Chapter 12

PREVENTION OF IMMOBILITY COMPLICATIONS THROUGH EARLY REHABILITATION

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INTRODUCTION

Putting a sick patient to bed has long been a tenet of medical care. Illness and injury require varying degrees of bed rest or immobilization to allow adequate healing. As our understanding of medicine has evolved, immobility itself has been found to be a major contributor in hampering a patient's recovery. In terms of morbidity and mortality, the consequences of immobility are legion. Financially, prolonged immobility is very costly, consuming a large percentage of each healthcare dollar. Militarily, the added morbidity incurred, from contractures and pressure ulcers alone, greatly prolongs the period of convalescence and delays or prevents return to duty. During times of emergency, such delays can potentially interfere with the military medical mission to conserve the fighting strength. Fortunately, awareness, scrupulous nursing care, and early rehabilitation intervention can prevent or minimize most of these complications without placing the patient in jeopardy.

HISTORICAL BACKGROUND

Until the twentieth century, bed rest had been held as the "basic principle in tissue healing."[1] Yet, the clinical importance of exercise as a treatment modality was known in the 16th century. The *Book of Bodily Exercise*, published by Spanish physician Cristobal Mendez[2] in 1533, presented a rationale for the use of exercise in medical treatment. The first modern scientific study to examine the effect of rest on metabolism was published in 1929 by Cuthbertson.[3] The 1940s work of Taylor and colleagues[4] and Widdowson and McCance[5] on the contraction of plasma volume with prolonged bed rest, spurred the current scientific interest in the effects of immobilization. When space travel evolved in the 1960s, the growing interest in the physiologic effects of the antigravity environment further heightened the concerns about immobilization. Hence, there is now a large body of knowledge on the deleterious effects of prolonged immobility.[6-9]

The impact of the consequences of immobilization on the practice of military medicine cannot be underestimated. Delay of return to duty as a result of these complications depletes manpower and undermines readiness. At the time of the Civil War, the strategy of "rest until healed" was in vogue.[10] Regarding casualty management, little changed in subsequent conflicts, undoubtedly contributing to loss of manpower from the insidious iatrogenic complications of immobility. During World War II, an appreciation of the consequences of immobility began to emerge. Building on the early work of Cuthbertson[3] and Dietrick and colleagues[11] observed a reduction in metabolic rate that occurs shortly after immobilization begins.

In 1945, Taylor and colleagues[4] reported reduced blood volume in otherwise normal young males who were put to bed. Widdowson and McCance[5] subsequently confirmed the resultant decrease in plasma volume with concomitant rises in hematocrit and hemoglobin. The deleterious effects of immobility, deconditioning, and contractures, and the importance of early rehabilitation was presented in a report from the Special Exhibit Committee on Physical Medicine in 1946.[12] In the years following World War II, a large body of scientific data regarding the physiologic effects of bed rest emerged. Much of the data were gathered as a result of the rapid development of the space program during the 1960s.[6,7,9]

Hertzman[13] was the first to describe the early rehabilitation of casualties in a combat theater. His reports during the Vietnam War emphasized the importance of proper bed positioning, early ambulation, and early institution of range-of-motion and strengthening exercises. Still, until the Persian Gulf War, no data had emerged to indicate the magnitude of some of the complications of immobility during wartime.

In an analysis[14] of 222 casualties referred to U.S. Army physical medicine services during the Persian Gulf conflict in 1991, 10% had lower limb contractures, 9% had upper limb contractures, 7% had pressure ulcers, and about 38% were referred for strengthening and range-of-motion exercises.[14] These complications adversely impact the length of hospitalization and full functional restoration.

