricular blocks, or presence of U waves following the T wave. Arrhythmias related to hypokalemia
become even more important in patients with preexisting cardiac disease taking medications such as digoxin or certain other antiarrhythmic drugs.

Serum potassium levels of 2.5 to 3.4 mEq/L can usually be treated by giving 20 mEq of oral potassium chloride two to four times daily based on the severity of hypokalemia. More severe hypokalemia (potassium <2.5 mEq/L) can also be treated orally unless the patient has an arrhythmia, muscle weakness, rhabdomyolysis, or is unable to tolerate oral intake. In these situations, potassium replacement is given intravenously in a monitored telemetry setting with frequent reassessments of serum potassium levels. Additionally, one should assess for the presence of hypomagnesemia, which occurs in up to 40% of patients with hypokalemia and is often related to a similar cause. If hypomagnesemia is present, magnesium must concurrently be administered as potassium replacement is often otherwise refractory.

Hyperkalemia

Hyperkalemia (serum potassium >5.0 mEq/L) is a common electrolyte abnormality and is often the result of acute or chronic kidney disease (CKD), hemolysis, metabolic acidosis, strenuous exercise, trauma, rhabdomyolysis, or insulin deficiency. Adverse effect of medications, such as angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers, direct renin inhibitors, aldosterone antagonists, potassium sparing diuretics, nonsteroidal anti-inflammatory drugs, digoxin, or beta blockers, can also result in hyperkalemia. Pseudohyperkalemia, related to movement of potassium out of cells during blood collection, can occur as the result of the use of excessive vacuum force, small gauge collection needle, tight tourniquet, difficult venipuncture, repeated fist clenching, or delay in the processing time of the specimen, and can be associated with severe thrombocytosis, leukocytosis, or erythrocytosis. If pseudohyperkalemia is suspected, when there is no obvious cause for hyperkalemia in an otherwise asymptomatic patient, it should be excluded by repeating the lab study. Symptoms associated with hyperkalemia may include muscle weakness and paralysis, in addition to, cardiac arrhythmias and conduction abnormalities. A 12-lead EKG should be performed when the serum potassium level is >5.5 mEq/L. Initial hyperkalemic EKG findings include peaked T waves, shortening of the QT interval, prolongation of the PR interval, and lengthening of the QRS duration, which may later evolve into sinus bradycardia, sinus arrest, idioventricular arrhythmias, ventricular tachycardia, ventricular fibrillation, and asystole.

Treatment for severe hyperkalemia (serum potassium >6.5 mEq/L) involves giving medications to stabilize the cardiac membrane to prevent arrhythmias, to shift extracellular potassium into cells and/or to eliminate excess potassium from the body. Thus, if hyperkalemia is present with EKG changes, or if the serum potassium level is >6.5 mEq/L, one should first administer either 1,000 mg of calcium gluconate IV or 500 to 1,000 mg of calcium chloride IV to stabilize the cardiac membrane. This
II. SPECIFIC MEDICAL COMPLICATIONS

should be followed by therapies to shift extracellular potassium into cells; therapies such as administration of 10 units of regular insulin IV, along with 50 mL of D50 if blood glucose is <250 mg/dL to prevent development of hypoglycemia are recommended. With the goal being to reduce serum potassium level to <5.5 mEq/L while avoiding concurrent hypoglycemia, the blood glucose should be repeated in one hour and the potassium level in two hours to document efficacy. Albuterol given along with insulin and dextrose has an additive potassium lowering effect and can be given as 10 to 20 mg in saline by nebulization over 10 minutes. Administration of sodium bicarbonate is usually reserved for patients with concomitant marked metabolic acidosis (serum bicarbonate ≤18 mEq/L). For removal of excess potassium in patients with persistently elevated serum potassium levels >5.5 mEq/L, available options are use of a cation exchange resin such as sodium polystyrene sulfonate (Kayexalate) 15 to 30 g orally every 4 to 6 hours to achieve a serum potassium level <5.5 mEq/L. Alternatively, Kayexalate may be given as an enema 50 g in 150 mL tap water to patients unable to tolerate oral medication; however, the use of Kayexalate in enema form should be avoided in postoperative patients, and in those with an ileus or bowel obstruction because of the risk of development of intestinal necrosis. If these measures are ineffective, or if treating a patient with severe acute kidney injury (AKI) or CKD (glomerular filtration rate [GFR] <30 mL/min), then a nephrology consult for removal of potassium via dialysis is indicated. Treatment of severe hyperkalemia should take place in a monitored telemetry setting with frequent lab reassessment until resolution. For patients prone to recurrent episodes of hyperkalemia such as those with CKD, preventive measures such as dietary potassium restriction, avoiding use of medications that may contribute to hyperkalemia, and the use of loop diuretics to increase urinary potassium loss may be beneficial.

HYPONATREMIA AND HYPERNATREMIA

Hyponatremia

Hyponatremia (serum sodium <135 mEq/L) can be seen in the rehabilitation population as the result of many conditions as shown in Table 11.1. Hyperglycemia may result in a phenomenon known as pseudohyponatremia in which a hyperosmolar state causes shift of intracellular water into the plasma volume which lowers serum sodium. Serum sodium falls about 2.4 mEq/L for every 100 mg/dL increase in serum glucose >100. Pseudohyponatremia can also result from hyperproteinemia and severe hyperlipidemia because of displacement of serum water by proteins or lipids. Once hyponatremia is recognized, whether there are associated neurologic symptoms present or not, the actual serum concentration for sodium is not as important as determining the acuity of the change. Symptoms of hyponatremia may include nausea, muscle cramps, fatigue, lethargy, gait disturbances, forgetfulness,
confusion, and, if severe and acute enough, coma or seizures. Asymptomatic chronic hyponatremia (>48 hours), down to 120 mEq/L, is not cause for alarm and does not require urgent correction. Treatment is tailored instead to the cause of hyponatremia. If it is because of volume depletion, if the serum sodium is >120 mEq/L, and if the patient is asymptomatic, hemodynamically stable, and is otherwise able to safely consume oral hydration, then the patient can be rehydrated via consumption of water. Patients with serum sodium <120 mEq/L and/or an inability to tolerate oral intake should receive IV fluid boluses of isotonic crystalloids (ie, normal saline or lactated ringers) of at least 2 liters as long as tolerated by cardiopulmonary status. Chronic hyponatremia related to syndrome of inappropriate antidiuretic hormone (SIADH) is treated by limiting free water intake to no more than 1 L daily in addition to treating the underlying cause if identified. Salt loading with salt tablets can also be used in patients with volume depletion or SIADH, but should be avoided in those with hypervolemia (ie, renal failure, cirrhosis, or congestive heart failure). For patients with SIADH who don’t respond to free water restriction or salt loading alone, the addition of a low-dose loop diuretic such as furosemide 20 mg twice a day administered orally along with salt tablets or IV saline is often effective. Hypervolemic causes of hyponatremia are managed by treatment of the underlying disease state in addition to free water restriction.

Acute hyponatremia, if severe (<120 mEq/L) and/or associated with neurologic manifestations, requires correction of serum sodium more urgently. This should be
done in a monitored setting such as the ICU where the patient can have frequent neurologic checks and timely labs for monitoring of serum sodium and is usually accomplished by the administration of IV hypertonic saline. Adjunctive therapies, such as demeclocycline in patients with SIADH or vasopressin receptor antagonists in patients who are not volume depleted, are also used in certain clinical settings. Care should be taken to avoid overly rapid correction of hyponatremia (not more than 10 mEq/L in a 24-hour period) because of concern about osmotic demyelination syndrome that can lead to severe neurologic sequelae. Nephrology consultation should be sought for assistance with management of refractory, severe, or symptomatic hyponatremia.

**Hypernatremia**

Hypernatremia (serum sodium >145 mEq/L) is not commonly encountered in the rehabilitation population given that most patients have an intact thirst mechanism and free access to water. Hypernatremia is most often related to water loss resulting from GI losses such as diarrhea or vomiting, or from urinary losses resulting from diabetes insipidus, or osmotic diuresis related to uncontrolled diabetes or urea excretion during recovery from renal failure. Less commonly it may be the result of inadvertent administration of hypertonic fluids. Symptoms of hypernatremia include lethargy, irritability, and generalized weakness which may progress to seizures or coma. Severe symptoms do not usually occur with serum sodium values <155 mEq/L. Treatment of hypernatremia should first focus on restoring intravascular volume in patients who are hypovolemic with administration of isotonic intravenous fluids such as normal saline. Once euvolemia is achieved, then treatment is shifted to the replacement of the free water deficit in addition to ongoing water losses with hypotonic fluid. This ideally should be accomplished orally or via the nasogastric tube with administration of water, however, intravenous infusion of 5% dextrose can be used if unable to replace enterally.

Calculation of the free water deficit can be determined by using the formula outlined in Figure 11.1. The free water deficit can then, under most circumstances, be safely replaced over 24 hours in the majority of patients with hypernatremia. The serum sodium should be monitored frequently to avoid overcorrection (one should not lower sodium to more than 10 mEq/L in a 24 hour period). In addition, the blood sugar should be monitored as well if dextrose is used. Correction of concomitant electrolyte abnormalities such as hypokalemia or hypomagnesemia

\[
\text{Volume to be replaced (in liters)} = \text{TBW} \times \frac{([\text{Na}] / 140) - 1}{\text{TBW} = \text{Weight (in kg)} \times 0.6 \text{ for men or 0.5 for women}}
\]

**FIGURE 11.1** Formula for calculating the free water deficit.
is also important. Consultation with endocrinology and/or nephrology should be sought if diabetes insipidus is suspected. Nephrology consultation is also indicated for management of severe or refractory hypernatremia.

**HYPOCALCEMIA AND HYPERCALCEMIA**

### Hypocalcemia

Hypocalcemia (serum calcium <8.5 mg/dL or ionized serum calcium <4.65 mg/dL) is an infrequent occurrence in the rehabilitation population, but when recognized, is often related to disorders involving parathyroid hormone (PTH) or vitamin D deficiency. Other etiologies include binding of serum calcium related to hyperphosphatemia as result of kidney disease or tumor lysis syndrome or deposition of calcium salts in tissues as seen in rhabdomyolysis. Severe hypomagnesemia can also be a contributing cause. In the setting of low serum calcium, the serum albumin concentration should be determined in order to correct for hypoalbuminemia if present (Figure 11.2). Alternatively, one may get an accurate assessment of calcium by ordering an ionized serum calcium level test. Hypocalcemia may be asymptomatic or can cause muscle cramps, paresthesias, fatigue, anxiety, carpopedal spasm, laryngospasm, or generalized seizures with severe tetany. Cardiovascular manifestations may include hypotension and various conduction abnormalities or arrhythmias. Diagnostic studies that should be ordered include PTH, phosphorus, magnesium, creatinine and vitamin D levels. An EKG should be done for serum calcium level <7.5 mg/dL. Asymptomatic mild hypocalcemia (serum calcium 7.5–8.4 mg/dL) does not require urgent treatment. Mild symptoms such as paresthesias associated with serum calcium levels of 7.5 mg/dL or greater can be treated with oral calcium supplementation such as calcium carbonate. Patients with more severe hypocalcemia (ie, calcium <7.5 mg/dL) or those with more severe symptoms such as tetany, seizures, or cardiac manifestations require more urgent correction of serum calcium with administration of IV calcium in the form of calcium chloride or calcium gluconate under telemetry monitoring. Concomitant hypomagnesemia should be addressed prior to correction of hypocalcemia since it is difficult to correct hypocalcemia until magnesium levels have been normalized. Those with recognized vitamin D deficiency

**Corrected calcium (mg/dL) = \[0.8 \times (4.0^* - \text{serum albumin \ (g/dL)}) + \text{serum calcium \ (mg/dL)}\]  

\(^*4.0\) represents normal albumin level in g/dL  

*Each 1 g/dL decrease of albumin will decrease 0.8 mg/dL in measured serum calcium*

**FIGURE 11.2** Formula for determining calcium concentration in setting of hypoalbuminemia.
II. SPECIFIC MEDICAL COMPLICATIONS

should receive appropriate vitamin D replacement. Chronic hypocalcemia accompanied by hyperphosphatemia related to CKD is managed with dietary phosphate restriction, phosphate binders such as calcium carbonate, or calcium acetate and active vitamin D supplementation with calcitriol. Hypocalcemia with concurrent hyperphosphatemia related to hypercatabolic disease states such as rhabdomyolysis or tumor lysis syndrome should not be treated with calcium until phosphorus levels normalize to avoid calcium-phosphate precipitation. If severe symptoms or refractory hypocalcemia is present, then endocrinology consultation is warranted. Nephrology consultation should be sought for patients with marked renal impairment (GFR <30 mL/min) with severe symptoms related to hypocalcemia and/or marked hyperphosphatemia for possible dialytic therapy.

Hypercalcemia

Hypercalcemia (serum calcium >10.5 mg/dL or ionized serum calcium >5.3 mg/dL) is a frequently seen disorder of calcium homeostasis and may be observed in the rehabilitation population. As described earlier in the chapter, accurate assessment of serum calcium requires the concomitant measurement of serum albumin, or alternatively, an ionized calcium level. Primary hyperparathyroidism and malignancy are the most commonly encountered etiologies. Other causes include immobility, milk alkali syndrome, vitamin D intoxication, thyrotoxicosis, Paget’s disease, granulomatous diseases such as tuberculosis or sarcoidosis, and side effect of medications such as thiazide diuretics or lithium. Symptoms of hypercalcemia may include constipation, anorexia, changes in mental status, weakness, bone pain, kidney stones, polyuria related to nephrogenic diabetes insipidus, cardiac conduction abnormalities, and less commonly, pancreatitis. Initial workup should include measurement of PTH, phosphorus, vitamin D levels, thyroid stimulating hormone and creatinine. For prolonged severe hypercalcemia, an EKG should be ordered.

Asymptomatic or mild hypercalcemia (calcium >10.5 to <12 mg/dL) does not require urgent treatment. Moderate hypercalcemia (calcium 12–14 mg/dL) does not require urgent treatment if it is chronic in nature and is not associated with symptoms. Adequate oral hydration should be encouraged and treatment of the underlying cause is appropriate. Treatment of severe hypercalcemia (calcium >14 mg/dL) or symptomatic hypercalcemia involves increasing the excretion of calcium by the kidneys with the infusion of intravenous saline at a rate of at least 200 mL/hr as tolerated, with close monitoring for signs of volume overload. If volume overload develops then loop diuretics such as Lasix 40 mg IV can be given. Because saline diuresis alone will not usually achieve normal calcium levels with severe hypercalcemia, intravenous bisphosphonate administration (ie, pamidronate or zoledronic acid) is usually the next step, barring any contraindications for its use such as advanced renal failure. Calcitonin, which has a more rapid onset but shorter duration of action as compared to the bisphosphonates, can also be used as an adjunct to therapy in patients with severe
symptomatic hypercalcemia. For persistent severe or symptomatic hypercalcemia, endocrinology and/or nephrology consultation is indicated.

AZOTEMIA

Azotemia, elevated blood urea nitrogen (BUN) and/or serum creatinine, is a common finding in rehabilitation patients. Its presence usually reflects a decline in GFR as the result of CKD, AKI, or a combination of both. However, elevations in BUN can be seen in patients with GI bleeding or hypercatabolic states and in those receiving systemic corticosteroids or high protein feedings. Similarly, elevations in serum creatinine can be seen in patients with increased muscle mass and in those taking medications such as cimetidine and trimethoprim. It is important to first determine whether azotemia is acute or chronic as this will dictate management. Labs ordered should include urinalysis as well as urinary sodium, creatinine, and urea to help determine the etiology of renal failure. Renal ultrasound is useful to evaluate the presence of an obstructive process manifested by hydroureter or hydronephrosis and may also provide information regarding chronicity of renal failure (small atrophic kidneys would suggest chronic disease).

Stable chronic elevations in BUN and creatinine require no urgent intervention as long as there are no associated signs of uremia (eg, alterations in mental status, malnutrition, bleeding, nausea/vomiting, pericarditis, neuropathy), volume overload, or significant electrolyte, or acid–base disturbances present. These patients can be managed for their CKD by nephrology in the outpatient setting. AKI, on the other hand, requires timely diagnosis and evaluation to prevent and manage its associated complications such as volume overload, acid-base and electrolyte disturbances and to reduce the incidence of irreversible renal damage. When AKI is recognized (ie, increase in serum creatinine >0.3 mg/dL in 48 hours, increase in serum creatinine >1.5 mg/dL from baseline and/or decline in urine output to <0.5 mL/kg/hr for >6 hours), then appropriate steps for diagnostic workup and treatment should be initiated. Given that most cases of AKI in the rehabilitation setting are because of prerenal azotemia, it is reasonable to administer an IV fluid bolus of 1 to 2 L of isotonic fluid such as normal saline or lactated ringers, as tolerated by cardiopulmonary status, and reevaluate labs for improvement in renal function. If azotemia persists, the next step would be to assess for urinary retention, including an assessment for bladder distention or post void residual >200 mL of urine as assessed by bladder ultrasound or straight urethral catheterization. If urinary retention is present, a Foley catheter should be inserted for accurate documentation of urinary output and for treatment of possible lower urinary tract obstruction. Nephrology should be consulted following the initial diagnostic workup if there is no improvement in renal function with the measures described above. Nephrology should also be involved if volume overload, uremia, or marked acid–base or electrolyte disturbances are present.
ABNORMAL LIVER FUNCTION TESTS

Derangements in liver function tests (LFTs) may be seen in the rehabilitation population. Abnormalities in serum aminotransferases (aspartate aminotransferase [AST] and alanine aminotransferase [ALT]), alkaline phosphatase, and bilirubin may reflect liver disease as well as other pathophysiology. For example, elevations in aminotransferases can be observed in conditions affecting skeletal or cardiac muscle or can be the result of medication side effects. Elevations in alkaline phosphatase may be observed in disorders affecting the bone. Bilirubin may be elevated as the result of hemolysis, gallbladder disease, disorders of bilirubin conjugation, inherited disorders or the result of medication side effects. Once LFT abnormalities are recognized, the provider should do a thorough medical history to assess for prior known hepatobiliary disease and for exposure to liver toxins such as alcohol, certain prescription medications, and excessive acetaminophen use. Clinical manifestations of hepatobiliary disease may include abdominal pain especially in the right upper quadrant, abdominal distention, anorexia, nausea, vomiting, malaise, lethargy, jaundice, pruritus, fever, chills, dark colored urine and light colored stools. Physical examination should focus on findings such as fever, jaundice, right upper quadrant tenderness, hepatosplenomegaly, ascites, and palpable liver masses which may be indicative of biliary tract obstruction or infection, decompensated liver disease, or malignancy of the hepatobiliary system. In those with chronic liver disease, gynecomastia, testicular atrophy, parotid gland enlargement, caput medusa, spider nevi, asterixis, or Dupuytren’s contractures may occur. A positive Murphy’s sign (holding or “catching” of breath during deep inspiration as the tender gallbladder descends toward and touches examiner’s fingers) may be present in patients with acute cholecystitis.

Useful laboratory studies may include gamma-glutamyl transeptidase (GGT) to determine if elevation of alkaline phosphatase is of hepatic origin. Elevated alkaline phosphatase with a normal GGT should prompt evaluation for bone disease. Viral hepatitis serology, urine toxicology, creatine phosphokinase (CPK), serum alcohol, and acetaminophen levels may be useful in the workup of aminotransferase elevations. Measurement of serum albumin and international normalized ratio (INR) can help detect problems with the synthetic function of the liver. Amylase and lipase should be obtained in the setting of abdominal pain, nausea, and vomiting to exclude acute pancreatitis. Abdominal ultrasound is the initial imaging study usually obtained and is useful to evaluate for hepatosplenomegaly, cirrhosis, liver nodules, ascites, bile duct dilatation, gallstones, and cholecystitis.

Hepatology or gastroenterology consultation should be sought for liver abnormalities that are accompanied by symptoms and/or associated physical examination findings, and for unexplained, persistent elevation (>6 months) of LFTs >1.5 times the upper limit of normal in the asymptomatic patient.
BIBLIOGRAPHY


II. SPECIFIC MEDICAL COMPLICATIONS


Patients in inpatient rehabilitation units who require bladder catheterization are prone to develop nosocomial (health care-associated) catheter-associated (CA) urinary tract infections (UTI). Thus, the vast majority of nosocomial UTIs occur in patients whose urinary tracts are currently or recently catheterized, including intermittent catheterization. Management of UTI is a problem in catheterized patients in inpatient units because CA bacteriuria and pyuria are common in such patients, and it is often not possible to determine whether there is a causal relationship with symptoms. Moreover, the prevalence of antimicrobial resistance to broad-spectrum drugs among uropathogens is rising.

DEFINITIONS

Definitions of terms used for UTI are summarized in Table 12.1. CA-UTI refers to symptomatic UTI in a catheterized patient whereas CA-asymptomatic bacteriuria (ASB) refers to bacteriuria with ≥10⁵ CFU/mL in a patient without symptoms or signs attributable to the urinary tract. CA-bacteriuria is a frequently used term that refers to both CA-ASB and CA-UTI, although the vast majority are CA-ASB. These definitions are important to consider because much of the published literature on this topic does not clearly distinguish between CA-UTI and CA-ASB and rather uses the more ambiguous term CA-bacteriuria. Distinguishing between the two is important because the former warrants treatment and the latter usually does not.

CA bacteriuria (mostly CA-ASB) is the source of most episodes of nosocomial bacteremia, and may be associated with increased mortality (1,2), although this latter point is controversial. One important consequence of CA-ASB is that it comprises a large reservoir of antimicrobial-resistant organisms that may be transmitted between patients who have urinary catheters or other invasive devices (3–5). CA-ASB is also a frequent target for inappropriate antimicrobial therapy in hospitals, which further contributes to the problem of antimicrobial resistance in hospitals. For example, in a study of 164 episodes of CA-ASB in VA patients, 53 (32%) were treated inappropriately
II. SPECIFIC MEDICAL COMPLICATIONS

with antimicrobials (6). In another VA study, CA-ASB accounted for 70% of antimicrobial-treated possible UTI episodes (7). Inappropriate antimicrobial use also exacerbates the growing problem of nosocomial Clostridium difficile colitis (8,9).

CA fungal infections are also common in hospitalized patients and can be symptomatic or asymptomatic. These infections are discussed at the end of this chapter.

Significant Bacteriuria

Significant bacteriuria is the level of bacteriuria that suggests true bladder bacteriuria rather than contamination, and is based on growth from a urine specimen collected and transported in a manner to minimize contamination and limit bacterial growth. The preferred method of obtaining a urine culture in a patient whose catheter has been in place for no more than a week is by sampling through the catheter port or, if a port is not present, puncturing the catheter tubing with a needle and syringe (10). In those with indwelling catheters for more than a week, a urine specimen should be obtained from a freshly placed catheter (11,12). Cultures should not be obtained from the drainage bag.

In symptomatic noncatheterized men and women, low colony counts of gram negative organisms have been shown to be significant. For example, in women with uncomplicated cystitis, colony counts of gram-negative organisms in voided urine as low as $10^2$ CFU/mL have been shown to reflect bladder infection (13). In men with urinary symptoms, a quantitative count of $\geq 10^3$ CFU/mL in a voided specimen differentiates sterile from infected bladder urine (14). In asymptomatic noncatheterized

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**TABLE 12.1 Definitions for Urinary Tract Infection (UTI)**

- **UTI**—nonspecific term that generally refers to bacterial or fungal infection of the urinary tract.
- **Catheter-associated bacteriuria (CA-bacteriuria)**—presence of significant bacteriuria in a catheterized or recently catheterized patient without regard to the presence or absence of urinary symptoms.
- **Catheter-associated asymptomatic bacteriuria (CA-ASB)**—presence of significant bacteriuria in a catheterized or recently catheterized patient without symptoms or signs referable to the urinary tract.
- **Catheter-associated UTI (CA-UTI)**—presence of significant bacteriuria in a catheterized or recently catheterized patient with symptoms or signs referable to the urinary tract.
- **Catheter-associated funguria (CA-funguria)**—presence of funguria in a catheterized or recently catheterized patient. Fungal colony counts have not been shown to be meaningful in interpreting the significance of funguria. CA-funguria should be distinguished as asymptomatic or symptomatic.

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*Quantity of bacteria in the urine suggestive of infection rather than contamination (see text).*
men and women, a higher colony count (≥10^5 CFU/mL) is used because, in contrast to symptomatic patients, specificity is more important than sensitivity in asymptomatic patients. In urine specimens obtained by urethral catheterization (or by suprapubic catheter or bladder aspirate) from symptomatic or asymptomatic men and women, periurethral contamination is less of a problem, and counts as low as ≥10^2 CFU/mL are considered to be significant (15). The significance of this colony count threshold was demonstrated by a study showing that the level of bacteriuria or candiduria rapidly increases from small quantities to >10^5 CFU/mL in catheterized individuals (16).

The National Institute on Disability and Rehabilitation Research (NIDRR) Consensus Statement, entitled “The Prevention and Management of Urinary Tract Infection among People with Spinal Cord Injuries,” has defined significant bacteriuria from indwelling catheter or suprapubic aspirate specimens as any detectable concentration ≥10^2 CFU/mL in a catheter urine specimen from a patient with intermittent catheterization; and ≥10^4 CFU/mL in a clean-catch specimen obtained from a catheter-free man with a condom collection device (15). The NIDRR Consensus Statement has defined UTI as bacteriuria with tissue invasion and resultant tissue response with signs and/or symptoms.

Given that most clinical laboratories, for reasons of feasibility and cost, do not routinely quantify urine cultures to 10^2 CFU/mL, defining CA-UTI as ≥10^3 CFU/mL in a symptomatic male or female is a reasonable compromise between sensitivity in detecting bladder bacteriuria and feasibility and cost for the microbiology laboratory (17). On the other hand, ≥10^6 CFU/mL is a reasonable criterion for the diagnosis of CA-ASB in asymptomatic women and men, even though lower counts probably represent true bladder bacteriuria, as increased specificity is desirable to reduce physicians’ tendency to treat, inappropriately, ASB. Definitions for significant bacteriuria are summarized in Table 12.2.

TABLE 12.2 Definitions for Significant Bacteriuria

<table>
<thead>
<tr>
<th>Noncatheterized, clean-catch voided specimen</th>
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<tbody>
<tr>
<td>• Symptomatic female or male</td>
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<tr>
<td>– ≥10^3 CFU/mL (based on data with gram-negative bacilli; sparse data on gram-positive organisms)</td>
</tr>
<tr>
<td>• Asymptomatic</td>
</tr>
<tr>
<td>– Female: ≥10^3 CFU/mL of same species in two consecutive voided specimens</td>
</tr>
<tr>
<td>– Male: ≥10^3 CFU/mL in single voided specimen</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Catheterized—urine from freshly placed catheter preferable</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Symptomatic female or male</td>
</tr>
<tr>
<td>– ≥10^3 CFU/mL</td>
</tr>
<tr>
<td>• Asymptomatic female or male</td>
</tr>
<tr>
<td>– ≥10^3 CFU/mL</td>
</tr>
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II. SPECIFIC MEDICAL COMPLICATIONS

EPIDEMIOLOGY

CA-bacteriuria is the most common nosocomial infection worldwide (18) and accounts for up to 40% of nosocomial infections in U.S. hospitals each year (19,20). Up to 25% of patients in general hospitals have a catheter inserted at some time during their stay (19,21), and most are catheterized for fewer than 4 days (22). In a recent report from the National Healthcare Safety Network (NHSN) (a Center for Diseases Control, national public health surveillance system for monitoring healthcare-associated infections with the use of standardized definitions) for 2011, the ratio of urinary catheter-days to patient-days was 7% in inpatient long-term care rehabilitation units, 9% in inpatient in-hospital or freestanding adult rehabilitation units, 19% in inpatient medical/surgical wards, and 52% in long-term acute care hospital adult wards (23). However, patients who are managed with intermittent catheterization are not considered to be catheterized for purposes of data collection for NHSN.

The duration of catheterization is the most important risk factor for the development of CA-bacteriuria (3,22,24). The incidence of bacteriuria associated with indwelling urethral catheterization with a closed drainage system is approximately 3% to 8% per day (21,25,26) and, thus, many patients catheterized for short periods of time and almost all those catheterized for a month or more will have CA-bacteriuria. In the NHSN analysis of 2011 data, the mean incidence of CA-UTI per 1000 catheter-days (intermittent catheterization is not considered a catheter-day in this analysis) was 7.1 in inpatient long-term care rehabilitation units, 3.1 in inpatient in-hospital or freestanding adult rehabilitation units, 1.3 in inpatient medical/surgical wards, and 2.2 in long-term acute care hospital adult wards (23).

The majority of patients with CA-bacteriuria do not have symptoms, as demonstrated in a study of 1,497 newly catheterized hospitalized patients (presumably medical/surgical patients) who were followed prospectively with daily urine cultures, urine leukocyte counts, and symptom assessment (27). Only 8% of 194 patients with CA-bacteriuria who could respond to symptom assessment reported symptoms referable to the urinary tract, although bacteriuria and pyuria had been present in most for many days. Additionally, there were no significant differences between catheterized patients with and without CA-bacteriuria in signs or symptoms commonly associated with UTI—fever, dysuria, urgency, flank pain, or leukocytosis.

However, bacteremia complicates CA-bacteriuria in up to 4% of cases (27–29), and about 15% of episodes of nosocomial bacteremia are said to be attributable to the urinary tract (28). Additionally, CA-bacteriuria is the most common source of gram-negative bacteremia in hospitalized patients (30). Of note, however, one recent study of hospitalized patients found that only 1 of the 235 episodes of CA-bacteriuria was unequivocally associated with bacteremia (27).

UTI is associated with poorer neurological outcomes, longer hospital stays, and increased cost of care after stroke (31). In a retrospective study of data from 4,971
patients collected from a stroke registry service in a national network of 8 centers, it was found that patients with nosocomial symptomatic UTI were 57% less likely to be discharged home compared with the other levels of care \( (p < .0001) \) (32). If poststroke care occurred, patients with UTI were more likely to receive inpatient stroke rehabilitation at the level of care suggestive of lower functional status.

Increased postvoid residual (PVR) may be associated with occurrence of UTI in stroke patients. Among 188 stroke patients who were admitted to an inpatient rehabilitation unit and who did not have UTI on admission (105 males, 83 females, mean age 67 years), UTI occurred in 74 patients (39.4%) during admission to the rehabilitation unit (33). The occurrence of UTI was 5 times higher in the patients with a mean PVR over 100 mL than in those with a mean PVR <100 mL. It was recommended that close monitoring of PVR and appropriate intervention is needed to reduce the occurrence of UTI in stroke patients. Likewise, other studies have shown an association between increased PVR and UTI (34,35). Nevertheless, the role of routinely measuring PVR in patients in rehabilitation units has not been established.

**MICROBIOLOGY**

Whereas uncomplicated UTIs are usually caused by a narrow and predictable spectrum of causative agents, a broad range of bacteria can cause nosocomial UTI, and many are resistant to multiple antimicrobial agents (10). Most episodes of CA-bacteriuria in patients catheterized for less than a month are caused by gram-negative bacilli (17). *Escherichia coli* causes most episodes, but UTI may also be caused by other gram-negative bacilli such as *Klebsiella* spp., *Serratia* spp., *Citrobacter* spp., *Enterobacter* spp., and *Pseudomonas aeruginosa*, and gram-positive cocci such as coagulase negative staphylococci and *Enterococcus* spp. (10). Funguria, mostly candiduria, is reported in up to 32% of patients catheterized for short periods of time (10,17).

**DIAGNOSIS**

The clinical diagnosis of CA-UTI is based on the presence of significant bacteriuria in a catheterized or recently catheterized person who has signs or symptoms of UTI not explainable by another condition after a thorough evaluation. As noted above, bacteriuria, UTI signs and symptoms, and pyuria in a catheterized patient are nonspecific, and, thus, the clinician must exercise clinical judgment as to whether treatment is warranted. Catheterized patients with CA-UTI usually do not manifest the classic UTI symptoms of dysuria, frequency, and urgency. Thus, in the presence of an indwelling urinary catheter, symptoms referable to the urinary tract, fever, or peripheral leukocytosis have little predictive value for the diagnosis of CA-UTI. Likewise, no studies...
have demonstrated that odorous or cloudy urine in a catheterized individual has clinical significance, although such complaints by patients or staff are often the reason patients receive treatment for “UTI.” Moreover, the presence or absence or degree of pyuria alone does not, by itself, differentiate CA-ASB from CA-UTI (17,27). Given the nonspecificity of symptoms and pyuria in a catheterized patient with bacteriuria, it is often difficult to decide whether such a patient who has symptoms or fever warrants treatment. Nevertheless, catheterized patients who have bacteriuria and who have symptoms or signs, which are compatible with UTI and which, after a thorough evaluation, cannot be explained by any other condition, warrant treatment. Signs and symptoms compatible with CA-UTI are listed in Table 12.3.

**PREVENTION**

Several evidence-based comprehensive guidelines have been recently published for prevention of CA-UTIs, with an emphasis on infection prevention in hospitals (17,36,37). UTI bundles that combine several prevention techniques to accomplish reduction in CA-UTI have been described (38–40). These strategies should be implemented throughout the hospital, including in inpatient rehabilitation units. It should be noted, however, that our ability to prevent CA-bacteriuria in patients who have appropriate indications for catheterization, especially in those patients requiring long-term bladder drainage, is quite limited with currently available infection prevention techniques (41).

Reducing unnecessary catheterization is the most effective way to prevent CA-bacteriuria (17). Studies have shown that urinary catheters are often inserted for inappropriate reasons or remain in place longer than necessary. In studies of hospitalized patients with urinary catheters, the initial indication for catheter use was judged inappropriate in up to 50% of cases, and continued catheterization inappropriate for

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**TABLE 12.3 Signs and Symptoms Compatible With CA-UTI**

- New onset or worsening of fever
- Altered mental status
- Flank pain
- Costovertebral angle tenderness
- Rigors
- Pelvic discomfort
- New or worsening incontinence, malaise, or lethargy

Patients with spinal cord injury (SCI) may, in addition, demonstrate the following:

- Increased spasticity
- Autonomic dysreflexia
- Sense of unease
almost half of catheter-days (42–44). In addition, the reason for catheter placement is often not stated and orders for catheterization are often not written (45), and clinicians may be unaware that their patients are catheterized (46).

Indwelling urethral catheterization appears to place patients at the greatest risk for CA-bacteriuria, and alternative bladder drainage modalities should be used when appropriate (17). Alternatives include the use of condom catheters, intermittent catheterization, or suprapubic catheterization. Each of these catheterization methods has been shown in selected populations to reduce the risk of CA-bacteriuria over the short term. Condom catheters have been shown in nonrandomized trials to result in a lower incidence of CA-bacteriuria compared with indwelling urethral catheters (24). These impressions were confirmed in a recent prospective, randomized trial of 75 men at a Veterans Administration hospital in which patients without dementia who had an indwelling catheter were about five times as likely to have an adverse outcome (CA-bacteriuria was the predominant outcome in a combined outcome variable) as those with appropriately sized condom catheters (47). No difference was seen in those patients with dementia, which may have to do with the increased risk of CA-bacteriuria in patients who manipulate their condom catheters (24). Thus, in men with low postvoid residual volume who are not cognitively impaired, appropriately sized condom catheters are preferable to indwelling urethral catheters. There is currently no satisfactory external catheter suitable for use by women.

Intermittent catheterization is widely viewed to be associated with fewer complications than indwelling catheterization, including CA-bacteriuria, hydronephrosis, bladder and renal calculi, bladder cancer, and autonomic dysreflexia (48–50). Although a meta-analysis of trials comparing catheterization methods in mostly postsurgical patients undergoing short-term catheterization found that indwelling urethral catheterization was associated with more CA-bacteriuria than intermittent catheterization (relative risk 2.90; 95% confidence interval 1.44 to 5.84), there are no randomized controlled trials that have compared intermittent urethral, indwelling urethral, suprapubic, or condom catheterization in patients on long-term catheterization, including those with neurogenic bladders (48,49).

Hydrophilic catheters, compared with standard catheters, reduce the friction of catheter insertion and urethral inflammation and are associated with improved patient satisfaction. Although previous studies have not supported their routine use to prevent CA-bacteriuria in patients managed with intermittent catheterization (51,52), a recent prospective, randomized, trial of 224 subjects with traumatic spinal cord injury of less than 3 months duration who used intermittent catheterization showed that the time to the first antibiotic-treated CA-UTI was significantly delayed in the hydrophilic-coated catheter group compared with the uncoated catheter group (53). During the period that subjects were hospitalized, the incidence of antibiotic-treated CA-UTIs was reduced by 21% (p < .05) in the hydrophilic-coated catheter group.
Several prevention strategies appear to have some benefit in prevention of CA-bacteriuria, but are not generally recommended for routine use. Thus, silver-alloy-coated catheters are protective against CA-bacteriuria in patients catheterized for a short-term, but studies have not clearly shown a beneficial effect on rates of CA-UTI, morbidity, secondary bloodstream infections, or cost savings (54,55). Although antimicrobial-coated urinary catheters appear to have some benefit in the prevention of CA-ASB in some trials of short-term catheterized patients, questions remain about their safety (potential for selection for antimicrobial resistance) and effectiveness and, thus, available data do not support their routine use to prevent CA-bacteriuria.

**MANAGEMENT**

**CA-ASB**

Screening and treatment of ASB have not been shown to be beneficial and may select for antimicrobial resistance and, therefore, are not recommended, except in pregnant women and patients who undergo traumatic genitourinary procedures (56). Populations that have been extensively studied and for whom these recommendations apply include persons with spinal cord injury and catheterized patients (56). As noted above, the problem often encountered by physiatrists and other physicians is not so much whether to treat a patient with CA-ASB, but instead whether signs or symptoms in a patient with CA-bacteriuria are because of the bacteriuria and thus whether the patient has CA-UTI.

**CA-UTI**

Bacteriuria in a catheterized person with symptoms or signs compatible with a UTI (usually fever) in the absence of another obvious cause of the symptoms or signs should be treated with antimicrobials. Even when another potential source of fever is identified, it is often appropriate to ensure antimicrobial coverage of the urinary organism, especially in sick patients. Antimicrobials alone may not be successful, if underlying anatomic, functional or metabolic defects are not corrected. Urinary catheterization itself should not complicate eradication of bacteriuria, although it predisposes to early recurrence.

Nosocomial CA-UTIs are often caused by multidrug-resistant uropathogens, so a urine culture should be obtained prior to treatment to confirm that the empiric regimen provides appropriate coverage and to allow tailoring of the regimen based on antimicrobial susceptibility data (10,57). If the catheter has been in place for two or more weeks, the culture should be obtained from a freshly placed catheter because the catheter biofilm may result in spurious culture results (11,12). Moreover, clinical outcomes are improved if the catheter is replaced, as shown in a prospective randomized
controlled trial in elderly nursing home residents with long-term indwelling catheters and CA-UTI. This study demonstrated that patients whose catheters had been in place for longer than 2 weeks and who underwent catheter replacement before antimicrobial treatment had a significantly shorter time to improved clinical status and significantly lower rates of polymicrobial CA-UTI after therapy, compared with those who did not undergo catheter replacement (58).