The monetary impact on healthcare in the United States cannot be underestimated. Although no data exist regarding total costs for all the ramifications of immobility, the costs for hospital based pressure sores alone amount to nearly $14 billion per year and an increase of inpatient bed days by as much as 50% in affected patients.[15,16]

PATHOPHYSIOLOGY

Basic to understanding the effects of inactivity on physiologic potential is the definition of functional capacity, maximum physiologic potential, and potential reserve. Kottke[8] defined these terms using the concepts of a person's ability at a given moment in time vs his or her maximum capacity. Functional capacity is the maximum metabolic rate achievable at the casualty's current state of training. Maximum physiologic potential is the maximum metabolic rate achievable in the same subject after a systematic program of physical training. The difference between these two levels is the potential reserve. While the maximum physiologic potential is fixed for a given individual, the functional capacity is dynamic and is a function of the subject's state of fitness. With inactivity, the functional activity falls, yielding an increase in the potential reserve. This gap between functional capacity and maximum physiologic potential must be closed when attempting to rehabilitate a patient who has suffered ill effects from immobility.[8]

Vallbona[17] indicated four types of inactivity that can lead to the complications of immobility:

1. prolonged bed rest,
2. restricted neuromuscular activity,
3. maintenance in a fixed position, and
4. a state of weightlessness.[17]

The first two types are the most important because they are most easily prevented. Maintenance in fixed positions may be unavoidable (such as repair of orthopedic trauma), and weightlessness is of concern only for space travel.

Clinical manifestations secondary to the effects of inactivity can become apparent in a matter of a few days. It is known that with absence of contraction, a muscle will lose up to 3% of its strength per day.[18] The quadriceps and extensors of the back atrophy most rapidly, impairing ambulation and the ability to climb stairs.[19] Bed rest induces decreased oxidative capacity, which can adversely effect endurance.[20] The severity of these complications can be reduced. While at bed rest, strength can be maintained by 20% maximum voluntary isometric contractions of muscle groups for 10 seconds each day.[18] In some medical centers, electrical stimulation has been applied to inhibit atrophy of disuse.[21,22] Gradual progressive tilting of bedbound patients can be utilized as necessary to restore autonomic tone and prevent postural hypotensive episodes prior to resuming ambulation.[7,17]

THERAPEUTIC USE OF IMMOBILIZATION

Although this chapter considers the ill effects of unnecessary immobility, there is no question that immobilization is the proper treatment of many conditions. The most important of these is orthopedic trauma. After the setting of broken bones, restricted motion is required for bone healing postfracture. The immobilization should be restricted to the smallest period required to ensure adequate stabilization, with an eye toward remobilization as early as the treating orthopedist deems safe. Another important example of the proper use of immobilization is the inflamed joint. An acutely inflamed joint, such as in rheumatoid arthritis, should be rested during periods of acute inflammation. In osteoarthritis, there is no inflammatory component, thus there is no contraindication for mobilization.

A long-standing area of controversy is the duration of needed bed rest for a patient who is suffering from uncomplicated acute back pain without neuromotor deficits. There have been many suggested answers to this question, but a recent study[23] has shown that the shorter periods of immobilization result in better outcomes. Objective research[24] suggests that the optimum period of rest should be no longer than 48 hours. Rest beyond this does not produce additional reduction in pain or better clinical outcome, but rather, contributes to further muscle weakening.

MANAGEMENT OF THE EFFECTS OF INACTIVITY ON ORGAN SYSTEMS

Musculoskeletal System

There is considerable loss of strength when a muscle is put at rest. This occurs even with relatively short periods of immobility. Muller[18] has shown that with each day of bed rest there is as much as 3% loss of muscle strength, or up to 20% loss of residual strength per week of immobilization. Lower extremity muscles lose their strength about twice as fast as upper extremity muscles.[25]

This means that there can be as much as a 50% loss of muscle strength in as little as 3 weeks of bed rest. Unfortunately, subsequent recovery of strength proceeds at a much slower pace. Once immobilization has ceased, the most rapid rate of strength recovery is approximately 10% per week.[26] Thus, it is far more efficient to prevent loss of strength secondary to immobilization. Prevention will have important ramifications on the speed at which injured soldiers can be returned to duty.