The choice of antimicrobial agent for empiric treatment should be based on available data, including the urine Gram stain results, previous urine culture results, and the hospital antibiogram showing susceptibility patterns of urinary pathogens (10,57). Depending on the antimicrobial susceptibility patterns in the hospital or the patient’s previous urine culture results, patients with mild-to-moderate illness without alterations in mental status or hemodynamic status may be treated with a urinary fluoroquinolone, such as ciprofloxacin or levofloxacin, or a broad-spectrum cephalosporin such as ceftriaxone or cefepime. Data from the NHSN between 2009 and 2010 showed a high prevalence of multidrug-resistant phenotypes among strains causing CA-UTI (59), which is cause for concern. Thus, 31.2% of *E. coli* strains were resistant to fluoroquinolones and 12.3% to extended spectrum cephalosporins (eg, cefepime), and 12.5% of *Klebsiella* spp. were resistant to carbapenems and 26.9% to extended spectrum cephalosporins.

If the patient has evidence of pyelonephritis or urosepsis (eg, severely ill, CVA tenderness, or high fever), an imaging study such as an ultrasound or a CT urogram should be considered to rule out anatomic abnormalities, and one should consider using a broader-spectrum drug such as piperacillin-tazobactam or a carbapenem for empiric treatment. If the urine Gram stain shows gram-positive cocci (most likely enterococci or staphylococci), treatment with vancomycin is reasonable. If the hospital has seen an increased prevalence of extended spectrum beta lactamase (ESBL)-producing uropathogens, a carbapenem should be used empirically. The antimicrobial regimen should be tailored as appropriate when the infecting strain has been identified and antimicrobial susceptibilities are known. Empiric treatment regimens for CA-UTI are shown in Table 12.4.

The optimal duration of antimicrobial treatment for CA-UTI is not known. Reviews of complicated UTI have recommended treatment durations from 7 to 21 days (17), depending on the severity of the infection. However, few studies have been performed that evaluate duration of treatment in populations with CA-UTIs. In a randomized, double-blind, placebo-controlled trial comparing 3-day and 14-day regimens of ciprofloxacin for the treatment of mild CA-UTI in 60 patients with spinal cord injury, there was no difference in clinical outcomes at long-term follow-up (60). Most recently, clinical and microbiologic success rates following treatment were almost identical in a noninferiority study of 619 patients with acute pyelonephritis or complicated UTI treated with a 5-day course of levofloxacin or a 10-day course of ciprofloxacin (61). These data suggest that a 7-day regimen is reasonable for most patients
II. SPECIFIC MEDICAL COMPLICATIONS

TABLE 12.4 Empiric Antimicrobial Management of Catheter-Associated UTI

<table>
<thead>
<tr>
<th>Antimicrobial and Dosing</th>
<th>Mild-to-moderate, afebrile</th>
<th>Severe illness and/or febrile</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Ciprofloxacin 500 mg PO twice daily or 1 g (extended release) PO once daily</td>
<td>• Ciprofloxacin 400 mg IV twice daily</td>
</tr>
<tr>
<td></td>
<td>• Levofloxacin 750 mg PO once daily</td>
<td>• Levofloxacin 500 to 750 mg IV once daily</td>
</tr>
<tr>
<td>Duration</td>
<td>5 to 7 days</td>
<td>Duration 5 to 14 days</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Ceftriaxone 1 to 2 g IV once daily</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Cefepime 1 g IV twice daily</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Piperacillin-tazobactam 3.375 g IV every 6 hours</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Meropenen 500 mg IV every 8 hours</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Imipenem-cilastatin 500 mg IV every 6 to 8 hours</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Doripenem 500 mg IV every 8 hours</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Ertapenem 1 g IV once daily</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Gentamicin 5- to 7 mg/kg IV once daily ± ampicillin 1 to 2 g IV every 6 hours</td>
</tr>
</tbody>
</table>

In choosing an empiric agent, consider the following:
- severity of illness and comorbidities
- antimicrobial susceptibility of prior urinary tract infections (UTI) strains
- local resistance data (hospital antibiogram)
- consider adding vancomycin if Gram stain shows gram-positive cocci
- use a carbapenem (meropenem, imipenem, doripenem, or ertapenem) if an extended spectrum beta lactamase (ESBL) strain is known or suspected
- tailor regimen based on susceptibility data, and transition to oral medications (usually a fluoroquinolone), as soon as condition allows


with CA-UTI, depending on their clinical response. Shorter regimens, such as a 5-day regimen of a urinary fluoroquinolone, are likely to be sufficient in those patients who are less severely ill, infected with uropathogens susceptible to the antimicrobial used, and have a rapid response to treatment.

FUNGURIA

*Candida* species cause the vast majority of fungal infections of the urinary tract and account for 10% to 15% of nosocomial UTIs (62,63). However, most episodes of nosocomial candiduria occur in catheterized patients, and most episodes are asymptomatic. In a large prospective study of nosocomial funguria, only 2% to 4% of patients had urinary symptoms (64). On the other hand, catheterized patients with candiduria may have UTI symptoms or signs such as fever or suprapubic or flank pain.
As with bacteriuria, determination of the clinical significance of candiduria can be problematic, as it can represent contamination of a voided specimen, colonization of catheters or stents, bladder infection, ascending kidney infection, or kidney infection associated with fungemia. Hematogenous dissemination is relatively much more likely to be the source of candiduria than is found with bacteriuria (65). Unlike bacteriuria, there are no established colony count thresholds to help distinguish contamination from bladder infection. In the catheterized patient with funguria, pyuria is a nonspecific finding.

Asymptomatic nosocomial candiduria rarely requires treatment, because it often resolves spontaneously, morbidity is low, and treatment is often followed by rapid recurrence and may select out for resistant organisms (66,67). In a randomized, placebo-controlled trial of 316 hospitalized patients with asymptomatic or minimally symptomatic candiduria, a 2-week course of fluconazole resulted in significantly higher eradication rates than placebo at 2 weeks of treatment (50% vs. 29%), but there was no significant difference in candiduria rates 2 weeks after completion of treatment (67). In asymptomatic patients with CA-candiduria, changing or removing the catheter will result in clearance of candiduria in 20% to 40% of cases (67), and discontinuation of antimicrobials may result in clearance (68). Pyelonephritis, candidemia, and fungus-related death in such patients are rare.

Candiduria should be treated in symptomatic patients, and those with systemic signs or symptoms should be evaluated for disseminated infection with imaging and blood cultures. Consultation with Infectious Diseases is recommended when considering treatment of funguria. Oral fluconazole is the drug of choice for cystitis and pyelonephritis due to most species of Candida (but should not be used for yeasts likely to be resistant to fluconazole, such as C. glabrata and C. krusei). Systemic amphotericin B deoxycholate is no more effective than fluconazole for susceptible strains. Lipid formulations of amphotericin B do not achieve appreciable levels in the kidneys or urine and should not be used for UTI. Echinocandins are minimally excreted and should not be considered first line agents for candiduria. Even with apparently successful local or systemic antifungal therapy for candiduria, relapse is frequent, and this likelihood is increased by continued use of a urinary catheter. Persistent candiduria, especially in immunocompromised patients, warrants radiologic imaging of the kidneys to evaluate for hydronephrosis or perinephric abscesses associated with ascending infection.

SUMMARY

Nosocomial bacteriuria and candiduria are very common, mostly associated with urinary catheterization, and usually asymptomatic. Routine screening to detect nosocomial bacteriuria or candiduria in asymptomatic patients is not recommended because treatment does not appear to alter the natural course of infection and an increase in antimicrobial resistance often results. Symptomatic UTI warrants treatment, as do
II. SPECIFIC MEDICAL COMPLICATIONS

infections where the clinician cannot be sure that bacteriuria or funguria is not causing the patient’s UTI signs or symptoms. The most effective way to reduce nosocomial UTIs is to reduce urinary catheterization by restricting use to patients who have clear indications and by removing the catheter as soon as it is no longer needed. Empiric treatment of CA-UTI should be broad-spectrum and tailored by the results of the urine culture, which should be obtained in all cases prior to treatment.

REFERENCES


A large proportion of patients in need of general rehabilitation services suffer from various forms of chronic pulmonary conditions. For such patients, physical rehabilitation has become the standard of care, with numerous studies demonstrating clear benefits in physiologic and psychological endpoints after successful completion of rehabilitation programs (1,2). For this reason, it is crucial that the physiatrist be familiar with the physiological changes associated with the most common respiratory disorders and their specific therapies. On the other hand, patients with no history of lung disease may also be at risk of developing pulmonary complications during the course of their rehabilitation hospitalization, such as pneumonia, atelectasis, and pulmonary embolism (PE), conditions that carry significant morbidity and mortality. This chapter summarizes the salient aspects of respiratory care during rehabilitation therapy and outlines the steps for early recognition of pulmonary complications.

**OBSTRUCTIVE LUNG DISEASE (ASTHMA AND CHRONIC OBSTRUCTIVE PULMONARY DISEASE)**

Common disorders that fall into the classification of obstructive lung disease include asthma and chronic obstructive pulmonary disease (COPD). Although not the same disorder, these conditions have certain pathophysiological mechanisms in common. The term “obstructive” refers to the impairment in airflow through the medium and small-sized airways due to inflammation of the bronchial mucosa. In both diseases, airway inflammation causes a reversible narrowing of the airway smooth muscle known as bronchoconstriction, swelling of the airway mucosa and excessive mucus production. These factors combine to create significant resistance to airflow, especially during expiration.

It is important to highlight the differences between asthma and COPD, as their treatment and prognosis are different (Table 13.1). Asthma is a condition that frequently starts during childhood. The airway inflammation is secondary to an abnormal reaction to environmental triggers and is therefore commonly associated with other
TABLE 13.1 The Differences Between COPD and Asthma

<table>
<thead>
<tr>
<th></th>
<th>COPD</th>
<th>Asthma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset</td>
<td>Usually fourth to fifth decade</td>
<td>Usually during childhood</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>Progressive</td>
<td>Episodic attacks</td>
</tr>
<tr>
<td>Cough</td>
<td>Chronic and productive</td>
<td>Dry and episodic</td>
</tr>
<tr>
<td>Family history</td>
<td>Rare</td>
<td>Common</td>
</tr>
<tr>
<td>Predominant association</td>
<td>Smoking</td>
<td>Allergies</td>
</tr>
<tr>
<td>Airflow limitation</td>
<td>Chronic</td>
<td>Reversible</td>
</tr>
<tr>
<td>First line treatment</td>
<td>Long-acting bronchodilators</td>
<td>Inhaled corticosteroids</td>
</tr>
</tbody>
</table>

allergic manifestations such as rhinitis, eczema, and sinusitis. Asthma can flare up episodically after exposure to cold temperatures, viral infections, or allergens such as smoke, pollen, pollution, mites, and strong odors. During these flares, subjects may experience shortness of breath, cough, and chest tightness. Wheezing is usually of a high pitch quality that can be auscultated during both inhalation and exhalation. Between flares, subjects whose disease is well controlled are usually asymptomatic and the physical exam generally reveals good air movement with little to no wheezing.

In contrast, subjects with COPD start to develop symptoms later in life after many years of inhalation of detrimental substances, usually via exposure to tobacco smoke. Persistent damage to the lung leads to destruction of normal architecture with permanent loss of tissue that is known as emphysema. In addition, there is chronic airway inflammation, easily collapsible airways, and an impaired ability to exhale (airflow obstruction). It is common to have progressive symptoms characterized by gradual worsening of shortness of breath and cough with persistent sputum production known as chronic bronchitis. Auscultation will usually reveal decreased breath sounds, prolongation in expiratory time, and wheezing during exhalation. As in asthma, patients with COPD can suffer from acute exacerbations triggered by pollution, viruses, or bacterial infections that can be severe enough to compromise respiratory status. The chronic progression of disease leads to weight loss, muscle wasting, and eventually impaired oxygenation. It is common for COPD patients to suffer from concomitant conditions such as cardiovascular disease, stroke, osteoporosis, and lung cancer (3).

Radiographs are not reliable for the diagnosis of airflow obstruction. Chest films may show hyperinflation caused by air trapping and increased lung volumes in particular during acute exacerbations and evidence of emphysema can be noted on the chest CT scans of COPD patients. The diagnosis of airflow obstruction relies on pulmonary function tests, a series of maneuvers to measure lung capacities and volumes.
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One of these procedures, spirometry, is the gold standard to detect and quantify airflow obstruction in both asthma and COPD. This test measures the volume of air as the patient forcefully exhales air over several seconds. In obstructive lung diseases, the amount of air exhaled during the first second (FEV₁) is less than 70% of the total air exhaled (FVC) (4). This impairment is persistent in COPD and episodic in asthma.

Considerations for Rehabilitation

In patients with COPD or asthma, it is critical to ensure that symptom control is achieved with optimal medical therapy prior to initiating a rehabilitation program. Treatment is mainly based on inhaled therapies with both short acting and long acting medications. Although most of these medications are used in both conditions, their indications are not identical (Table 13.2). In asthma, inhaled corticosteroids represent the cornerstone of therapy whereas in COPD the primary agents are long-acting bronchodilators (3,5). In both conditions, acute relief of bronchoconstriction is provided by short-acting bronchodilators such as albuterol, which should readily be available in the rehabilitation unit.

Asthmatic patients should be free of symptoms before starting each session of physical or occupational therapy. One way to assess whether a patient is at his baseline

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**FIGURE 13.1** Lung volumes and capacities as measured by pulmonary function testing.

(Figure 13.1). One of these procedures, spirometry, is the gold standard to detect and quantify airflow obstruction in both asthma and COPD. This test measures the volume of air as the patient forcefully exhales air over several seconds. In obstructive lung diseases, the amount of air exhaled during the first second (FEV₁) is less than 70% of the total air exhaled (FVC) (4). This impairment is persistent in COPD and episodic in asthma.

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Asthmatic patients should be free of symptoms before starting each session of physical or occupational therapy. One way to assess whether a patient is at his baseline
is to measure the degree of airflow obstruction with a peak flow meter, a portable and widely available device that respiratory technicians are familiar with and should be freely available to the patient. Subjects should have measured peak airflows above 70% of either their previously recorded best value or their predicted maximum that is derived from charts based on height and weight. Not infrequently, patients with asthma may develop bronchoconstriction during exercise because of changes in the temperature and humidity of the airway mucosa induced by hyperventilation. This exercise-induced bronchoconstriction can be prevented with the use of prophylactic short-acting bronchodilator therapy (ie, 2 puffs of albuterol) 10 to 15 minutes before starting to exercise.

In COPD, the permanent structural damage to the lung causes a phenomenon called air trapping. Because of airway collapse, patients have incomplete exhalation and retain air in their lungs causing the lungs to increase in size. With exercise, the

### TABLE 13.2 Pharmacotherapy in Obstructive Lung Disease

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Representative Agents</th>
<th>Representative Brand Names</th>
<th>Use in COPD</th>
<th>Use in Asthma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Short-acting beta agonists</td>
<td>Albuterol, terbutaline</td>
<td>Proventil, Ventolin</td>
<td>Rescue agent</td>
<td>Rescue agent</td>
</tr>
<tr>
<td>Short-acting anticholinergics</td>
<td>Ipratropium</td>
<td>Atrovent</td>
<td>Rescue agent</td>
<td>Rescue agent</td>
</tr>
<tr>
<td>Inhaled corticosteroids (ICS)</td>
<td>Beclomethasone, mometasone, fluticasone, budesonide</td>
<td>Qvar, Asmanex, Pulmicort, Flovent</td>
<td>Third line therapy</td>
<td>First line therapy</td>
</tr>
<tr>
<td>Long-acting beta agonists (LABA)</td>
<td>Salmeterol, Formoterol, Indacaterol</td>
<td>Serevent, Foradil, Arcapta</td>
<td>First or second line therapy</td>
<td>Second line therapy, only with an ICS</td>
</tr>
<tr>
<td>Long acting anticholinergics</td>
<td>Tiotropium, aclidinium</td>
<td>Spiriva, Tudorza</td>
<td>First or second line therapy</td>
<td>Not indicated</td>
</tr>
<tr>
<td>Combination agents</td>
<td>LABA + ICS</td>
<td>Advair, Symbicort, Dulera</td>
<td>Third line therapy</td>
<td>Second line therapy</td>
</tr>
<tr>
<td>Oral leukotriene inhibitors</td>
<td>Montelukast, zafirlukast</td>
<td>Singulair, Accolate, Zyflo</td>
<td>Not indicated</td>
<td>Occasional therapy</td>
</tr>
<tr>
<td>Phosphodiesterase inhibitors</td>
<td>Roflumilast</td>
<td>Daliresp</td>
<td>Occasional therapy</td>
<td>Not indicated</td>
</tr>
<tr>
<td>Monoclonal anti-IgE antibody</td>
<td>Omalizumab</td>
<td>Xolair</td>
<td>Not indicated</td>
<td>Occasional therapy</td>
</tr>
</tbody>
</table>
II. SPECIFIC MEDICAL COMPLICATIONS

High respiratory rate results in less time to evacuate the breath and causes the chest to fill up with increasing amounts of air. As this “dynamic hyperinflation” progresses and no further air can be inhaled, the patient rapidly develops severe shortness of breath and quick fatigue which results in a reduction in inspiratory capacity. To overcome this, it is important for the patient to learn the strategy of pursed lip breathing and prolonged exhalation while performing exercise. This technique involves consciously slowing the respiratory rate and exhaling completely through pursed lips. This process allows the patient to decompress the chest by fully expelling all of the air prior to the next inhalation, which translates into significant increases in the patient’s overall exercise capacity. Exercise load should be graduated at a pace that the patient can manage using this breathing technique.

Oxygenation should be monitored with a pulse oximeter at rest and frequently during the rehabilitation process. Normal oxygen saturation values are around 98% to 100% and decrease progressively in subjects with COPD as their lung function worsens over time, with continuous oxygen supplementation indicated when O₂ saturation levels drop below 88% at rest (approximately a PaO₂ of 55 mmHg). However, patients with less severe decrements in lung function may experience significant drops in O₂ saturation during exercise despite normal values at rest, an indication to administer supplemental oxygen during exertion only. It is, therefore, advisable to monitor oxygenation at baseline and frequently during physical therapy as the exercise level and duration is gradually increased. Saturations measured by pulse oximetry should be maintained above 88% at all times.

Both asthma and COPD patients may experience acute worsening of symptoms (disease exacerbations). Although unlikely to be triggered by the rehabilitation process, they can occur during the course of therapy and warrant early recognition for prompt intervention to reduce complications (6). Acute exacerbations are generally treated with nebulized short-acting bronchodilators and systemic corticosteroids in both conditions. Supplemental oxygen is administered if needed and severe cases may require respiratory support (mechanical ventilation). COPD exacerbations may require antibiotic therapy if sputum becomes mucopurulent. Rehabilitation should be placed on hold while the subject recovers from an acute exacerbation. Prompt evaluation by a physician is recommended.

INTERSTITIAL LUNG DISEASE

Interstitial lung diseases (ILDs) encompass a group of pulmonary disorders characterized by an increase in lung stiffness leading to decreased total lung capacity (TLC) and a restrictive ventilatory defect. This means that on pulmonary function testing, there is a proportional decrease in both FEV₁ and FVC as well as a significant reduction in the total size of the lungs (4). A major effect of having small and stiff lungs is an increase in the work of breathing needed to physically expand the lungs and the chest
wall. As a result, most patients with ILD adopt a pattern of rapid, shallow respirations to minimize their effort of breathing. In many instances, gradual scarring of the lung tissue occurs, with destruction of normal lung tissue and pronounced impairment in oxygenation capacity. Although many patients complain of cough, progressive shortness of breath is the most prominent complaint.

In some patients, ILD occurs without an apparent underlying cause and is termed “idiopathic” (7). It can also be secondary to a number of conditions such as sarcoidosis, hypersensitivity pneumonitis, asbestos exposure, adverse reactions to medications, or autoimmune diseases such as lupus or rheumatoid arthritis. In all these instances, unchecked ILD may eventually progress to permanent lung scarring known as pulmonary fibrosis. At this point imaging studies show permanent scarring and a typical radiologic pattern called “honeycombing” (Figure 13.2). Treatment is mainly targeted towards the underlying disease process associated with the ILD (ie, steroids for connective tissue disease) or avoidance of the offending agent/exposure. General pulmonary therapies include oxygen, rehabilitation, and lung transplantation. To date, there is no effective drug therapy to reverse the fibrotic process that occurs in the lungs.

Considerations for Rehabilitation

The main consideration while working with a patient with ILD is to ensure adequate oxygenation during exercise. Subjects with ILD tend more often to be hypoxemic than patients with COPD and many require supplemental oxygen even at rest (8). Close monitoring of \( O_2 \) saturations during exertion is therefore crucial. For patients already
II. SPECIFIC MEDICAL COMPLICATIONS

on supplemental oxygen, it is advisable to increase $O_2$ flow at least 2 L/min above the requirements at rest before engaging in activity and grade the exercise level to a point where subjects can keep an adequate $O_2$ saturation. Relative to other forms of exercise, activities of lower intensity and longer duration are preferable for ILD patients. Some subjects may require more $O_2$ than can be supplied with a nasal cannula and exercise may need to be performed gradually with the patient using devices that provide higher oxygen flow (Table 13.3).

**TABLE 13.3 Oxygen Delivery Methods**

<table>
<thead>
<tr>
<th>Oxygen Delivery Method</th>
<th>$\text{FiO}_2$ Provided</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nasal cannula</td>
<td></td>
<td>Flow should not be $&gt;6$ L/min. Humidity required for $&gt;4$ L/min</td>
</tr>
<tr>
<td>1 L/m$^a$</td>
<td>24%</td>
<td></td>
</tr>
<tr>
<td>2 L/m</td>
<td>28%</td>
<td></td>
</tr>
<tr>
<td>3 L/m</td>
<td>32%</td>
<td></td>
</tr>
<tr>
<td>4 L/m</td>
<td>36%</td>
<td></td>
</tr>
<tr>
<td>5 L/m</td>
<td>40%</td>
<td></td>
</tr>
<tr>
<td>6 L/m</td>
<td>44%</td>
<td></td>
</tr>
<tr>
<td>Simple mask</td>
<td>35%–55%</td>
<td>Flow must be $&gt;5$ L/min to prevent rebreathing of $CO_2$</td>
</tr>
<tr>
<td>Aerosol mask</td>
<td>28%–100%</td>
<td>Employs flow rates of 8 to 15 L/min</td>
</tr>
<tr>
<td>Venturi mask</td>
<td></td>
<td>Appropriate flow rate must be used as indicated in each connector</td>
</tr>
<tr>
<td>Blue connector</td>
<td>24%</td>
<td></td>
</tr>
<tr>
<td>Yellow connector</td>
<td>28%</td>
<td></td>
</tr>
<tr>
<td>White connector</td>
<td>31%</td>
<td></td>
</tr>
<tr>
<td>Green connector</td>
<td>35%</td>
<td></td>
</tr>
<tr>
<td>Red connector</td>
<td>40%</td>
<td></td>
</tr>
<tr>
<td>Orange connector</td>
<td>50%</td>
<td></td>
</tr>
<tr>
<td>Purple connector</td>
<td>60%</td>
<td></td>
</tr>
<tr>
<td><strong>Nonrebreathing mask</strong></td>
<td>80%–100%</td>
<td>Flow must be sufficient to keep bag $\geq$ half inflated</td>
</tr>
</tbody>
</table>

Actual oxygen delivery is always less than the ideal values listed above. The discrepancy increases with the respiratory rate.

$^a$L/m: liters/minute.
NEUROMUSCULAR DISEASE

Multiple different disorders affecting the nerves and muscles can cause impairment in respiratory muscle function and include, but are not limited to, myasthenia gravis, amyotrophic lateral sclerosis (ALS), muscular dystrophy, spinal trauma, and medication-induced myopathy. Neuromuscular weakness leads to a decreased ability to take deep breaths and forcibly exhale as well as a restrictive ventilatory defect. The respiratory status of these patients is monitored using spirometry by measuring FVC as well as maximal inspiratory force and maximal expiratory force. These measures reflect the patient’s ability to take deep breaths and cough forcefully. As neuromuscular disease worsens, there is a progressive inability to exhale CO₂ because of respiratory muscle weakness referred to as chronic ventilatory failure, which may require invasive or noninvasive assistance with a ventilator. The natural history of this syndrome is variable and depends on the underlying etiology. Some conditions, such as ALS, are refractory to therapy and unavoidably lead to chronic respiratory failure.

Considerations for Rehabilitation

In most cases, rehabilitation is required to maintain muscle strength and in severe cases, to keep muscles stretched and joints mobile. When working with patients with neuromuscular disease, it is important to periodically assess O₂ saturations at rest and during exertion. The physiatrist should also be aware of signs of ventilatory failure that may reflect acute worsening of CO₂ retention, such as tachycardia, excessive sweating, use of accessory respiratory muscles, and “abdominal breathing.” CO₂ retention (respiratory acidosis) may be associated with low O₂ saturations and should be considered before simply dialing up the supplemental oxygen and allowing the process to get worse. This can be done by obtaining an arterial blood gas or using a capnometer (measures exhaled CO₂ through a special nasal cannula). Significant CO₂ elevations from baseline and decreases of pH below 7.35 are a cause for concern and warrant prompt physician referral.

POST-ICU CARE

A common entity treated in intensive care units (ICUs) is the acute respiratory distress syndrome (ARDS), a condition in which the lungs are filled with fluid (edema) as a result of an acute inflammatory process. It is commonly a result of infections (pneumonia, sepsis) but may be secondary to other conditions such as burns, trauma, or pancreatitis. Patients require intubation and usually depend on high levels of mechanical ventilator support. In addition, ARDS is often associated with multiorgan failure and carries a significant mortality. Patients fortunate enough to survive often endure
II. SPECIFIC MEDICAL COMPLICATIONS

various consequences of critical illness, such as severe weakness because of polyneuropathy, myopathy, and severe deconditioning. Therefore, it is not uncommon that ICU survivors are referred for intense rehabilitation.

Considerations for Rehabilitation

Patients who suffer from ARDS may have transient or permanent lung damage leading to hypoxemia and oxygen dependence and may require supplemental oxygen. Not infrequently they may have a “restrictive physiology” that resembles that of ILD. The principles of oxygen monitoring are just as important as in the conditions described before. Recent studies have placed emphasis on the psychological effects of long ICU stays, which can be severe and may include posttraumatic stress disorder. All of these complications emphasize the importance of medical rehabilitation after discharge from the ICU.

PULMONARY COMPLICATIONS IN REHABILITATION

The physiatrist should be aware of the pulmonary complications that may occur during therapy. Although they are often related to underlying comorbidities that are common to rehabilitation patients, most of these conditions can occur regardless of whether they have underlying lung disease or not. Rapid diagnosis is crucial to allow for timely and appropriate treatment.

PNEUMONIA

Pneumonias are infections of the lower respiratory tract (small airways and alveoli) caused by microorganisms that are either inhaled or aspirated from the upper airway (pharynx) and are usually bacterial in origin. Pneumonias are clinically sub-classified by where the patient acquired it, as it may provide insight into the underlying etiology and potential resistance to antimicrobial therapy. Hospital-acquired pneumonia (HAP) or nosocomial pneumonia refers to any pneumonia contracted by a patient in a hospital setting at least 48 to 72 hours after being admitted. Health care-associated pneumonia (HCAP) is a category of pneumonia that extends to patients who are in close contact with health care settings such as rehabilitation centers, dialysis centers, or nursing homes, or have been recently hospitalized. Along the same lines, a ventilator-associated pneumonia (VAP) is a term used for pneumonias acquired while the patient is on a mechanical respirator. HAP, HCAP, and VAP are all associated with significantly worse outcomes compared to pneumonias acquired in the community (CAP) (9), largely because of the tendency of these pneumonias to be caused by pathogens that are resistant to common
antibiotics and to follow a more aggressive clinical course. In fact, the later into a hospital admission the pneumonia develops, the more likely it is to be associated with a multidrug resistant organism. Because of its impact on patient survival, prompt recognition is crucial to institute proper antibiotic treatment. Effective preventive strategies include proper hand hygiene at all times by health care staff, including rehabilitation personnel, at all times.

Cardinal symptoms that raise suspicion of pneumonia include fever, cough with purulent sputum production, and worsening shortness of breath. Laboratory analysis usually shows an increase in white blood cells and imaging studies of the chest reveal a new or worsening infiltrate. Typically, such infiltrate contrasts with the air present in the airways, a finding known as “air bronchograms” (Figure 13.3). Considering the complications of untreated HAP, clinicians should have a high index of suspicion for this infection and a low threshold for initiating treatment in patients who exhibit clinical change in the medical wards. Respiratory cultures should routinely be obtained in order to guide treatment. If a sputum specimen cannot be collected by noninvasive means, a more invasive procedure such as a bronchoscopy should be considered. Available microbiology information regarding bacterial speciation and sensitivities allows for appropriate antibiotic selection as well as for discontinuation of unnecessary agents. Sampling should ideally be performed prior to initiation or change of the antibiotic regimen as the yield will progressively decrease thereafter.

Frequent monitoring of oxygenation and clinical status is indicated because pneumonias can affect oxygenation and may progress to sepsis and ARDS. An
important complication to be aware of is the extension of the infection into the pleural space called empyema because of the significant morbidity that this diagnosis carries if left untreated. A diagnostic thoracentesis should be performed in all cases of pulmonary infiltrates accompanied by a new pleural effusion that is at least moderate in size or that is present in a patient who is clinically deteriorating. A pleural effusion that is either loculated radiographically or meets criteria for a parapneumonic effusion/empyema by fluid analysis should be treated with drainage and placement of a chest tube.

The key to successfully treat any pneumonia is the early initiation of broad-spectrum antibiotics. In HAP and HCAP, the bacterial organisms most commonly isolated from the respiratory tract are gram-negative bacilli (Pseudomonas aeruginosa, Klebsiella pneumoniae, Escherichia coli and Acinetobacter species) and gram-positive cocci, of which the most notable is methicillin-resistant Staphylococcus aureus (MRSA) (10). Therefore, empiric coverage with an agent with good activity against Pseudomonas (ie, cefepime, piperacillin/tazobactam, or meropenem) and MRSA (ie, vancomycin, linezolid) should be used. Once a specific pathogen has been isolated and its sensitivities identified, the broad antibiotic coverage can be changed (de-escalated) to a more targeted therapy. In cases of bacterial resistance, specialists from the Infectious Disease specialty should be involved. Treatment duration of 7 to 10 days in patients with uncomplicated HAP who have received appropriate initial coverage is usually associated with a good clinical response.

### Atelectasis

Atelectasis is a term applied when the ventilation of a portion of the lung is interrupted with lack of aeration leading to alveolar collapse. Since these areas of collapsed lung maintain their blood supply, it causes a mismatch of ventilation and blood perfusion that may result in hypoxemia and shortness of breath if extensive. Risk factors to develop atelectasis include prolonged immobility, muscle weakness, mucous plugging, ineffective cough, and suboptimal inspiratory effort. Atelectasis is not uncommon in rehabilitation patients who are weak and have a poor inspiratory effort. On imaging studies, atelectasis is seen as an opacity with evidence of lung volume loss, evidenced by the shifting of normal intrathoracic structures towards the side of the lesion (Figure 13.4). In many instances, it may pose a diagnostic dilemma since the radiographic lesion may be mistaken or even coexist with pneumonia.

Treatment of simple atelectasis focuses on re-expanding the affected lung segments by optimizing patient mobility and inspiratory effort. Frequent incentive spirometry exercises are both effective for treatment and prevention of this complication. Patients with atelectasis caused by mucous plugging will benefit from aggressive chest physiotherapy, which may be administered manually, using chest wall oscillation therapy (with a vibrating vest) or with positive expiratory pressure (PEP) masks.
Atelectasis of right upper lobe
Atelectasis of entire left lung
Upward shift of fissure
Ipsilateral shift of trachea

FIGURE 13.4 Two examples of atelectasis seen on chest x-rays. Note the shift of intrathoracic structures.

Significant mucous plugging causing symptomatic atelectasis (shortness of breath or hypoxemia) requires pulmonary consultation for direct aspiration of secretions with a bronchoscope. Although lung collapse may result in a low fever, atelectasis not associated with an active pneumonia is unlikely to cause a high fever, an elevated white blood cell count, or purulent secretions. The presence of these features should alert the possibility of a concomitant infection and the need to start antimicrobial therapy.

Pulmonary Embolism

Pulmonary embolism (PE) is a condition in which a blood clot (thrombus) formed in a distal vein dislodges and migrates to the lungs, acutely occluding a portion of the pulmonary artery circulation. Depending on the extent of the occlusion, symptoms may vary from being completely asymptomatic, to developing acute and sharp chest pain, hypoxemia, shortness of breath, or coughing blood (hemoptysis). Large pulmonary emboli can lead to shock and sudden death.

Subjects undergoing rehabilitation may have a higher risk to develop deep vein thrombosis (DVT) that can lead to PE. Known as the Virchow’s Triad, there are three main factors that are recognized as contributing to the development of DVT: a propensity to clot (hypercoagulable state), venous stasis, and vein (endothelial) injury. The latter two can easily be brought about by poor mobility and a chronic inflammatory state present in many rehabilitation patients. Subjects who have undergone orthopedic procedures are particularly vulnerable because of immobility and tissue debris that enters the bloodstream during the preparation of bones for the artificial joints. For this reason, different groups of high risk patients need to receive low dose anticoagulants such as heparin as a prophylactic measure against thrombosis (11).
An asymmetric swelling of a limb should prompt evaluation for DVT using a Doppler ultrasound, while PE should be kept in the differential diagnosis of patients who develop acute dyspnea and tachycardia, particularly if associated with sharp pain upon inspiration (pleuritic pain) and hypoxemia. High suspicion of PE should be followed by a confirmatory test such as CT angiography (Figure 13.5). Alternatives include a nuclear medicine ventilation/perfusion scan or a Doppler ultrasound for confirmation of occult DVT.

Treatment of DVT/PE involves immediate anticoagulation with intravenous (heparin) or subcutaneous (heparin or low-molecular heparins) agents. Patients who are hypoxemic or have hemodynamic compromise such as hypotension or severe tachycardia as a result of the embolus occluding large portions of the pulmonary circulation should be considered for rapid transfer to an intensive care unit for closer monitoring and may be candidates for more aggressive (and riskier) therapies to dissolve the clots.

After patient stabilization with intravenous or subcutaneous therapy, overlapping with oral anticoagulation over a few days is usually performed (warfarin) and continued for 3 to 6 months. Specific coagulation laboratory parameters are used to monitor the dosage of anticoagulation agents used and include prothrombin time (PTT) for heparin, international normalized ratio (INR) for warfarin, and sometimes anti-Xa...
levels for low-molecular weight heparins. For example, oral warfarin dosing should be adjusted to target an INR between 2 to 3 (normal value: 1).

In the presence of acute DVT or PE, it is advisable to hold rehabilitation treatments until the patient’s condition is stabilized. For PE, patients should no longer feel dyspneic and be able to oxygenate well with no or little oxygen requirements. For DVT, early walking exercise is safe and recommended to help reduce acute symptoms, improve quality of life, and may help to prevent or improve the postthrombotic syndrome, a condition that causes leg swelling and pain that may persist for months as a result of venous insufficiency (12).

REFERENCES

Osteomyelitis refers to any infection of bone tissue and has long been recognized as one of the most difficult infectious diseases to manage. In inpatient rehabilitation services, osteomyelitis is a commonly encountered diagnosis and may arise in a number of distinct settings. Trauma patients who have suffered penetrating injuries or open fractures are at high risk for acute osteomyelitis as a result of direct inoculation of organisms. Spinal cord injury patients may develop contiguous osteomyelitis (acute or chronic) because of chronic skin ulcerations and direct exposure to pathogens. Additionally, patients in the rehabilitation setting may have catheters for long-term administration of intravenous medications, resulting in increased risk for catheter-related bloodstream infections and the possibility of developing hemato-genous osteomyelitis. All of these types of osteomyelitis require long-term administration of antimicrobials, often via the intravenous route in the outpatient setting, and such patients should be managed in consultation with the infectious diseases specialist.

CLASSIFICATION

Many formal classification schemes have been proposed for osteomyelitis (1–3). Waldvogel introduced a classification scheme according to the mode of introduction of infecting organisms (hematogenous, contiguous, or associated with vascular insufficiency) (2). Other classification schemes assess acute versus chronic infection. It is important to note, however, that osteomyelitis is generally defined as chronic in the presence of fragments of necrotic bone (sequestrum), regardless of the time since initiation of infection (1,4). However, much of current thinking regarding diagnosis and treatment of osteomyelitis is based on the Cierny and Mader classification scheme (3). This method categorizes osteomyelitis according to the anatomy of the infected bone (medullary, superficial, localized, or diffused) and also considers the physiology and immune status of the host (1,3).
14. OSTEOMYELITIS

DIAGNOSIS

Clinical

Clinical signs and symptoms of osteomyelitis are often nonspecific and depend on the location of the infection. Fevers, chills, general malaise, difficulty with weight-bearing, decreased range of motion, and localized swelling or tenderness may be present (5). In the context of trauma, nonhealing wounds, expression of purulence, and surrounding erythema are suggestive of underlying infection, but the depth or extent of the infection is often difficult to determine clinically. A draining sinus tract, when present, is highly suggestive of underlying chronic osteomyelitis (6), as is the presence of exposed bone. The ability to “probe to bone” has a positive predictive value of 89% for the presence of osteomyelitis in the setting of diabetic patients with lower extremity ulcers (7). This tool has not been systematically studied in other settings and patient populations.

Imaging Studies

In most cases, imaging studies are needed to establish the diagnosis and extent of osteomyelitis. Although conventional radiographs are not sensitive or specific for detecting osteomyelitis, particularly when infection has been present for less than 2 weeks (8–11), they are a useful first step in the evaluation of the anatomy of the affected bone. In chronic osteomyelitis, findings may include lytic lesions, periosteal reaction, sclerosis, and cortical erosions (8–10). Trauma, fractures, or other anatomic distortions, including changes induced by previous surgery, can complicate the interpretation of conventional radiographs (8).

MRI is the most sensitive imaging modality for acute osteomyelitis as, within one week of infection, detectable signal changes occur as a result of marrow edema (8,10). However, the finding of marrow edema is not specific to osteomyelitis and can be difficult to distinguish from neoplastic processes (12). Additionally, as marrow edema caused by infection cannot be reliably distinguished from surrounding reactive edema, MRI may at times overestimate the affected area of bone. Interpretation of MRI findings can be challenging in the setting of concurrent malignancy, recent trauma, or recent surgery (12).

The sensitivity of MRI to osteomyelitis is reported to be 82% to 100% (8). In the absence of typical findings of osteomyelitis, MRI generally has an excellent negative predictive value for osteomyelitis and may therefore be useful for excluding osteomyelitis when clinical suspicion is low (9,11). Additionally, MRI provides excellent visualization of anatomy and can be helpful in the planning of debridement and other surgical interventions. Contrast enhancement is not required to visualize changes due to marrow edema. However, when a contrast medium such as gadolinium...
II. SPECIFIC MEDICAL COMPLICATIONS

is used, MRI can also reveal abscesses and fistula tracts as well as sequestra (9). There is a low risk of nephrogenic systemic fibrosis after administration of gadolinium-based contrast agents in individuals with decreased renal function (glomerular filtration rate [GFR] <30 mg/mL/min), with hepatorenal syndrome, or following kidney transplant. Nephrogenic systemic fibrosis consists of pathological deposition of collagen in tissue, particularly in the skin of the extremities, resulting in immobility and joint contractures (13). For this reason, administration of gadolinium-based contrast to individuals with renal dysfunction should be avoided when possible (14). MRI is susceptible to image artifact in the presence of nearby high-attenuation objects such as a metal implant. MRI is not practical for whole body scanning or scanning of very large anatomic areas.