Ultrastructural Changes in Muscle

Structural changes occur in muscle tissue that has been immobilized. The contractile properties of muscle are adversely effected by immobilization. Davies and associates[27] showed that the mean time to peak tension and the half relaxation time increased significantly with 3 weeks' immobilization of the triceps surae. Maximal voluntary contraction force was reduced. This was associated with a 10% decrease in muscle cross-sectional area. Maximal tension and contraction times recovered within 2 weeks following removal of the long leg cast. Sale and colleagues[28] found that after 5 weeks of immobilization of human thenar muscles there was an average 42% reduction in maximum voluntary contraction force. Likewise, Duchateau and Hainaut[29] found that 6 weeks of immobilization of the adductor pollicis brevis muscle caused a 55% reduction in maximum voluntary contraction force. This correlated with a 19% increase in duration, 15% decrease in amplitude, and 26% decrease in area of the compound muscle action potential recorded from the surface.

Literature regarding fiber type atrophy in immobilization is conflicting. Haggmark et al[30] investigated muscle biopsies taken from the quadriceps of patients immobilized in long leg plaster casts and found a selective slow twitch muscle fiber atrophy with reduced cross-sectional area and reduced oxidative enzyme activity in slow twitch fibers. In his review of muscular atrophy following immobilization, Appell[31] indicated that slow twitch muscles with predominantly oxidative metabolisms are most susceptible to atrophy. The rate of protein synthesis is reduced and catabolism is increased. However, in independent studies, Sirca and Susec-Michieli[32] and Robinson and colleagues[33] found that in patients with osteoarthritis, there was a selective atrophy of fast twitch muscle fibers. This atrophy was interpreted as a direct consequence of decreased muscular activity.

Duchateau and Hainaut[34] showed that the immobilized muscle produced more high threshold motor units than the control muscle. The order of recruitment was maintained, however, in accordance with the size principle of Henneman.[35] The motor unit firing rate at recruitment was unchanged, but maximum firing rate was reduced. This reduction was found to be greatest in low threshold units. Serra and colleagues[36] found that electromyographic (EMG) spectral analysis was altered in patients who sustained muscle atrophy secondary to immobilization, compared to controls. Thus, there is the potential for electrophysiologic evaluation of muscular atrophy secondary to immobilization.

The best strategy to prevent muscular atrophy due to immobilization is to limit the immobilization only to the region of the body in which it is absolutely required, and to make the period of immobilization as brief as possible. In the immobilized patient, an exercise program should still be implemented to retard atrophy. A 30% maximum voluntary isometric contraction (MVC) for 5 seconds each day is sufficient to prevent disuse atrophy.[18] Alternatively, a 50% MVC for 1 second each day will also prevent disuse atrophy.

Vallbona[17] recommends a daily program where the supine patient applies pressure with the feet against a footboard for 5 seconds, relaxing for 10 seconds, and repeating this cycle three additional times.[17] This maneuver requires contraction of most muscle groups of the legs and back. This should not be performed in patients with unstable spines, however. To exercise the upper extremities, a similar routine can be employed by having the patient extend the arms and make a strong grip action. This can be done with or without a hand roll.

The role of electrical stimulation in preventing atrophy from immobilization is controversial, and findings reported in literature are conflicting. Eriksson's[37] group found that intermittent electrical stimulation for up to 5 weeks did not cause any significant changes in enzymatic activities, muscle fiber characteristics, or mitochondrial properties, but did result in improvements in muscle strength comparable to the results of a program of voluntary exercise. More recently, Gibson and colleagues[22] examined the effect of percutaneous electrical stimulation in preventing muscle atrophy secondary to immobilization, by measuring quadriceps mass, composition, and rate of protein synthesis in seven males with tibial fractures who were immobilized in long leg casts for 6 weeks. The results were compared to 14 others with similar injuries

who did not receive electrical stimulation. In those not receiving electrical stimulation, quadriceps cross-sectional area (measured by ultrasonography) fell by a mean of 10%, and the rate of protein synthesis was 10% lower than in the control group. In contrast, those who received electrical stimulation showed no significant difference in muscle cross-sectional area or protein synthesis vs the control group.