CT, although less sensitive than MRI for detection of osteomyelitis, provides excellent visualization of bony sequestra typical of chronic bone infection, and increased marrow density caused by edema and inflammation may be seen in early infection (8). CT is generally the imaging modality of choice when MRI cannot be performed. Contrast administration is useful for definition of soft tissue abnormalities as well as bone changes. Additionally, CT imaging can reveal areas of necrotic bone, soft tissue involvement, and abscesses (9,10,15). As with MRI, streak artifact from high-attenuation objects such as metallic implants may severely limit the interpretation of nearby images, limiting usefulness in device-associated infection.

Nuclear imaging modalities currently in widespread use for evaluation of osteomyelitis are triple-phase bone scans, gallium scans, and tagged white blood cell scans. Single-photon emission computed tomography (SPECT) and positron emission tomography (PET) scanning are also promising for evaluation of osteomyelitis in patients who cannot have MRI performed on them. In all cases, these nuclear imaging studies rely on flow of isotopes through the bloodstream to affected areas to identify areas infiltrated by inflammatory molecules or cells and are therefore less sensitive when blood flow is compromised (16). Additionally, alternative causes of inflammation or bone turnover may cause false positive results (17).

In standard triple-phase bone scans, a radiolabeled tracer is injected, and scans are performed just following injection (to measure blood flow to the area of interest), 15 minutes after injection (to measure inflammation in the area of interest), and four hours after injection (to measure accumulation in bone). Images are planar. In osteomyelitis, increased signal is expected in all three phases, whereas cellulitis with normal adjacent bone will reveal increased signal only in the first two phases (17). Using this evaluation criterion in the setting of normal radiographs, both the sensitivity and specificity of triple-phase bone scan are considered to be approximately 95% (17,18). However, abnormal anatomy or increased bone metabolism unrelated to infection may cause a false-positive result. Therefore, in real-world settings with frequently abnormal baseline radiographs, the overall estimated specificity of triple-phase scanning is approximately 50% (18).
Another planar nuclear imaging study frequently utilized in the setting of suspected osteomyelitis is gallium-67 imaging. This modality takes advantage of gallium-67 binding to transferrin and lactoferrin, acute phase reactants that accumulate at sites of inflammation. Gallium scanning is more sensitive and specific than triple-phase bone scans but produces lower quality images and requires imaging 24 hours after injection, therefore producing potential delays in diagnosis and management (18,19).

Tagged white blood cell scans, in which leukocytes are radiolabeled ex vivo and reinjected, have also demonstrated increased specificity for osteomyelitis when compared with the triple-phase bone scan but sensitivity is low for chronic osteomyelitis in the central skeleton as a result of the active bone marrow producing increased background signal and decreased migration of leukocytes in a chronic infection (16).

PET and SPECT imaging provide functional information with high contrast resolution. PET generally has higher resolution and sensitivity compared with SPECT (18). 18F-FDG PET has been reported to have a sensitivity of 95% and specificity above 85% for osteomyelitis, including spinal infections (20–22). Limitations include a drop in specificity to 75% in the recent (within 6 months) postoperative period and to 65% when metal implants are present (22).

In general, planar nuclear imaging studies are not as clinically useful as MRI or CT for planning surgical interventions or identifying collections or fistula tracts because of lack of anatomical visualization and differentiation of soft tissue from bone (8–10). Therefore, MRI or CT is generally preferred over nuclear imaging studies for evaluation of osteomyelitis. However, within the limitations outlined above, nuclear imaging can be useful for evaluation of the whole body or large anatomical areas when MRI or CT are impractical. 18F-FDG PET is the most sensitive imaging modality available for patients with suspected osteomyelitis and metallic implants in place that preclude MRI, although specificity is limited in this setting (18,22).

Laboratory

Most laboratory findings of osteomyelitis are nonspecific. Whereas the peripheral white blood cell count may be increased in the setting of acute osteomyelitis, leukocytosis is not specific and not predictably present in acute or chronic infection. The presence or absence of leukocytosis should not alter the clinical suspicion for osteomyelitis (23,24).

The erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) are frequently obtained when osteomyelitis is suspected. These measures have been assessed in the context of suspected acute and chronic osteomyelitis in adults and children, but studies are largely retrospective, and use of differing cut-off values complicates generalizations. Pooled data suggest that normal levels of both ESR and CRP support absence of osteomyelitis when the clinical suspicion is also low (25). Likewise,
II. SPECIFIC MEDICAL COMPLICATIONS

Elevated markers (ESR greater than 30 to 60 mm/hr or CRP greater than 10 to 30 indicates variability in the study methods used) are highly suggestive of the need to perform further assessment for osteomyelitis in the appropriate clinical setting (25–27).

Serum procalcitonin, a marker intended to distinguish bacterial infections from other inflammatory conditions (28,29), has been recently assessed for its utility in the diagnosis of bone and joint infections. In a meta-analysis of 7 available studies evaluating procalcitonin levels in osteomyelitis and septic arthritis, pooled sensitivity was 0.67 and specificity 0.90, indicating lower sensitivity and higher specificity than CRP in this population (30). In diabetics with lower extremity wounds, procalcitonin measurements were elevated to similar levels in soft tissue and bone infection (30). Because of heterogeneity in the studies and the patient populations, the utility of this marker in clarifying the diagnosis of osteomyelitis is currently unclear.

Bone Biopsy

Bone biopsy should be obtained whenever osteomyelitis is present or suspected to be present to establish the diagnosis and/or to obtain culture and susceptibility information (2,5,6). When possible, percutaneous biopsy should be done through uninvolved skin (31). An exception to the need for biopsy occurs in hematogenous osteomyelitis of the vertebral bodies in which a combination of positive blood cultures with a consistent microorganism as well as imaging findings indicating osteomyelitis may be considered presumptive diagnostic evidence of osteomyelitis (2). When bone biopsy is performed and histopathology is found to be consistent with osteomyelitis, estimates of culture positivity vary, with reports of 34% to 87% cultures positive for a likely organism (32,33). Open biopsies are more reliable than percutaneous needle biopsy due to potential sampling error with the latter (34). Biopsies that involve aspiration of >2 cc of purulent fluid are more likely to result in positive cultures (32). Stopping antimicrobials when possible for 24 to 72 hours prior to the biopsy procedure is common practice and may increase the yield of cultures, but there are no data to suggest a specific timeframe for stopping antimicrobials and the resulting increase in culture positivity (32).

Growth in cultures obtained from superficial swabs of draining or non-draining wounds or sinus tracts do not reliably correspond to the pathogen causing bone infection and should not be used in place of bone cultures to determine treatment of osteomyelitis (34–36). Material for culture should be sent promptly in a sterile container for gram stain as well as aerobic and anaerobic culture and a separate specimen sent for histopathology. Specialized cultures for mycobacteria and fungal organisms should be performed when evaluating immunocompromised patients at risk for opportunistic infections, in circumstances such as open trauma with exposure of bone to the environment and when evaluating those individuals not responding to conventional antibacterial antibiotics particularly when standard cultures have been negative.
When hardware is present and removed, sonication of the removed hardware to disrupt biofilms may increase the yield of cultures, especially in patients who have received antimicrobials within the previous 14 days (37,38). Sonication, however, is not feasible in many clinical settings.

**MICROBIOLOGY**

Positive cultures from bone revealing a microbiological etiology for osteomyelitis are found in up to 87% of cases when appropriate biopsies are performed (33). Bone infected by contiguous spread frequently tests positive for multiple organisms by culture. Hematogenous spread usually results in a monomicrobial infection (5). In cases of traumatic inoculation, puncture, or penetration, organisms present in the environment at the time of the injury must also be considered. *Staphylococcus aureus* is the most commonly isolated pathogen in most series of osteomyelitis. Streptococci, enterococci, coagulase negative staphylococci, as well as *Pseudomonas* spp., *Morganella* spp., and other gram negative rods are frequently isolated (2,34,39). Candida may cause hematogenous osteomyelitis in patients with recent intravascular catheter infections (40). Mold and mycobacteria may also cause bone and joint infections in patients with environmental exposure to these organisms (41,42). All culture material should be sent to the laboratory for isolation of routine aerobic and anaerobic bacteria, and in the appropriate clinical context, also for fungi and mycobacteria. Patients who have had recent and/or prolonged hospitalizations are at risk for multidrug resistant organisms, and culture information is essential to appropriate treatment.

**TREATMENT**

Treatment of osteomyelitis most frequently requires a combined medical and surgical approach. Initial surgical goals include obtaining diagnostic specimens for culture and histopathology to facilitate an accurate diagnosis and appropriate antimicrobial treatment, adequate debridement of infected tissue and bony sequestra, drainage of fluid collections, and removal of infected hardware (3,5). Appropriate antimicrobial therapy is based on culture results, pharmacokinetics of the available antimicrobials, and allergy history.

For methicillin-susceptible *S. aureus*, a penicillinase-resistant penicillin such as oxacillin, nafcillin sodium, or cefazolin, is optimal (5). Vancomycin is clearly inferior to beta-lactam antimicrobials for methicillin-susceptible *S. aureus* (43). For methicillin-resistant *S. aureus* (MRSA), careful assessment of in vitro laboratory sensitivities of the organism to vancomycin is essential for optimization of treatment (44). Although vancomycin is frequently used as first line therapy for these infections, failure rates of greater than 40% have been reported (44–46). For all pathogens, treatment must be
individualized and carefully monitored. Recent data suggests that treatment of chronic osteomyelitis with oral medications that have good oral bioavailability and activity against the causative pathogen can be as successful as parenteral treatment and avoids complications related to intravascular catheters (47,48). Fluoroquinolones are excellent oral choices for susceptible gram negative rods, and combinations of trimethoprim-sulfamethoxazole with rifampin have been demonstrated effective for MRSA infections with susceptibility to both antimicrobials (49). Rifampin is added to many regimens because of its ability to penetrate bacterial biofilms and bone and its theoretical benefit in treatment of chronic infections; but resistance to rifampin develops rapidly, and this antimicrobial should be used only in combination with other effective antimicrobials (50). Likewise, fluoroquinolones should not be used for monotherapy of staphylococcal infections because of the possibility of the development of resistance during the course of therapy (44). Oral beta-lactam antimicrobials generally do not reach concentrations in bone considered adequate for treatment of osteomyelitis (48).

When culture information cannot be obtained, or cultures are negative despite best efforts, empiric therapy directed at the most likely pathogens with consideration to the patient’s known previous colonization or infection with antimicrobial resistant pathogens may be considered. Usually, this includes empiric treatment for MRSA with vancomycin and a second agent for gram negative bacteria such as a fluoroquinolone or an antipseudomonal cephalosporin (5). Consultation with an infectious disease specialist is advised to determine the best regimen when culture information is not available, is complex, or is conflicting, and when the patient is at risk for unusual infections as a result of exposures or immunosuppression.

The duration of antimicrobial therapy for osteomyelitis has not been established in prospective randomized studies. Animal models of osteomyelitis that do not include surgical debridement demonstrate consistently superior bone sterilization rates after 4 weeks of parenteral antimicrobial therapy compared with 2 weeks of therapy (51). Additionally, when surgical debridement is performed, revascularization of surrounding tissue requires approximately 6 weeks of healing (52). Most practitioners advise at least 4 to 6 weeks of treatment for osteomyelitis following the last surgical debridement (5,6). For MRSA osteomyelitis, guidelines recommend at least 8 weeks of treatment (44). The optimal duration of parenteral antibiotic treatment for osteomyelitis prior to switch to oral antibiotics has not been established. When parenteral treatment is utilized, it is often administered in the home setting for the majority of the duration of the therapy. For antimicrobial agents requiring frequent dosing such as oxacillin sodium, continuous infusion of the antimicrobials with use of a portable pump is frequently advised. Close follow-up for complications of antimicrobial therapy and monitoring of the indwelling infusion catheter are required for the duration of the therapy (53).

Generally, removal of foreign bodies, including hardware, is advised in the setting of osteomyelitis. This strategy is occasionally not possible because of the prospect of anatomic destabilization with the removal of the hardware prior to bone healing.
or surgery may be precluded due to the patient’s overall medical condition. In these cases, the treatment plan may include debridement followed by parenteral antimicrobials to reduce bacterial burden and maintenance with suppressive doses of oral antimicrobials until bone healing occurs and the hardware may safely be removed (1,3). Antimicrobials should be carefully chosen in consultation with an infectious disease expert to minimize toxicity and appropriately address the cultured bacteria. Later surgical interventions may focus on placement of muscle flaps or other measures to facilitate closure of wounds, stabilization procedures, and reconstruction (5).

Serum markers are frequently used for follow-up during and after treatment for osteomyelitis. CRP and procalcitonin appear to decline and normalize more quickly on antimicrobial treatment than ESR. Based on studies in vertebral osteomyelitis, it is known that persistently elevated CRP and ESR after 4 weeks of treatment may warrant concern regarding an ongoing infection or complication (54,55). In one study of individuals with diabetic foot infections, persistent elevations in ESR at 3 months were observed only in the subset with ongoing osteomyelitis (56). Guidance on the use of CRP and ESR to assist in clinical decision making during treatment and follow-up in other circumstances is currently lacking, but many clinicians use an increasing CRP after an initial decline following debridement as a marker for relapsing infection (57). It has not been established that serum markers must be in normal range prior to discontinuation of antimicrobials.

SUMMARY

Bone infection presents challenges in diagnosis and treatment. Bone biopsy remains essential for establishing appropriate treatment in most cases. A multidisciplinary approach to diagnosis, treatment, rehabilitation, and/or reconstruction is required. Whereas the optimal duration of antimicrobials for osteomyelitis has not been established, treatment with oral antimicrobials with good bioavailability or intravenous antimicrobials based on culture and susceptibility results for at least four weeks after debridement is generally recommended. Consultation with specialists in infectious diseases is recommended for establishing the optimal treatment and follow-up regimen for individuals with these challenging infections.

REFERENCES


42. Cruz AT, Antekeier SB. Chronic multifocal Mycobacterium fortuitum osteomyelitis following penetrating plantar trauma. *Am J Orthop (Belle Mead NJ).* 2012;41:E109–E111.
II. SPECIFIC MEDICAL COMPLICATIONS


Clostridium difficile Colitis

Lilian M. Abbo

Clostridium difficile infection (CDI) is a significant and growing problem worldwide (1,2). The importance of CDI in the United States is underscored by the 14,000 deaths and over $1 billion in excess costs annually (1). Traditionally regarded as a consequence of acute-care hospitalization and prior antibiotic exposure, the epidemiology and treatment of this disease are rapidly changing. Patients in Physical Medicine and Rehabilitation are vulnerable to CDI because of age, prior hospitalization, prior exposure to antimicrobial therapy, and diminished immune status (3,4). C. difficile can be found in asymptomatic patients as part of the bowel flora (colonized/carrier state) or as an infectious organism causing a wide range of manifestations from mild to extremely severe colitis. The purpose of this chapter is to review the changing epidemiology, risk factors, clinical manifestations, diagnosis, treatment, and prevention of CDI, in particular C. difficile colitis.

C. difficile is an anaerobic gram-positive, spore-forming bacillus that causes diarrhea via the production of two large molecular weight toxins, toxin A and toxin B (5). Binding of these toxins to the colonic epithelial cells leads to disruption of vital cell-signaling pathways causing inflammation and mucosal injury leading to intestinal fluid secretion and diarrhea (6,7). C. difficile can exist in spore and vegetative forms. Outside the colon, it survives as spores that are heat, acid, and antibiotic resistant. Colonization of the gastrointestinal tract occurs via the fecal-oral route following environmental exposure to C. difficile spores or from contact with an infected person or health care worker (2). Once the spores enter the colon, they can convert to functional vegetative, toxin-producing forms. Infection is facilitated by treatment with antimicrobials, which disturb the normal colonic microbiota, allowing toxigenic C. difficile to flourish (8). If patients are unable to mount a protective antibody response, infection can lead to a wide range of symptoms from mild diarrhea to pseudomembranous colitis, toxic megacolon, and sometimes death (9).
ANTIBIOTIC-ASSOCIATED DIARRHEA

Most cases of antibiotic-associated diarrhea are mild and nonspecific episodes without a definitive cause. They usually resolve with discontinuation of antimicrobial therapy (10,11). No mechanism has been clearly established as a cause of antibiotic-associated diarrhea, but studies suggest that changes in fecal microbiota are a contributing factor (11,12). Some theories suggest that antibiotics, by substantially altering the colonic flora, reduce the concentration of fecal anaerobes that are normally present and, thus, alter the metabolism of carbohydrates, causing osmotic diarrhea (10,11). In many suspected cases, nonantibiotic drugs are the cause of diarrhea attributed to antibiotics; these include laxatives, antacids, contrast agents, products containing lactose or sorbitol, nonsteroidal anti-inflammatory drugs, antiarrhythmic drugs, and cholinergic agents (13). Although \textit{C. difficile} accounts for only 15% to 25% of the cases of antibiotic-associated diarrhea, it accounts for the majority of cases of colitis associated with antimicrobial therapy (11).

TOXIGENIC VERSUS NONTOXIGENIC CLOSTRIDIUM DIFFICILE

The development of \textit{C. difficile} colitis requires production of toxins A and/or B. Some studies suggest that toxin B is the more potent toxin in CDI pathogenesis. However, some strains do not express any of these toxins, and these nontoxigenic \textit{C. difficile} (NTCD) strains have garnered attention for their capacity to colonize patients and potentially reduce the risk for symptomatic colitis caused by toxigenic strains. Among healthy volunteers without symptoms, the prevalence of \textit{C. difficile} carriage has been reported to be between 4% and 7.6% of adults and up to 80% of healthy newborns (14–16). Of the isolates in these studies, NTCD strains accounted for 42% to 50% of the total. This percentage of NTCD is similar to what has been observed in asymptomatic hospitalized patients (17).

Although NTCD isolates are thought to be nonpathogenic, there are several reports of association with infection in susceptible patients. However, in those reports, patients were also exposed to antimicrobials and chemotherapeutics, making it unclear whether NTCD was the true cause of the diarrhea. In addition, NTCD isolates have been cultured from toxin-positive patients. This observation suggests that NTCD isolates may be involved in mixed (toxigenic and nontoxigenic) infections and such cases could be misidentified as solely associated with the nontoxigenic strain (17). Isolates of NTCD have also been obtained from the environment and from animal and human sources. Studies in a hamster CDI model have demonstrated a protective effect of NTCD against toxigenic infection (18). The extent to which this protective effect of NTCD occurs in humans remains to be defined. Evidence for a therapeutic or preventive role for NTCD is limited, but clinical prophylaxis studies are ongoing (17). For the purpose of this chapter, we focus only on toxigenic \textit{C. difficile} infections.
CHANGING EPIDEMIOLOGY

Almost every antimicrobial has been associated with CDI (19). It was first recognized in 1978 when *C. difficile* was identified as the causative pathogen of antibiotic-associated pseudomembranous colitis, with clindamycin being the most common antibiotic involved (20). The increasing widespread use of broad-spectrum antimicrobials, including beta-lactams and fluoroquinolones, subsequently led to the implication of other antimicrobials in CDI in the community and hospitalized patients (21–23). Although antimicrobial exposure is the most important risk factor for CDI, not all cases of CDI are preceded by antimicrobial use.

The incidence of CDI remained relatively stable until the early 2000s when a hypervirulent strain of *C. difficile* (ribotype NAP1/BI/027) emerged. This NAP1 ribotype has been implicated as the responsible pathogen in selected *C. difficile* outbreaks in North America and Europe (4,24). This strain produces binary toxin, an additional toxin that is not present in other *C. difficile* strains, and is resistant to fluoroquinolones in vitro (an infrequent observation in *C. difficile* strains prior to 2001) (25). The hypervirulent strain has been associated not only with an increase in the frequency of disease encountered worldwide over the last decade, but also with more severe symptoms and significantly elevated mortality rates (4,26). Data on discharge diagnosis rates in U.S. hospitals showed that rates of CDI more than doubled, from <150,000 cases in 2001 to >300,000 initial cases per year, incurring costs of up to $3.2 billion annually (1,27). The estimated number of deaths attributed to CDI, based on multiple cause-of-death mortality data, increased 400% from 3,000 deaths per year during 2000 to 14,000 deaths per year during 2007, with more than 90% of deaths in persons aged ≥65 years (1). There is clear evidence to suggest that *C. difficile* is transmissible and acquired from external sources. Cases of CDI often appear in clusters and outbreaks within institutions. Subsequently, many epidemiologic studies have confirmed the importance of *C. difficile* as a transmissible nosocomial pathogen (4,24,28,29).

RISK FACTORS

Major risk factors for CDI initial and recurrent episodes are summarized in Table 15.1. In many cases, the cause of CDI is multifactorial, but it can also occur in the absence of any known risk factors (30). A significant risk factor for CDI is recent health care exposure (31). Frequent hospitalization and increased length stay have been identified as risk factors for CDI (32). Data from the CDC’s Emerging Infections Program in 2010 determined that 94% of the CDI cases were associated with receiving health care despite 75% of cases occurring outside the hospital, including recently discharged patients, outpatients, and those in long-term care facilities (1).

Antimicrobial use has been the most widely recognized and modifiable risk factor for *C. difficile* intestinal colonization and infection (22,23,28,33,34). Various roles
have been described for antimicrobials in the pathogenesis of CDI. First, antimicrobials disrupt the normal colonic microflora, including anaerobes such as *Bacteroides* species, thereby allowing *C. difficile* to multiply and elaborate toxins in high concentrations (35,36). Second, patients who develop CDI are likely to contaminate their environment, which increases the probability of transmission, particularly to persons with an increased risk of *C. difficile* colonization (secondary to antimicrobial exposure) (35). Third, the development of *C. difficile* antimicrobial resistance to clindamycin or fluoroquinolones appears to be an important virulence factor causing severe disease (4). The antibiotics most frequently implicated in diarrhea associated with *C. difficile* infection are clindamycin, expanded-spectrum penicillins, cephalosporins and over the last decade fluoroquinolones (25,37,38). However, virtually any antibiotic may be implicated, including brief courses of antibiotics that are given prophylactically before surgery (11).

CDI disproportionately affects older patients (31). In the United States, a total of 93% of deaths from CDI occurred in persons ≥65 years of age and was reported as the 18th leading cause of death in this age group in 2008 (1,39). The Agency for Healthcare Research Quality (AHRQ) recently reported an analysis of the Healthcare Costs and Utilization Project (HCUP) database, indicating that patients ≥85 years of age have the highest rate of hospital stays for CDI (1,089 per 100,000 population), followed by patients ≥65 years of age (465 per 100,000 population). Collectively, those ≥65 years of age represented 92% of CDI-related hospital stays in the United States in 2009 (39).

### TABLE 15.1 Patient Risk Factors for Initial and Recurrent *Clostridium difficile* Infection (CDI)

<table>
<thead>
<tr>
<th>Risk Factors for Initial Episode</th>
<th>Risk Factors for Recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Advanced age &gt;65 years</td>
<td>Advanced age &gt;65 years</td>
</tr>
<tr>
<td>Antimicrobial therapy</td>
<td>Use of non-<em>C. difficile</em> antimicrobials during or following an episode of CDI</td>
</tr>
<tr>
<td>Gastric acid suppressing agents</td>
<td>Gastric acid suppressing agents</td>
</tr>
<tr>
<td>Health care exposure</td>
<td>Long hospital stays</td>
</tr>
<tr>
<td>Impaired immune response (ie, solid organ transplantation, hematopoietic stem cell transplantation, HIV infection, inflammatory bowel disease)</td>
<td>Impaired immune response</td>
</tr>
<tr>
<td>Cancer chemotherapy</td>
<td>Previous episodes of CDI</td>
</tr>
<tr>
<td>Enteral feeding and gastrointestinal surgery</td>
<td>Underlying chronic comorbidities</td>
</tr>
<tr>
<td>Smoking and history of smoking</td>
<td>Inadequate antitoxin antibody response</td>
</tr>
<tr>
<td>Underlying chronic comorbidities</td>
<td>Persistent disruption of the colonic flora</td>
</tr>
</tbody>
</table>
In addition, several host factors are probably important, including low antitoxin antibody levels and comorbid conditions. However, new at-risk populations, including children and peripartum women, have been recognized (40). For example, a study of children with diarrhea who presented to a large pediatric emergency department in Seattle found *C. difficile* cytotoxin in 6.7% of the 372 children tested; the mean age of *C. difficile*-positive patients was 19 months, and there was a strong association between the recent use of antibiotics and the presence of the toxin (41). In addition, a report from the U.S. Centers for Disease Control and Prevention described severe CDI in 10 peripartum women from four states; 50% of these women experienced a recurrence (40).

Cancer chemotherapy has also been shown to be a risk factor independent of antibiotic exposure. Several agents have been implicated, including carboplatin, cisplatin, cyclophosphamide, doxorubicin, methotrexate, topotecan, paclitaxel, vinorelbine, and 5-fluorouracil as well as others (42). The mechanism is thought to be a result of alterations in gut flora due to the antimicrobial activity of the chemotherapeutic agent. Additional mechanisms include severe inflammatory changes induced by chemotherapy, intestinal necrosis promoting an anaerobic environment within the gastrointestinal tract, decreased degradation of *C. difficile* toxins, and delayed reestablishment of indigenous microbiota (31).

Populations with underlying chronic comorbid conditions, including those with chronic kidney disease, HIV, solid organ or hematopoietic stem cell transplantation, and inflammatory bowel disease, also appear to be at an increased risk of developing CDI (42,43). It is not entirely clear whether these patients are at increased risk because of their underlying immunosuppression, their inability to develop an adequate immune response, exposure to specific medications, frequent exposure to antimicrobials, frequent and prolonged exposure to the health care environment, or a combination of these factors (31).

In a recent meta-analysis of 12 studies that assessed risk factors for CDI, the authors found that continued use of non-*C. difficile* antibiotics after diagnosis, concomitant receipt of antacid medication, and older age were significantly associated with recurrent CDI (44).

**CLINICAL MANIFESTATIONS**

The clinical manifestations of infection with toxin-producing strains of *C. difficile* are discussed in the following text. There is a wide range of manifestations from asymptomatic carriage, to mild or moderate diarrhea, to fulminant and sometimes fatal pseudomembranous colitis (28). The underlying reasons for the wide range of manifestations is not clearly understood, but may be related to complex host (ie, immunity) and pathogen factors (45). The diagnosis of CDI should be based on a combination of clinical and laboratory findings.
II. SPECIFIC MEDICAL COMPLICATIONS

ASYMPTOMATIC CARRIER

Asymptomatic *C. difficile* carriers shed *C. difficile* in their stools but do not have diarrhea. Although asymptomatic, these individuals serve as a reservoir for environmental contamination. Studies have found that the prevalence of asymptomatic *C. difficile* colonization among adults hospitalized in acute and/or long term care facilities ranges between 7% and 50% (46,47). The risk of colonization increases at a steady rate during hospitalization, suggesting a cumulative daily risk of exposure to *C. difficile* spores in the health care setting (28). The host immune response to *C. difficile* and the acquired strain (toxigenic vs. nontoxigenic) may play a role in determining an individual’s carrier status (15,33,46).

DIARRHEA WITH COLITIS

*C. difficile* colitis is usually manifested by watery diarrhea (up to 10–15 stools daily), mild to severe abdominal pain, tenderness and cramping with associated low grade fever and leukocytosis (48). Diarrhea may be associated with the passage of mucus or occult blood in the stool, but melena or hematochezia are rare (28). Some patients with CDI and fever or leukocytosis do not have diarrhea, and diagnosis is difficult. Physical examination may reveal variable findings that range from mild to severe abdominal pain, tenderness and cramping with associated low grade fever and leukocytosis (48). Fever (temperature >38.5°C) is associated with *C. difficile*-associated diarrhea in about 15% of cases, and is a sign of severe disease. These symptoms generally occur in the setting of antibiotic administration; they may begin during antibiotic therapy or 5 to 10 days following antibiotic administration or even with limited exposure as a single-dose (31). Infrequently, symptoms present as late as 10 weeks after cessation of therapy. Extraintestinal manifestations such as bacteremia or arthritis are very rare (28). *C. difficile* pouchitis or ileitis has been a traditionally rare manifestation, but it is increasingly recognized in patients who have undergone a total colectomy (49).

Depending on the course of the illness and clinical response to treatment, sigmoidoscopic or colonoscopic exams may be normal or reveal mild erythema, friable mucosa, or manifestations of severe infection with pseudomembranes (Figure 15.1) (50). Unexplained leukocytosis in hospitalized patients (with or without diarrhea) may reflect underlying CDI. Clinicians must have a high index of suspicion to make a timely diagnosis, ordering appropriate stool studies, initiating treatment, and then implementing appropriate infection control precautions.

SEVERE CDI COLITIS

There is no consensus definition of severe CDI colitis. Some of the parameters described in the literature by expert opinion include leukocytosis >15,000 cells/mL and a serum creatinine level ≥1.5 times the premorbid level (28). Patients with clinical signs and symptoms suggestive of severe CDI may develop a colonic ileus and present
with severe abdominal pain, if sensation is intact, and distention, but minimal or no diarrhea. Abdominal plain films may demonstrate small bowel dilatation, air–fluid levels, and scalloping of the bowel wall because of submucosal edema (Figure 15.2).

**FIGURE 15.2** Supine abdominal plain film shows diffuse mild dilatation of the small bowel loops. Note the haustral polypoid thickening of the colon (arrows).

Courtesy of Javier Casillas, MD.
II. SPECIFIC MEDICAL COMPLICATIONS

Pseudomembranous colitis has been used as a marker of severe CDI. However, it can only be diagnosed by direct visualization of pseudomembranes on lower gastrointestinal endoscopy (either sigmoidoscopy or colonoscopy) or by histopathologic examination. Direct visualization using any of these techniques will detect pseudomembranes in only 51% to 55% of CDI cases that are diagnosed by combined clinical and laboratory criteria that include both a culture positive for *C. difficile* and a positive stool cytotoxin test result (28). Therefore, the absence of pseudomembranes does not rule out severe CDI.

Complications of severe CDI include dehydration, electrolyte abnormalities, hypotension or shock, renal failure, lactic acidosis (plasma lactate >2.2 meq/L), hypalbuminemia (serum albumin <2.5 mg/dL), toxic megacolon, bowel perforation, systemic inflammatory response syndrome, sepsis, and death (28). Toxic megacolon is a specific clinical diagnosis based upon signs of systemic toxicity and radiological findings of colonic dilatation >7 cm in its greater diameter (Figure 15.3) (51). Given the risk of perforation, prompt surgical consultation is warranted in cases of severe disease to assess the need for colectomy.

LABORATORY DIAGNOSIS

Accurate diagnosis is extremely important in the management of CDIs. Efficiently and effectively making the diagnosis of toxigenic CDI remains a challenge to the clinician and the microbiologist. The diagnosis of CDI should be based on a combination of clinical and laboratory findings. A case definition for the usual presentation of CDI includes the presence of diarrhea, defined as passage of 3 or more unformed stools in
24 or fewer consecutive hours (47,52,53), a stool test result positive for the presence of toxigenic *C. difficile* or its toxins, and/or colonoscopic or histopathologic findings demonstrating pseudomembranous colitis (28).

According to the Clinical Practice Guidelines for *C. difficile* by the Society of Healthcare Epidemiology of America (SHEA) and the Infectious Disease Society of America (IDSA) (28), empirical therapy without diagnostic testing is inappropriate and should be avoided if diagnostic tests are available, because even in an epidemic environment, only approximately 30% of hospitalized patients who have antibiotic-associated diarrhea will have CDI (54). In a recent study conducted at a single institution, Sunkesula et al demonstrated that empiric CDI therapy results in conversion of CDI test results from positive to negative in a significant proportion of patients within 1 to 3 days compared to patients where the stool was sent prior to starting empirical CDI treatment (55). False-negative CDI test results associated with empirical therapy could result in several potential adverse consequences, including progression of illness or increased risk for recurrence if CDI therapy is discontinued due to a false-negative test (55). If a patient has severe diarrhea and there is a high suspicion that *C. difficile* is the causative organism, it is appropriate to implement infection control measures, send stool for diagnostic testing, and start empirical therapy while awaiting results (31).

According to the SHEA/IDSA *C. difficile* guidelines (28), testing for *C. difficile* should only be conducted on unformed, diarrheal stool. The only exception would be in patients with a severe ileus when no stool is produced and patients have to be treated based on a high index of suspicion based on clinical and radiological findings. There is no role for laboratory testing among patients on treatment or soon after treatment for acute disease (“test of cure”), except in epidemiological studies. The rationale to avoid these tests is that stool assays may remain positive for months during or after clinical recovery (28,56). Repeat testing following a positive test is appropriate if a patient improves on therapy and there are recurrences after the completion of a regimen (clinical recurrence) (56).

Many laboratories currently utilize an enzyme immunoassay (EIA) to test for toxin A/B because of its ease of use. However, multiple studies indicate that utilizing this test alone is not appropriate for toxigenic *C. difficile* detection because of low sensitivity (28). No single method is perfect and all assays must be undertaken with clear rules concerning diarrheal disease. Many laboratories have adopted Nucleic Acid Amplification testing (NAAT) alone or a 2 to 3 step algorithm for the most sensitive diagnosis of CDI as recommended by professional societies and guidelines (Figure 15.4) (28,52,53,56–58). The selection of the best test will depend on each institution’s clinical needs, costs, and personnel. Recommendations for laboratory testing of toxigenic *C. difficile* published by the American Society for Microbiology (ASM) (52,59) are shown in Table 15.2. Testing should be performed only if the stool is mushy or watery (conforms to the shape of the container) in patients who pass 3 or more such unformed stools in a 24-hour period unless an ileus is suspected.
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Step 1
Enzyme Immunoassays for GDH and Toxin(s) A/B

GDH positive
Toxin negative

GDH negative
Toxin negative

Step 2
Polymerase chain reaction (PCR) or Nucleic acid amplification (NAAT)

Negative Result (do NOT treat)

Positive Result (treat)

Positive Result (treat)

Negative Result (do NOT treat)

FIGURE 15.4 Algorithm for the laboratory diagnosis (52) and treatment of Clostridium difficile associated diarrhea. Repeat stool assays are not warranted during or following treatment in patients who are recovering or are symptom free.


TABLE 15.2 Recommendations for Clostridium difficile Laboratory Testing

1. Utilizing toxin A/B EIA for C. difficile diagnosis is insensitive and no longer recommended as a stand-alone test.

2. Glutamate dehydrogenase (GDH) antigen assays have been found to be good screening tests for C. difficile infection (CDI) in many studies with high sensitivity and negative predictive values.

3. Positive GDH assay results must be confirmed with a cytotoxin assay and/or nucleic acid amplification (NAAT) testing. A GDH positive result along with a positive toxin A/B EIA, a positive cytotoxin neutralization, or a positive NAAT result may be reported as positive for toxigenic C. difficile. If the A/B EIA or cytotoxin neutralization assay is used and is negative, specimens should be further tested by either NAAT or toxigenic culture.

4. Laboratories can also use a NAAT to detect C. difficile toxin genes as a stand-alone diagnostic test.

5. Repeat testing following a positive test (test of cure) is not recommended since patients may carry toxigenic C. difficile for months after clinical cure. Repeat testing following a positive test is appropriate if the patient improves with therapy and there are recurrences after the completion of a treatment regimen (clinical recurrence).

6. Repeat testing following a negative test is not recommended if one of the suggested algorithms is used because nearly all-positive patients will be detected (high sensitivity). Testing a second specimen from a negative patient is more likely to be a false positive.

7. Up to 50% of neonates may be colonized with toxigenic C. difficile. Testing for CDI in this population should proceed only after consultation with a clinician.
TREATMENT OPTIONS

Patients diagnosed with CDI-associated diarrhea should stop all concomitant antimicrobials when possible other than those used to treat the CDI. Antimicrobial recommendations are provided below. Supportive care with correction of fluid losses and electrolyte imbalances is important. Appropriate management also includes implementation of strict infection control policies. All patients with suspected or proven CDI should be placed on contact precautions, and health care providers should wash hands before and after contact with the patient or the patient’s environment. Hand hygiene with soap and water is preferred over alcohol-based hand sanitizers, since *C. difficile* spores are resistant to killing by alcohol (28).

In 2010, guidelines for the diagnosis and management of CDI were published by the SHEA and IDSA (28). Those guidelines are currently being updated and projected for publication in 2015 (60). So far, the most commonly used antimicrobials to treat *C. difficile* infections are metronidazole and vancomycin. Fidaxomicin (Difucid®) is a new macrocyclic antibiotic with bactericidal activity against *C. difficile* (61). Studies have shown that fidaxomicin may decrease recurrence rates compared to vancomycin in patients infected with non-NAP1 strains, but recurrence rates are similar in patients with the NAP1 strain (62). Therapeutic options depend on severity of symptoms and number of episodes and are discussed in the following text.

ASYMPTOMATIC COLONIZATION

As previously mentioned, asymptomatic patients should not be tested or treated routinely except in epidemiologic studies (28). The rationale for identifying and treating these asymptomatic patients is that they potentially serve as a reservoir for horizontal spread of *C. difficile* to other patients, either by way of the environment or by way of the hands of medical personnel (28). Delmee et al (63) demonstrated a significant reduction in new *C. difficile* infections in a leukemia unit after extensive environmental renovation and cleaning in addition to prophylactic oral vancomycin therapy (500 mg four times daily for 7 days) for asymptomatic colonized patients. In contrast, metronidazole therapy was ineffective in reducing the incidence of CDI when administered to all *C. difficile* carriers in a chronic-care facility, even when contact precautions and antibiotic restrictions were concurrently used (28). Further studies are needed to determine if treatment of asymptomatic *C. difficile* carriers might be effective. Optimer Pharmaceuticals, Inc. is currently investigating the use of fidaxomicin for prophylaxis against CDI in adults undergoing hematopoietic stem cell transplantation and also for the treatment of CDI in pediatric patients (64). In addition, it has been suggested that identification of asymptomatic carriers and institution of more stringent barrier precautions may be useful in interrupting outbreaks, but there are no available data to support such measures (28).
MILD AND MODERATE DISEASE

Symptomatic CDI is usually treated with oral metronidazole or oral vancomycin for 10 days. Oral metronidazole (500 mg three times daily or 250 mg four times daily) and oral vancomycin (125 mg four times daily) have similar rates of efficacy, with response rates of 90% to 97% (11). Vancomycin doses of 250 mg or 500 mg four times daily, frequently used in clinical practice, have not been shown to be more effective than the lower dose. Metronidazole is the preferred treatment in the SHEA/IDSA C. difficile guidelines (28) because it is less expensive than vancomycin and avoids the potential risk of promoting vancomycin-resistant enterococci in nosocomial cases. Indications for oral vancomycin, as opposed to metronidazole, are pregnancy, lactation, intolerance of metronidazole, or failure to respond to metronidazole after 3 to 5 days of treatment. The anticipated response to treatment is resolution of fever within 1 day and resolution of diarrhea in 4 to 5 days.