The impact of electrical stimulation on muscle protein metabolism has also been shown by Bouletreau and colleagues.[38] They demonstrated a reduction in urinary excretion of nitrogen, creatinine, and 3-methyl histidine in intensive care patients who received intermittent muscular electrical stimulation. In a comparison of the effect of isometric exercise vs isometric exercise with electric stimulation on retarding quadriceps atrophy, Arvidsson and colleagues[39] found that there was no difference between the two methods in males, but in females, the results favored electrical stimulation. The degree of atrophy was determined by use of computed tomography. In a study of the effects of electrical stimulation on the quadriceps during postoperative knee immobilization, Morrissey et al[40] found that the decrease in isometric quadriceps torque resulting from immobilization could be signifi-cantly lessened by applying electrical stimulation during the period of immobilization. However, it was found not to significantly alter thigh circumference changes that occurred during immobilization.

Gould and colleagues[41] compared three treatment regimens designed to prevent atrophy of normal thigh and calf muscles immobilized in a long leg cast. One treatment group received nonisometric exercise, the second received isometric exercise, and the third received electrical stimulation. In the electrostimulated group, muscle atrophy was one half that of the exercise group in the thigh and one fifth that of the other two groups in the calf.

In a subsequent study, Gould et al[42] compared isometric quadriceps exercise to electrical stimulation in a group of 20 patients who underwent open meniscectomy. The electrical stimulation applied was a tetanizing, 5-second contraction to the quadriceps approximately 400 times per day. The electrically stimulated group had a significantly reduced loss of quadriceps muscle volume and strength, had reduced postoperative knee swelling, required less pain medication, had a greater range of knee motion, and group members were able to walk earlier without crutches. Buckley and colleagues[21] applied electrical stimulation to major lower extremity muscle groups in four paraplegic patients. Electrical stimulation to achieve tetanic contractions was applied 15 seconds out of each minute for 10 hours per day over 3 weeks. Although the stimulation produced significant growth of thigh and calf muscles, no significant changes in nitrogen balance or phosphate balance could be identified.

Based on these recent studies,[21,41,42] it appears that electrical stimulation is of potential benefit in minimizing immobilization atrophy when immobilization is restricted to a specific anatomic region (such as about the knee). A reasonable protocol is to provide 5 to 15 seconds of tetanizing electrical stimulation to the muscle or muscles of interest per minute for 8 to 10 hours per day. It is not practical to apply electrical stimulation to all major muscle groups of the body for the patient on bed rest, and it is not a substitute for isometric exercise.

Contractures

During immobilization, the balance between collagen synthesis and degradation is altered, resulting in a progressive shortening of connective tissue around joints with contracture formation and loss of range of motion.[43] A muscle immobilized in a shortened position for 1 week will show contraction of the muscle belly with subsequent remodeling of loose connective tissue into dense connective tissue.[19] In addition, immobilization of a muscle in a shortened position can exacerbate immobilization atrophy.[44] If immobilization is necessary, the joint should be maintained in a neutral position in order to keep agonist and antagonist muscles at equal lengths and tensions.[19] The clinical impact of contracture formation results in impaired range of motion, mobility, and ability to perform activities of daily living.

In a study[14] of Persian Gulf War casualties referred for physiatric evaluation, 10% had lower limb contractures compared with 9% in the upper extremity. These contractures could have been due to immobilization for fracture healing, peripheral nerve injuries, or lack of early intervention with range-of-motion exercises. It is unclear whether, or to what extent, these contractures could have been prevented. Haher and colleagues[45] have shown that flexion contractures interfere with the healing of pressure sores, providing further evidence that the complications of immobility are additive and can interact to further hinder recovery.

There are three basic forms of contracture[19(p450)]:

1. soft tissue (skin, subcutaneous tissue, tendons, and ligaments);
2. myogenic (muscle); and
3. arthrogenic (fibrosis and ankylosis of joint capsule).

Soft tissue contracture results from progressive shortening of connective tissue around joints with contracture formation and loss of range of motion.[43] The soft tissue structures include skin, subcutaneous structures, tendons, and ligaments. Myogenic contractures result when a muscle is immobilized in a shortened position with contraction of the muscle belly and subsequent remodeling of loose connective tissue into dense connective tissue[19]; and, as will be discussed below, immobilization of a muscle in a shortened position can exacerbate immobilization atrophy.[44] Arthrogenic contractures result from capsular fibrosis and ankylosis of joints.

Range-of-Motion Therapy

The most important management strategy is preservation of range of motion by moving each joint (either passively, with assistance, or actively) through its full range of motion 3 to 5 times at a minimum of twice a day.[46] The additional steps that can be employed to prevent contractures in the patient at bed rest or one unable to actively move an extremity include proper positioning in the bed.[47]

Simple steps to maintain neutral anatomic position when the patient is in bed and not undergoing range-of-motion therapy should be employed. A firm mattress with solid support is recommended to reduce hip flexion. Starting at the foot, a footboard or boot should be used to maintain ankle position in neutral. Because of gravity and the fact that the posterior compartment of the leg is stronger than the anterior compartment, plantar flexion contractures of the ankle are all too common, particularly if spasticity is present. Trochanteric rolls will assist in preventing external rotation of the hip. Prone lying should be encouraged for at least one half hour per 8-hour shift as an additional measure to prevent hip flexion contractures, as well as to give pressure relief. Periodic side lying, alternating between left and right every 2 hours, will allow for knee and hip flexion.

The superior extremities should be supported with pillows. Positioning of the upper extremities should also alternate at least every 2 hours among three basic positions:

1. shoulder abducted and externally rotated with elbow flexed and forearm pronated,
2. shoulder abducted and internally rotated with elbow flexed and forearm pronated, and
3. shoulder adducted with elbow extended and forearm supinated.

There are two basic wrist and hand positions to provide for alternating flexion and extension. A hand roll can be used to allow flexion of the wrist and hand and, if needed, a wrist hand orthosis can be used to maintain the wrist and hand in extension. Extension and flexion should be alternated at least every 4 hours. It must be remembered that these positioning strategies are adjuncts to, but not substitutes for, an adequate range-of-motion program.

Diathermy

When contracture at a joint is present, use of prolonged stretch within the limits of pain and without tearing of tissues has proven effective, particularly when combined with diathermy.[48-50] As described above, contractures can result from shortening of soft tissue structures, remodeling of muscle tissue, and fibrosis of joint capsules. The effectiveness of a stretching regimen will be enhanced through use of diathermy.

Diathermy is deep heating of biologic tissue. Heating of connective tissue to 41°C to 45°C causes molecular changes in collagen that result in increased extensibility.[51] Superficial heating modalities such as heat packs, whirlpool, and radiant heat lamps do not provide sufficient temperature elevations in muscle and pericapsular structures to effectively alter collagen extensibility.[49,51]

Available deep heating methods include short-wave diathermy, microwave diathermy, and ultrasound diathermy. Of these modalities, ultrasound diathermy is the most commonly utilized and widely available. Ultrasound has the advantage over the other two diathermy methods in that the equipment is much more portable, and its depth of penetration is superior. Both short-wave and microwave diathermy applications rely on conversion of electromagnetic radiation into heat in the tissues and will result in therapeutic temperature elevations at a depth up to 3 cm below the skin surface. Although this is sufficient for adequate warming in superficial muscles and joints, such as the hand, it does not provide for therapeutic temperature elevations in deeper structures, particularly the hip.[52]

Ultrasound utilizes the reverse piezoelectric effect by applying high frequency alternating current to a crystal, thereby producing acoustic vibrations that are converted to heat energy when absorbed by biologic tissues. Ultrasonic energy is selectively converted to heat energy at different tissue interfaces. Bone absorbs approximately 10-fold as much acoustic energy as muscle, which energy is then conducted to the surrounding tissues.[53] For this reason, ultrasound is a very effective modality for achieving therapeutic temperature elevations in contracted joint capsules. Ultrasonic frequencies used in diathermy are on the order of 1 MHz, and ultrasonic intensity is expressed in W/cm^2. To achieve therapeutic temperature elevations in deep tissues, the output of the instrument should be able to attain an average of 4 W/cm^2.[50]