Ideally, all antibiotic treatment should be oral, as C. difficile is restricted to the lumen of the colon. If oral therapy is not feasible, metronidazole can be given intravenously at a dose of 500 mg every 8 hours. Intravenous metronidazole provides therapeutic concentrations in the fecal flora because of biliary excretion and exudation across the intestinal mucosa. Side effects of metronidazole include peripheral neuropathy, nausea, and metallic taste (11). Intravenous vancomycin is not recommended for C. difficile associated diarrhea because of its limited excretion in the colon. Most C. difficile infections respond to either vancomycin or metronidazole, and the lack of a response should prompt an evaluation of compliance, a search for an alternative diagnosis, or an assessment for ileus or toxic megacolon, as these conditions may prevent the drug from reaching the target site.

SEVERE DISEASE

Patients with severe disease should receive prompt antimicrobial therapy, supportive care, and close monitoring. Urgent surgical evaluation is recommended in patients with peritoneal signs, severe ileus, or toxic megacolon. In critically ill patients with fulminant disease, oral vancomycin 500 mg four times a day with or without intravenous metronidazole 500 mg every 8 hours should be used (28). For patients with ileus, transport of the antibiotic to the colonic lumen may be facilitated by instilling vancomycin through long tubes inserted orally or anally (enemas). The optimal enema dose has not been studied in clinical trials, but retention of enemas using 500 mg of vancomycin in 100 mL of normal saline solution every 6 hours have been described. The dose should be adjusted based on renal function and patient’s weight to avoid toxicity (28,65). Severely ill patients who have no response to metronidazole or vancomycin may, in rare instances, require colectomy (11). Colectomy can be life saving for selected patients. Colectomy has usually been performed for patients with
megacolon, colonic perforation, or an acute abdomen, and sometimes for patients with septic shock. Among patients with a lactate level of 5 mmol/L or greater, postoperative mortality is 75% or higher, and early colectomy should be considered before the patient becomes so acidotic (11,28).

Several Phase II and Phase III trials have been recently published comparing fidaxomicin with oral vancomycin for the treatment of moderate to severe CDI (61,66,67). The combined North America and International phase III trials showed that the clinical cure rates of fidaxomicin were noninferior to vancomycin, but rates of recurrence were significantly lower and global cure rates significantly higher with the fidaxomicin treatment (66). The approved dose of fidaxomicin by the Food and Drug Administration for the treatment of CDI is 200 mg orally twice daily for 10 days. No dose adjustment is recommended based on the renal function. From the evidence available to date, fidaxomicin could be used for mild to moderate or severe CDI; however, it appears to have the most benefit in preventing recurrence in patients with severe disease if the patients are not infected with the NAP1 strain. It is important to know that only a limited number of patients had severe disease in the published studies, and the beneficial results were obtained from a subgroup analysis. The major limitations of fidaxomicin are the high cost compared to alternative treatments, a lack of an IV formulation, and lack of data in pediatric patients (61).

RECURRENT OR RELAPSING INFECTION

Recurrence is defined as the complete resolution of symptoms while on appropriate therapy, followed by reappearance of diarrhea with or without other symptoms after stopping the treatment. Recurrence can occur within 1 to 3 weeks or as late as 3 months after completing a course of treatment for C. difficile (28). Recurrence has been reported in approximately 20% to 25% of the cases initially treated with oral vancomycin or metronidazole and about 15% in patients treated with fidaxomicin (68). Patients with at least one episode of recurrent CDI have a 45% to 65% chance of additional recurrences. Recurrence should be distinguished from persistent diarrhea without resolution during the first course of therapy; the latter should prompt evaluation for other etiologies. Risk factors for recurrence include age >65 years, severe underlying medical illness, and use of concomitant antimicrobials during treatment for CDI (Table 15.1).

There are different options recommended to treat recurrences of CDI (69). Patients with mildly symptomatic initial recurrence following therapy for CDI can be treated with metronidazole. The decision to administer vancomycin for a first recurrence should be based upon the presence of markers of severe disease at the time of first recurrence, rather than on previous drug exposure. Fidaxomicin is an alternative agent for treatment of an initial recurrence of CDI. There are no rigorous studies of management for multiple recurrences of CDI; new and promising therapies are being investigated (69).
Patients with multiple CDI recurrences might benefit from oral vancomycin in a pulse-tapered or intermittent fashion. The use of intermittent antibiotic therapy is based upon a theory that recurrence may be due to the presence of persistent spores that survive antibiotic therapy. Intermittent therapy is hypothesized to allow the spores to germinate on the days when no antibiotics are administered. Once the spores have converted to the vegetative, toxin-producing forms, they are susceptible to killing when antibiotics are readministered. A tapered oral vancomycin regimen consists of a stepwise decrease in dose over a period of time. Intermittent (or pulsed) therapy consists of administering the drug every few days. Guidelines have been published on treatment recommendations for recurrent CDI and are currently being updated (28, 60). Fidaxomicin may be an appropriate therapy in patients with recurrent CDI or perhaps as initial therapy in patients at high risk of developing recurrent disease, although parameters for its most appropriate use are still being defined (69).

### MONOCLONAL ANTIBODIES

The use of monoclonal antibodies against *C. difficile* toxins A and B in addition to antibiotic therapy has been reported to reduce the recurrence rate of CDI in some studies; however, they are not yet available for routine clinical use. In a study of 200 patients with CDI treated with metronidazole or vancomycin in addition to monoclonal antibodies or placebo, recurrence rates were 7% vs. 25%, respectively (70). Studies are needed to confirm these results, as well as to determine whether monoclonal antibodies are useful in the management of severe disease or if there is a role for prophylactic passive immunization for patients at highest risk.

### STOOL TRANSPLANTATION

Fecal bacteriotherapy (stool transplantation) is an alternative modality that aims to restore the normal fecal microbiota by administering a sample of healthy donor stool (12); success rates have been very high compared to oral vancomycin in curing recurrent CDI (71, 72). In a recent randomized control study comparing oral vancomycin with duodenal stool infusion, van Nood et al demonstrated that the infusion of donor feces was significantly more effective for the treatment of recurrent CDI than the use of vancomycin (72). Of 16 patients in the stool infusion group, 13 (81%) had resolution of *C. difficile*-associated diarrhea after the first infusion. The three remaining patients received a second infusion with feces from a different donor, with resolution in two patients. Resolution of CDI occurred in 4 of 13 patients (31%) receiving vancomycin alone and in 3 of 13 patients (23%) receiving vancomycin with bowel lavage ($p < .001$ for both comparisons with the infusion group).

Methods of administration of donor stool include by enema, whole bowel irrigation through a nasogastric tube, or colonoscopy. Screening of donors for possible
enteric or systemic communicable diseases is a standard practice. Many patients affected with recurrent or severe refractory disease have a rapid and durable clinical response. Postfetal-transplant evaluations show resurgence of native *Bacteroides* species frequently missing in the flora of those afflicted with CDI. There is some concern for possible spread of pathogenic organisms from donor to host, which may be of particular concern in immunocompromised hosts. Neemann et al (73) recently reported a case of severe CDI successfully treated with fecal transplantation in a nonneutropenic allogeneic hematopoietic stem cell transplant patient that previously failed conventional CDI treatment, and was cured after 48 hours of stool transplantation; future studies are needed to determine the safety of fecal bacteriotherapy in patients with impaired immune systems.

Despite reported overall success rates of approximately 90% with stool transplantation, this approach has been limited for aesthetic and logistical reasons, but is becoming more common in many clinical settings as a cost-effective treatment of recurrent CDI (72,74,75).

**PREVENTION**

Prudent use of antimicrobials has been shown to be a fundamental element in reducing CDI (23,29). Prescriber education though campaigns or antimicrobial stewardship programs restricting the use of broad spectrum agents such as fluoroquinolones, clindamycin, and cephalosporins have been shown to be successful at reducing the rate of CDI in acute and long term care facilities (3,34,76). In order to achieve and sustain reductions in CDIs, the principles of antimicrobial stewardship such as appropriate selection and duration of antimicrobial therapy should be reinforced in both community and hospitalized patients. Avoiding the use of unnecessary antimicrobials in patients colonized, but not infected, is extremely important.

CDI rates often strongly correlate with increasing antimicrobial use, poor attention to environmental cleaning, and waning compliance with good infection control practices. The prevention and control of CDIs must involve bundled interventions aimed at improving antimicrobial use across the health care system and in individual patients, as well as interventions targeting environment control, personnel hand hygiene, and barrier precautions (35).

**REFERENCES**

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II. SPECIFIC MEDICAL COMPLICATIONS


Hematological Disorders

John Byrnes

This is an overview of disorders of red blood cells (RBC), white blood cells, and platelets that may either be part of the complex of comorbidities frequently associated with patients entering a rehabilitation program or that may become manifest during the rehabilitation process. The intention is not to provide an overview of hematological disorders that could be encountered in an equivalent general patient population. It is presumed that the patients have recently met prerequisite criteria to qualify for a rehabilitation program and are reasonably medically stable without significant undefined or unresolved acute issues. Of course, hematological disorders completely unrelated to the rehabilitation issues may coincidentally present during the time frame of the rehabilitation process but these are outside the purview of this discussion. In addition, the focus of the rehabilitation program and the demographics of its participants make up may make some issues more prevalent.

ANEMIAS

Iron Deficiency and Anemia of the Inflammatory Response

Anemia is very prevalent in the chronic care population. Although iron deficiency anemia is the most common RBC abnormality in the acute care population, the anemia of chronic disease is the most prevalent anemia in the chronic care population and iron deficiency is less prevalent. The anemia of chronic disease has similarities to iron deficiency anemia and is often misdiagnosed and mistreated. Both can be microcytic and hypochromic, but iron deficiency more so. Both are involved with iron metabolism, and both are manifested by a low serum iron level. Patients with iron deficiency anemia should be treated with iron and they respond quickly to adequate replacement. On the other hand, the patient with the anemia of chronic disease does not respond to iron administration and the affected patients generally should not be given iron as explained in the following text.
The anemia of chronic disease is better described as the anemia of the inflammatory response and is now known to be part of the inflammatory defense mechanism (1). Consequently, I will refer to it as such and not as the anemia of chronic disease. Furthermore, it can manifest during acute illness as well as be found in chronic disorders. The primary feature of the anemia of the inflammatory response is the uptake and retention of iron into the cells of the reticuloendothelial system, primarily macrophages in the bone marrow and liver. A major distinguishing feature of iron deficiency anemia is the absence of iron in the bone marrow of patients, whereas in the anemia of chronic inflammation, iron is abundant in the marrow. The iron content of a bone marrow is routinely evaluated by Prussian Blue staining of the bone marrow aspirate.

The pathophysiology of the anemia of the inflammatory response has recently been elucidated (2). It is multifactorial and is primarily driven by cytokines of the immune response, inducing changes in iron homeostasis. Lesser factors are impaired proliferation of RBCs in the bone marrow, shortening of the life span of RBCs, and decreased production of erythropoietin. Central to understanding the pathophysiology of the anemia of inflammation is the recently described role of hepcidin in normal iron homeostasis and its role in the inflammatory response. Hepcidin was discovered in 2000 and is the major iron regulating hormone. It is a 23 amino acid polypeptide produced primarily in the liver. Normally it regulates iron absorption out of the enterocytes of the duodenum and macrophages into the circulation. Hepcidin binds to and inhibits ferroportin, the cell membrane iron transporter. Increases in hepcidin cause internalization of ferroportin molecules on cell membranes, preventing the extracellular transport and release of stored iron. Normally, hepcidin inhibits the transport of absorbed iron out of the duodenal enterocytes into the circulation, thus blocking dietary iron absorption when it is not needed, preventing excessive iron absorption. It also regulates internal iron homeostasis, releasing just enough iron from storage sites to transferrin as needed for red cell production. Transferrin, the major iron transport protein in plasma, transports iron in the circulation—one molecule binds two atoms of iron very tightly. Transferrin delivers iron via transferrin receptors to red cell precursors and other cells needing iron.

However, hepcidin is an acute phase protein induced by interleukin-6 during inflammation. In response to IL-6, the liver produces increased amounts of hepcidin. When hepcidin is high, serum iron levels drop because it is trapped in the gut enterocytes, inside the liver, and bone marrow macrophages and not able to enter the circulation (2). Trapping of iron and reduction in plasma iron is in fact a protective mechanism to limit the amount of iron available to bacteria and parasitic invaders. Barely enough iron is made available to make RBCs. Hemoglobin values modestly decline but generally do not compromise the patient significantly.

Distinguishing between iron deficiency anemia and the anemia of chronic inflammation often is not readily apparent. Both are hypochromic, but the mean corpuscular volume of the RBCs in iron deficiency generally is lower for the same degree
of anemia of chronic inflammation. The serum levels of transferrin are low in both. In iron deficiency, levels of transferrin increase, but transferrin has little iron available to transport, thus the transferrin saturation percent expressed as the ratio of iron bound to transferrin compared to its capacity to bind iron (Fe/total iron binding capacity [TIBC]), is very low, typically less than 13%. On the other hand, in the anemia of the inflammatory response, the serum iron concentration is low, and the transferrin level often decreases along with many other plasma proteins such as albumin. Generally, the resulting transferrin saturation is higher than 13%.

Measurement of another serum protein, ferritin, can also help distinguish between iron deficiency anemia and the anemia of the inflammatory response. Ferritin is a large protein shell composed of 24 subunits covering an iron core of several thousand atoms of iron. It is the soluble storage form of iron in the tissues and its level in the circulation reflects the body’s stores. In iron deficiency the serum ferritin is very low, generally less than 30 ng/mL, whereas in the anemia of chronic inflammation the serum ferritin level is high, generally greater than 100 ng/mL, reflecting the fact that it is an inflammatory reactant and that stored iron in the anemia of chronic inflammation is high. Furthermore, almost always a significant inflammatory process with elevation of other serum inflammatory markers is evident in the anemia of the inflammatory response.

Uncomplicated iron deficiency can be quite severe but quickly responds to standard oral iron replacement. In contrast, giving iron to patients with anemia of chronic inflammation is ineffective and possibly counterproductive as sequestering iron is likely an adaptive beneficial response for the reason given earlier in the chapter. The anemia of chronic inflammation resolves only when the inflammatory process is eliminated. Moreover, the anemia of chronic inflammation generally is not severe or clinically compromising, unless other factors exacerbate the degree of anemia. Certainly iron deficiency and chronic inflammation may coexist and the serum studies may be ambiguous, in which case, a bone marrow examination may be necessary to evaluate the iron stores. As one might guess, marrow iron stores are low or absent in patients with iron deficiency and high in patients with anemia of chronic inflammation.

**Anemia of Chronic Kidney Disease**

Another form of anemia frequently found in patients in a chronic care program is the anemia of chronic kidney disease (CKD). It is distinct from the anemia of chronic inflammation. The anemia of CKD is caused by deficient production of erythropoietin by the kidneys. The RBC mass is regulated by the serum erythropoietin, which is produced by the kidney in response to oxygen demand. With CKD there is less ability to produce erythropoietin and, consequently, fewer RBCs are produced. Today human recombinant erythropoietin is available to treat the anemia of CKD. However, caution
must be exercised as adverse effects of thrombotic complications (3), progression of some cancers, and decreased patient survival (4), have been observed in patients treated with recombinant erythropoietin. Overtreatment leading to excessively high hematocrits is associated with venous and arterial thrombotic complications. Consequently, guidelines for the use of recombinant erythropoietin in the treatment of CKD have been promulgated by the FDA. In controlled clinical trials, patients experienced greater risk of death, serious adverse cardiovascular reactions, and stroke when administered erythropoiesis-stimulating agents (ESAs) to target a hemoglobin level greater than 11 g/dL. ESAs have also been shown to shorten overall survival and/or risk of tumor progression or recurrence in clinical studies of patients with breast, non-small cell lung, head and neck, lymphoid and cervical cancers. Enrollment of providers in the ESA APPRISE Oncology Program is necessary to prescribe or to dispense ESAs to patients with cancer. Therefore, the recommendation of the FDA is to use the lowest ESA dose to reduce the need for RBC transfusions (5).

Anemia has implications for functional recovery during rehabilitation, and its management is an important issue. Practice trends in the management of anemia in the acute rehabilitation setting were recently surveyed (6). Ninety-four medical directors of inpatient rehabilitation units reported on their use of transfusion thresholds and human recombinant erythropoietin. Forty-six percent reported recommending the use of recombinant erythropoietin in anemic patients. The majority responded that they recommended transfusion in patients with a hematocrit less than 25%. It was concluded that practice guidelines should be developed to aid the rehabilitation medicine specialist in the management of anemic patients in the acute rehabilitation setting and that further study of the relationship between hematocrit, tolerance for exercise, and long term functional outcome should be performed.

The efficacy of recombinant human erythropoietin in patients admitted to a long term-care facility was studied in a randomized, double blind, placebo controlled trial (7). The objective was to assess the efficacy of recombinant erythropoietin in decreasing the occurrence of red cell transfusions. After 84 days, patients receiving recombinant erythropoietin had received 39% fewer red cell transfusions compared with those on placebo. It was concluded that the administration of recombinant erythropoietin resulted in a significant reduction in transfusions, and despite fewer transfusions, patients treated with recombinant erythropoietin achieved a higher hemoglobin level.

**THROMBOCYTOPENIA**

One may be prompted to get a platelet count as part of the evaluation of an evident hemostasis problem manifest by easy bruising or bleeding, or it may be discovered coincidentally in a complete blood count (CBC) obtained for another reason.
Impaired hemostasis is especially a concern for patients with a platelet count less than 50,000/mm³. Significant thrombocytopenia most often would be of recent onset as ordinarily a normal platelet count would generally be a part of the entry criteria to a rehabilitation program (except in the case of cancer rehabilitation). Often the new onset of thrombocytopenia, especially in an otherwise stable medical setting, is medication related. However, it is advisable to recheck a low platelet count to make sure it is not an artifact. The blood smear should be examined by the laboratory to visually confirm the deficiency of platelets. Platelet clumping may occur in the blood collection vial, and this interferes with the automated machine counting of platelets. If platelet aggregates or clumping is seen upon visual inspection of the blood smear, a more accurate platelet count can be obtained using a citrate anticoagulant vial for blood collection (blue top) rather than the usual purple topped ethyldiaminetetraacetic acid (EDTA) anticoagulant vial.

If thrombocytopenia is confirmed, the next action is to look over the patient’s list of medications and consider the likelihood of each being causative, based upon the timing of the onset of thrombocytopenia in relation to the introduction of medications and the known association between some medications and thrombocytopenia. Empiric discontinuation of unnecessary medications and switching to alternatives is generally advisable. It is recommended that this be done in conjunction with a hematology consultation especially if the thrombocytopenia is severe, less than 50,000/mm³.

Certain medications are especially suspect in the setting of thrombocytopenia. A special and frequent culprit is heparin. Heparin induced thrombocytopenia (HIT) is suspect with a 50% or more drop in platelet count shortly after the introduction of heparin. HIT is more likely to occur with higher doses, standard heparin versus low molecular weight heparin, and sicker patients, but it can occur in a patient in a rehabilitation setting on a relatively low dose (8). The greatest concern regarding HIT is the further development of heparin induced thrombocytopenia and thrombosis (HITT). HIT is the result of an autoantibody directed against heparin in association with the platelet surface protein known as platelet factor 4. The antibody attaches to and activates the platelets resulting in thrombocytopenia and thrombotic problems rather than bleeding.