The application of ultrasound diathermy requires the use of a coupling medium or gel to transmit the acoustic energy into the tissue and not reflect it into the surrounding environment. To prevent the occurrence of hot spots and to provide uniform heating, the applicator is moved continuously in multiple planes (stroking technique) about the contracture for 10 to 12 minutes. This should be concurrent with, or immediately followed by, passive stretching to take advantage of the extensibility of the collagen. Dosimetry is determined by patient response to the internal heating, and output should be immediately reduced if the patient complains of pain. Therefore, the patient's nociceptive abilities must be assessed prior to initiating treatment. Contraindications to application of ultrasound diathermy therapy include[51] (*a*) application to anesthetic regions, (*b*) applications over regions of vascular insufficiency, (*c*) application over cemented joint prostheses, (*d*) application over malignant tumors, (*e*) application over the heart, (*f*) application to the eyes, and (*g*) application to the pregnant uterus. When applying it over metallic implants, caution must be taken due to selective heating.

A nonthermal consequence of ultrasound application to biologic tissues is the risk of cavitation. Cavitation refers to the formation and oscillation of gas bubbles within the tissues experiencing ultrasonic energy; these gas bubbles may subsequently coalesce and collapse, resulting in tissue damage. The risk of cavitation is minimized with intensity outputs of under 4 W/cm^2 when a stroking technique is employed. An additional, nonthermal consequence of applying ultrasound is the production of standing waves that can result in blood cell aggregates and stasis of blood flow.[54] Again, this can be avoided if the stroking technique is used.

Splinting

The major goals of splinting are to assist, resist, align, and simulate function.[55] Thus, for sustained stretch or maintenance of neutral position, splinting is useful. The splinting may be static or dynamic. Dynamic splinting has the advantage of allowing the patient to perform active range-of-motion exercises while maintaining the desired positioning when at rest. The splint itself can prevent secondary contracture. Serial casting can be particularly useful in maintaining sustained stretch to reduce contracture.[56] As gains are made, the cast can be reformed to adjust to these gains so that sustained stretch is maintained. By bivalving the cast it can be removed for therapy, exercise, and inspection for areas of excess skin pressure.

Continuous passive motion (CPM) machines have been used for early mobilization of joints in both lower and upper extremities in the early postoperative period.[57,58] Joints are mechanically ranged without patient effort. A predetermined joint range of motion can be applied passively at a slow continuous rate to prevent soft tissue contracture and maintain joint homeostasis and nutrition. During the first few days postoperatively, the CPM machine is applied for up to 12 hours per day. Its use is generally restricted to joints that have been operated upon and it is impractical in many situations because the device is cumbersome. Patient mobility is restricted while the CPM machine is in use.

Whether through manual or mechanical means, early mobilization is the mainstay of contracture prevention. Once formed, contractures are difficult to overcome and require intensive therapy to reverse.

Immobilization Osteoporosis

Bone homeostasis is altered during immobilization. Immobilization in plaster, by bed rest, and the weightless state can all result in detectable demineralization.[59-61] The bony changes of disuse osteoporosis may mimic neoplastic disease, particularly myeloma.[62] Acute osteoporosis has been shown to occur following immobilization and is related to an increase in osteoclastic bone resorption.[63,64] In less than 10 days of immobilization (bed rest), there is an increase in urinary excretion of hydroxyproline, a necessary building block for bone remodeling and maintenance.[65] Similarly, there is up to a four-fold rise in urinary glycosaminoglycans following immobilization.[66] An associated increase in serum calcium and phosphate is observed as well. Serum

1,25-dihydroxyvitamin D decreases significantly during immobilization, reaching its nadir at the end of 1 week. This can lead to a local reduction in bone mass. There is potential for recovery during the early phase of immobilization, but this ability to recover may be lost after 6 months of immobility.[67] Minaire[67] points out in his review of immobilization osteoporosis that the cumulative effect of repeated periods of immobilization in promoting osteoporosis remains hypothetical.

Mechanical stress is an important factor in the maintenance of normal cortical bone remodeling. Immobilization is characterized with reduced osteon densities and cross-sectional area, and with an observed decrease in radiologic density in long bones.[68,69] Vico and colleagues[70] have shown that in rats exposed to 5 days of zero gravity, there is an increase in the number of osteoclasts per square millimeter of trabecular bone.[69] Lips and associates[71] evaluated degrees of mobility and parameters of bone turnover in 70 nursing home residents. An increased urinary excretion of hydroxyproline and a decrease in serum 1,25-dihydroxyvitamin D concentrations were observed, indicating that lower mobility leads to higher bone resorption, which may suppress formation of 1,25-dihydroxyvitamin D.

Bone loss may be averted and potentially reversed by maintaining physical activity.[72] Primary prevention of immobilization osteoporosis is based on exercise, particularly loading of bone intermittently through the day.[67,73,74] However, the type, intensity, duration, and frequency of the exercise has not been determined according to recent literature.[67] Weight bearing should be initiated early during the period of immobilization in order to prevent or possibly reverse osteoporosis.

Drug trials to reverse or prevent osteoporosis secondary to immobilization have shown promise. Administration of 100 International Units (Medical Research Council, London, England) of salmon calcitonin daily, if initiated within the first 2 weeks of immobilization, may retard bone loss and can be effective in preventing or treating immobilization induced hypercalcemia.[67] Recent clinical research[75–79] has centered on antiosteoclastic agents, particularly the bisphosphonates. In a trial to observe the effect of diphosphonate EHDP (disodium ethane-1-hydroxy-1, 1-diphosphonate) on bone mineral metabolism, Lockwood and colleagues[80] evaluated low- and high-dose regimens in four healthy young male subjects placed on bed rest for 20 weeks. At the high dose (20 mg/kg/d) there was some decrease in urinary hydroxyproline excretion and in the rate of bone resorption.

Chappard and associates[64] evaluated the effect of the bisphosphonate (1-hydroxy ethylidene-1,1 bisphosphonic acid) on osteoclast number during prolonged bed rest (120 days) in 15 healthy subjects. Insignificant bone loss and a marked reduction in osteoclast number were observed. Recently, etidronate disodium (disodium diphosphonate) has been found to increase bone mineral density in postmenopausal osteoporosis. Cyclic, low doses of etidronate have been successfully used in multiple studies.[75–77] The regimen is 400 mg/d given over 2 weeks followed by 13 weeks off the medication. This 15-week cycle is then repeated.[78,79] Addition of phosphates provided no additional benefit.[76,79]

Miller and associates[77] compared the effectiveness of cyclic etidronate vs both fluoride and estrogen in postmenopausal osteoporotic women. All three groups had gains in bone mineral density over the 2-year treatment period, but to varying degrees. Sixteen percent gains were observed in the etidronate and fluoride treated groups and a 5% gain was observed in the estrogen treated group. Etidronate, however, was found to be very well tolerated, and superior to fluoride, given the latter's side effect and toxicity profile,[75–77] and was deemed superior to giving supplemental calcium and vitamin D.[77] Calcium supplementation is probably only necessary in postmenopausal patients whose calcium intake is less than 400 mg/d.[81] Whether this regimen will prevent or reverse immobilization osteoporosis remains to be established.

Clodronate, an investigational antiosteoclastic drug, has shown promise in a recent trial comparing its efficacy in preventing demineralization and resorptive hypercalcemia against etidronate and calcitonin.[82] Oral clodronate was found to be superior to etidronate and equally effective as calcitonin.

Currently, there are no satisfactory medications that absolutely prevent immobilization osteoporosis. The best way to prevent this complication is daily weight bearing when possible and stressing bones through exercise.

Nervous System

Nervous system manifestations of immobilization are many. They include sensory, motor, autonomic, central, and psychologic factors. Sensory deprivation in immobilized patients has been associated with altered perception of sensory input.[17,83] This can result in lowered threshold to painful stimuli.