While on any dose of heparin, if a patient develops new thrombosis or recurrent thrombosis, HITT must be considered along with stopping heparin and instituting alternative anticoagulation. Warfarin can exacerbate the thrombotic process by initial depletion of vitamin K dependent anticoagulant proteins and must not be used. Obtaining a heparin platelet antibody study can quickly help determine if heparin is the culprit and a negative result is strongly predictive that heparin is not responsible and may be continued. However, a positive antibody result is less strongly predictive and the decision to use an alternative anticoagulant must be made on clinical grounds while a more definitive test, the platelet serotonin release assay is sent to a reference laboratory. If the serotonin release assay is negative one can be fairly confident that
heparin is not responsible for the thrombocytopenia (9,10). A positive test strongly suggests HIT. A hematology consultation should be obtained in cases of suspected HIT or HITT as the management involves special testing and use of anticoagulant medication not generally familiar to the nonhematologist.

A recent review of all published reports of medications associated with thrombocytopenia, excluding heparin, listed 317 medications. The most frequently implicated medications were quinidine, quinine, and trimethoprim-sulfamethoxazole (11). Virtually all categories of medications commonly used in internal medicine have been reported to cause thrombocytopenia by a variety of different mechanisms. Generally, stopping the culprit medication is all that is required. In general, platelet transfusions should not be given prophylactically. Platelet transfusions should be given to thrombocytopenic patients only if compromised hemostasis is manifest as significant bleeding or if the patient is to undergo an invasive procedure.

LEUKOPENIA

Leukopenia, much like thrombocytopenia, discovered in a rehabilitation setting, is probably of recent onset as the patient likely had a relatively normal white blood cell count as part of the entry criteria to the program. Also, a primary consideration in this circumstance would be a causative medication. Many medications can cause nonchemotherapy-induced myelosuppression. In general, a neutrophil count greater than 500/mm³ does not significantly compromise the patient, but measures should be taken to identify and eliminate the offending agent before the leukopenia exacerbates and infectious complications ensue (12). Generally, there is the medication-associated, rare entity of agranulocytosis where neutrophils are absent, resulting in presentation with fever. Agranulocytosis is an emergency, and the patient should be transferred to an acute care setting. Medications should be reviewed and potential suspects immediately eliminated. A systematic review of agranulocytosis induced by nonchemotherapy drugs identified 125 of them that were definitely or probably related to agranulocytosis. Drugs for which 10 or more reports were available included carbimazole, clonazapine, dapsone, methimazole, penicillin G, procainamide, propylthiouracil, rituximab, sulfasalazine, and ticlopidine (13). A hematology consultation should be obtained for the evaluation and management of severe leukopenia.

DISORDERS INVOLVING MORE THAN ONE CELL LINE

Hematological disorders involving more than one cell line often involve cells being prematurely removed from the circulation as in hypersplenism and are generally chronic in nature and should be evident before entering a rehabilitation program. More
rarely, such conditions are because of a bone marrow production problem requiring a bone marrow examination for definition, such as myelodysplasia. Hematological expertise is generally required for better definition of the problem. It may be necessary to exclude afflicted patients from participation in a rehabilitation program.

**HIGH LEVELS OF A HEMATOLOGICAL CELL LINE**

Presuming that the hematological values met criteria upon acceptance into a rehabilitation program, the development of increased levels of RBC, white blood cells, or platelets, most often is reactive and the following considerations apply. An unexpected increase in the hematocrit likely reflects volume changes, most often, a degree of dehydration. An increase in granulocytes above the normal range should prompt consideration of an infection, particularly as a debilitated patient may not manifest the usual fever. A significant increase in the platelet count may indicate occult bleeding, even without a significant change in the hematocrit, as the blood loss may be compensated for by increased RBC production.

**ACTIVITY LEVELS IN PATIENTS WITH HEMATOLOGIC ABNORMALITIES**

Guidelines for the degree of activity based upon hematological parameters have been proposed. Some physical therapy programs use the Winningham Contraindications for Aerobic Exercise Guidelines. Based upon these guidelines aerobic exercise is contraindicated when the platelet count is <50,000/mm³ or hemoglobin <10 gm/dL. However, the therapist needs to work with the patient’s health care team to establish individualized parameters to assure safety and maximize rehabilitation benefits. A more complete discussion of limitations for oncology patients is discussed by Bilek-Sawhney and Wells (14).

**SUMMARY**

The hematological comorbidities often encountered in a rehabilitation setting may impact the rehabilitation process and outcome. Concomitant disorders of inflammation and renal impairment often are responsible for anemia in these patients, and anemia in particular would seem to compromise the rate of rehabilitation progress. However, rigorous, evidence-based guidelines for the management of anemia in this setting are needed and cannot be presumed. Studies of the role of ESAs are in progress, and results are pending. It is hoped better guidance will soon be available.
The exposure to multiple medications in the rehabilitation setting increases the risk of otherwise infrequent adverse reactions occurring. Not infrequently, leukopenia or thrombocytopenia results. If it is detected early, and the offending medication is promptly discontinued, minimal consequences are likely. An awareness of changes in hematologic parameters in relation to the introduction of medications will prevent a minor perturbation from becoming a crisis.

REFERENCES
Gastrointestinal Bleeding

Aaron Bellows and Paul A. Feldman

Gastrointestinal bleeding (GIB) can complicate the course of recovery of patients in an inpatient rehabilitation setting. GIB, significant enough to impede the patient’s rehabilitation program or require a change in the management of the patient’s medical condition, has a reported incidence of 0.3% (1). Significant risk factors that predispose to GIB include advanced age (greatest risk above 80 years), administration of anticoagulation with warfarin, unfractionated heparin or low-molecular-weight heparin, use of clopidogrel or glucocorticoids, prior GIB, and a history of diabetes, renal insufficiency, diverticulosis, or colitis (1,2).

Many patients on the inpatient rehabilitation unit are on anticoagulation therapy for the prevention of thromboembolic events; the anticoagulation therapy imposes a significant risk of GIB when underlying gastrointestinal (GI) pathology is present (3–7). One study showed that anticoagulation therapy resulted in a six-fold increased risk of GIB in the first two weeks after total hip replacement and a two-fold increased risk after knee replacement. The relative risk remained elevated for up to 12 weeks after total hip replacement (2). Nonsteroidal anti-inflammatory drugs (NSAIDs) commonly used in patients with osteoarthritis may exacerbate the negative effects of anticoagulation on bleeding (8–10).

GIB can occur at any location along the GI tract, although bleeding is most commonly found in the upper GI tract proximal to the ligament of Treitz and in the lower GI tract distal to the ileocecal valve. In a recent study of patients in a rehabilitation setting, the most common causes of GIB included gastric ulcers, esophagitis or esophageal ulcers, duodenal ulcers, rectal ulcers, and diverticular bleeding (1). Other causes were ischemic colitis, colon ulcers, proctitis, vascular ectasias, aortoenteric fistulas, and GI tumors.

**UPPER GIB**

GIB in the upper GI tract usually presents with coffee-ground emesis, melena, hematemeisis, hemoglobin-positive stools, and/or decreased hemoglobin. Hematochezia, the
passage of fresh blood from the anus, when associated with hemodynamic instability is usually indicative of a brisk and severe GIB. The most common sites for upper GIB are described below.

**Peptic Ulcer Disease**

Peptic ulcer disease (PUD), defined as a benign disruption of the gastro-duodenal mucosa, is among the most common causes of upper GIB in rehabilitation patients and is frequently associated with the use of NSAIDs (including low-dose aspirin) and *Helicobacter pylori* infection (11,12). In the outpatient setting, NSAIDs impart a relative risk of bleeding, ranging from 2.7 to 33.9, with the elderly being at highest risk as a result of the reduced protective effect of prostaglandins on gastric mucosa associated with advancing age (13). Whereas corticosteroids by themselves have not been shown to result in increased risk for peptic ulcers, the concurrent use of corticosteroids and NSAIDs has been associated with a 15-fold increased risk of peptic ulcer disease compared with the use of either drug alone (14,15). Bleeding from PUD usually manifests with symptoms of hematemesis, coffee-ground emesis and/or melena. Epigastric pain or discomfort may or may not be experienced by the patient. Hemodynamic compromise is usually associated with more severe bleeding. Gastritis and/or duodenitis can also cause GIB but usually to a lesser degree.

**Esophagitis and Esophageal Ulcers**

Esophagitis and esophageal ulcers frequently occur in a setting of immobility and prolonged periods of recumbency (16). The most common cause of esophagitis is gastroesophageal reflux. Pill retention, which increases the likelihood of esophageal injury, is more likely in persistently recumbent patients. Medications associated with esophageal injury include aspirin and other NSAIDs, tetracycline, potassium chloride, iron compounds, and bisphosphonates. Bleeding from esophagitis typically manifests with coffee-ground emesis, melena, or hematemesis. More severe bleeding is rare but can occur with more extensive esophagitis and ulceration.

**Gastric Antral Vascular Ectasia**

Gastric antral vascular ectasia (GAVE) is a less common cause for GIB. The condition is characterized by tortuous dilated blood vessels in the distal stomach and usually presents with decreased hemoglobin in the absence of melena or hematemesis. GAVE is often associated with advanced age, chronic liver disease, and renal or connective tissue disease but can also be idiopathic (17,18).
II. SPECIFIC MEDICAL COMPLICATIONS

LOWER GIB

Lower GIB usually presents with hematochezia or melena, with or without significant hemodynamic compromise. It usually manifests as a result of the following medical conditions.

Diverticular Disease

Elderly patients may comprise a significant proportion of patients in an inpatient rehabilitation setting. The prevalence of diverticular disease increases with age, affecting up to two-thirds of people over 80 years old. In patients with diverticulosis, the incidence of bleeding ranges from 5% to 50% (19). Accounting for about half of all lower GIB, diverticular hemorrhage is typically characterized by acute, intermittent and painless, large-volume arterial bleeding that resolves spontaneously.

Ischemic Colitis

Patients of advanced age, those suffering from dehydration, peripheral vascular disease and patients who have recently undergone cardiopulmonary bypass, aortoiliac reconstruction, or renal transplant or who are in rehabilitation after myocardial infarction are more susceptible to decreased intestinal blood flow and occlusive disease of the mesenteric vasculature and may develop ischemic colitis (20–22). Ischemic colitis due to decreased intestinal blood flow typically affects the splenic flexure and descending colon. The disease is frequently characterized by acute-onset left-sided abdominal pain followed by bloody diarrhea within 24 hours. Bleeding usually resolves with restoration of mesenteric blood flow through administration of adequate intravenous or, in milder cases, oral hydration. Ischemic colitis resulting from occlusive vascular disease (thrombotic or embolic) usually involves the superior mesenteric artery and presents with severe abdominal pain, with or without rectal bleeding. This condition typically affects the colon proximal to the mid-transverse colon and the small intestine and may progress to bowel necrosis, shock, and death. Revascularization remains the treatment of choice for mesenteric ischemia.

Rectal Ulcers and Hemorrhoids

Rectal ulcers can occur as a result of iatrogenic rectal injury with rectal probes or tubes, rectal prolapse, or ischemia. The condition is usually identified in patients with a chronic debilitated status. Bleeding episodes typically present with bright red blood per rectum, with or without clots, and are not usually associated with hemodynamic
instability. Hemorrhoidal bleeding typically manifests with the passage of bright red blood per rectum and is associated with bowel movements; it is rarely associated with significant anemia or hemodynamic compromise and can be managed conservatively.

**Malignancy**

GI neoplasms, including benign, malignant, primary, and metastatic disease account for approximately 5% of upper GIB and up to 17% of cases of lower GIB (11). The presentation of bleeding in these patients varies with the location of the neoplasm. Bleeding from neoplasm in the upper GI tract typically presents with melena and/or hematemesis, whereas bleeding from neoplasm in the lower GI tract usually presents with hematochezia. Iron deficiency anemia is a common manifestation of malignancy involving the upper and lower GI tracts. Malignancy may be suspected in individuals with a history of unintentional weight loss, tobacco use, or a family history of GI cancer.

**CRITICAL ILLNESS, AORTIC REPAIR, AND INCREASED INTRACRANIAL PRESSURE**

Individuals who have been transferred to inpatient rehabilitation for recovery after critical illnesses (such as sepsis, respiratory failure, trauma, severe burns, and hemorrhage) are predisposed to stress-induced mucosal injury along the GI tract. The resulting stress-related ulcers and erosions increase the risk of GIB, especially in patients with respiratory failure requiring mechanical ventilation.

**Aortoenteric Fistulas**

Aortoenteric fistulas as etiologies of GIB are relevant among postsurgical rehabilitation patients who have recently undergone aortic repair with synthetic graft placement. Patients typically present with a self-limited “herald bleed” that manifests with hematemesis and/or hematochezia followed by massive bleeding and exsanguination. Intermittent bleeding can be seen if a blood clot temporarily seals the fistula. The condition may be diagnosed by the extravasation of contrast into the bowel on CT scan and angiography. Treatment involves emergency surgical intervention (23).

**Increased Intracranial Pressure**

Increased intracranial pressure as a result of head injury, intracranial neoplasm, or cranial surgery may lead to a Cushing’s ulcer at locations along the proximal GI tract from the esophagus to the duodenum. These ulcers, which are thought to be mediated
by a hypersecretory state of gastric acid and pepsin, have a propensity to bleed (24). Treatment is designed to increase gastric pH with proton pump inhibitor (PPI) therapy and to decrease intracranial pressure.

II. SPECIFIC MEDICAL COMPLICATIONS

EVALUATION AND MANAGEMENT OF PATIENTS WITH GIB

Evaluation

Initial management of any GIB requires assessment of vital signs, abdominal and rectal examinations, and monitoring of complete blood counts and coagulation profiles. Vital signs can indicate the severity of bleeding. Tachycardia is the first sign of hypovolemia, whereas orthostatic hypotension indicates at least a 15% loss of blood volume. Hypotension in the supine position indicates more significant hypovolemia, with at least a 40% loss of blood volume (25).

Abdominal guarding or rebound tenderness raise suspicions for perforation. Perforation may occur in severe PUD, which, if present, requires immediate surgical intervention. On rectal examination, the presence of bright red blood in the rectal vault or melena will indicate the presence of a GIB. Active hematemesis, melena, or hematochezia associated with hemodynamic instability warrants urgent attention.

In the acute phase of significant hemorrhage, the early measurement of hemoglobin and hematocrit may not accurately reflect the actual decrease in red blood cells because whole blood is being lost. Within 8 hours of the onset of bleeding, however, approximately 50% of the actual decrease may be detected by evaluation of red blood cell indices. A decline of 1 unit of hemoglobin or 3 units of hematocrit from baseline is considered significant. Serial blood counts should be drawn every 4 to 12 hours, depending on the severity of the bleed.

Management

Patients presenting with active melena or hematemesis or GIB associated with hemodynamic instability (heart rate greater than 100 beats per minute, systolic blood pressure less than 90, a decrease in systolic blood pressure of 40 mmHg, or orthostatic changes), require intravenous volume resuscitation with normal saline or lactated Ringer’s solution. Patients with underlying cardiac or renal disease should be frequently evaluated for volume overload. Hemodynamically unstable patients or those with brisk bleeding should be transferred to an intensive care unit (26). Immediate consultation with a gastroenterologist is warranted. Patients with GIB without evidence of active bleeding or hemodynamic instability and a hemoglobin drop of less than 1 gram may be observed in the rehabilitation unit with monitoring of vital signs and serial blood counts every 12 hours. Consultation with a gastroenterologist within 6 to 12 hours is recommended.
The transfusion of blood products is typically reserved for patients who have any of the following symptoms: symptomatic anemia (lightheadedness, dizziness, shortness of breath, chest pain, or fatigue), a hemoglobin level less than 7.0 g/dL (or less than 10.0% in the elderly or those with coronary artery disease), or a brisk, high-volume GIB (27,28). Anticoagulation medications should be withheld in the acute phase of active or brisk GIB. If coagulopathies are present, fresh frozen plasma should be transfused to a normalized prothrombin time, and platelets to a goal of greater than 50,000/mm$^3$ (3,29). Management of anticoagulation in clinically stable patients without active GIB should include a careful risk versus benefit analysis in consultation with a gastroenterologist and cardiologist.

For patients with suspected upper GIB, intravenous PPI therapy should be administered (80 mg intravenous bolus followed by 8 mg/hr infusion of either pantoprazole or esomeprazole) (30). Early administration of PPIs in patients with upper GIB has been shown to facilitate ulcer healing and to reduce the rate of rebleeding from PUD (31,32).

After initial resuscitation with fluid and blood products, endoscopic evaluation is warranted. When an upper GIB is suspected, a nasogastric tube (NGT) can be used prior to endoscopy to determine the severity of the hemorrhage and may assist to differentiate an upper from a lower GIB. The presence of bright red blood that does not clear upon lavage indicates an ongoing active bleed, which should be investigated by endoscopy on a more urgent basis. Most patients with upper GIB should ideally undergo endoscopy usually within 24 hours from onset of bleeding. When performed within this window of time, upper endoscopy has been associated with a reduction in both the length of hospitalization and the requirement for blood transfusions (32). For patients with hemodynamic compromise or active bleeding, endoscopy should be performed within 6 to 12 hours. Such early intervention has been shown to improve clinical outcomes (33). If an ulcer in the stomach or duodenum is identified on endoscopy, the presence of \textit{H. pylori} infection should be determined. Methods to test for \textit{H. pylori} infection include histological analysis of gastric biopsies, detection of \textit{H. pylori} antigen in stool or serological detection of \textit{H. pylori} IgG from blood. In a setting of active GIB, serological testing is preferred. Effective eradication of \textit{H. pylori} infection has been shown to significantly reduce the incidence of recurrent ulceration and bleeding (34,35). First line therapy consists of a combination therapy with amoxicillin 1 gram twice daily, clarithromycin 500 milligrams twice daily, and a PPI twice daily for 2 weeks. Metronidazole and tetracycline can be used instead of amoxicillin in cases of penicillin allergy.

The initial diagnostic test for suspected lower GIB is colonoscopy after bowel preparation with a polyethylene glycol-based solution administered orally or by NGT. Urgent colonoscopy has not been shown to offer better outcomes than non-urgent colonoscopy in terms of mortality, hospital stay, transfusion requirements, or rebleeding rates (36). In cases of brisk bleeding that is not self-limiting, patients may benefit from angiography to localize and treat the active bleeding source. Surgical
intervention should be reserved for patients who fail angiography treatment and experience ongoing hemorrhage.

In 5% of cases of GIB, the source of bleeding cannot be identified following endoscopy and colonoscopy (obscure GIB). In these cases, an evaluation of the small intestine using wireless capsule endoscopy (WCE) should be considered (37). Approximately 75% of obscure GIB emanates from the small bowel, which can readily be visualized on WCE. The most common finding is vascular ectasias of the small bowel. Other less common findings include ulceration and neoplasm (38).

PREVENTION OF GI BLEED

Because the overall rate of GIB in an inpatient rehabilitation setting is low, routine use of GI prophylaxis with PPI therapy is unnecessary and may predispose patients to the adverse side effects of the medication. Side effects that have been associated with agents to reduce gastric acidity include aspiration pneumonia and electrolyte imbalance with antacids, confusion and thrombocytopenia with histamine-2 receptor antagonists, nosocomial pneumonia, Clostridium difficile colitis, and interstitial nephritis with PPIs (39–42).

PPI prophylaxis, however, should be considered in patients at higher risk of GIB, including those with a known history of PUD, those taking aspirin or NSAIDs (37,43), those with traumatic brain injury (44), intracranial neoplasm, or cranial surgery (45), and in those recovering from recent severe trauma, prolonged mechanical ventilation, end-organ failure, severe burns, and sepsis. PPI therapy may be considered in a select population of patients receiving anticoagulation therapy as has been reported in cases of patients following total hip replacement surgery (2). NSAIDs should be discontinued prior to administration of anticoagulation therapy or corticosteroids. However, in cases where NSAIDs cannot be discontinued, PPI therapy should be coadministered.

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