Orthostasis as a result of autonomic nervous system compromise stemming from immobilization is

a known complication. This is discussed in more detail in the cardiovascular section that follows. Other autonomic nervous system functions can be adversely effected or exacerbated by immobilization. The course of reflex sympathetic dystrophy, though not occurring directly as a result of immobilization, can be influenced adversely by immobilization. The painful limb involved is not actively moved by the patient due to the sympathetically medicated pain, and subsequently undergoes varying degrees of disuse atrophy and contracture.

Lagier and Van Linthoudt[84] reported two cases of reflex sympathetic dystrophy involving the foot, in which articular changes occurred. The abnormalities included superficial pannus, erosions, and fibrous and bony ankylosis, conditions that can be resolved only through range-of-motion and strengthening programs. Patient tolerance of these programs will determine the ultimate success of rehabilitation. Various physical, medical, and surgical procedures have been employed to alleviate pain and allow ranging and strengthening to prevent and reverse these complications of immobility. These interventions range from contrast baths and desensitization with various textures, to sympatholytic medications and blockades, and surgical sympathectomies. Detailed treatment of reflex sympathetic dystrophy is beyond the scope of this chapter. The reader is referred to the excellent review by Schwartzman and McLellan.[85]

Unlike the autonomic nervous system, the effect of immobilization on the function of the peripheral nervous system is not so clear. Whether an increased risk of peripheral neuropathy results as a consequence of immobility has not been demonstrated in the recent literature. Malathi and Batmanabane[86] demonstrated a reduction in the mean axon diameter in large myelinated fibers of the tibial nerve in cats that was directly proportional to the duration of immobilization. Prolonged immobilization of more than 8 weeks caused splitting of the myelin lamellae and collagen replacement. Marciniak[87] investigated the effect of immobilization on nerve terminals in birds and found reduced numbers of synaptic vesicles and mitochondria. Marciniak reported that prolonged immobilization produced fragmentation of axonal endings with resorption by Schwann cells. Robinson and colleagues[33] demonstrated slower axonal conduction velocities in immobilized limbs of the cat.

Impaired neural control emanating from the central nervous system (CNS) has been described by Haines.[88] Balance and coordination can be adversely affected independently from muscular weakness.[89] Dupui and colleagues[90] found that 30 days of bed rest induced sensorimotor changes that resulted in impaired balance and gait performance. Gait alterations included decreased step length, walking velocity, and stability. Seizures secondary to immobilization hypercalcemia have been reported, and this is discussed in greater detail in the section on the effects of immobilization on the endocrine and metabolic systems.

The association of immobility with dementia has recently been investigated. Selikson and associates[91] examined the risk factors associated with immobility in 34 nonambulatory patients. Factors associated with immobility are contractures, severe dementia, poor vision, and history of fractures. Factors not associated with immobility include age, osteoarthritis, mild to moderate dementia, weight gain, and medications. The effect of immobilization on the development or exacerbation of dementia was not addressed. Intellectual embarrassment, including impaired orientation and concentration, has been shown to occur with immobilization within days.[92]

Psychologic disturbances result as a consequence of immobilization and the attendant reduced sensory stimulation.[83] This may manifest as increased anxiety and be expressed as hostility, worry, jitteriness, tearfulness, insomnia, depressed mood, and feelings of hopelessness.[93] The immobilized patient is at risk for clinical depression and the clinician should be aware of its manifestations, which include the presence of at least five of the following for at least 2 weeks, representing a change from previous functioning[94]:

- depressed mood
- poor appetite or overeating
- insomnia or hypersomnia
- low energy or fatigue
- loss of interest or pleasure
- poor concentration or difficulty making decisions
- feelings of worthlessness
- psychomotor agitation or retardation
- recurrent thoughts of death or suicide ideation.

All of these factors can adversely effect morale and motivation to participate in rehabilitation, and thereby prolong the period of immobilization and reinforce its negative effects.[95-97]

Prevention and management depend on minimizing the period of immobilization and, during that required period, providing adequate sensory stimulation from the environment. Patients should

be positioned such that they may interact with their surroundings, particularly with fellow patients and the clinical staff. Patients who have suffered CNS injury, such as right hemisphere stroke, and have resultant left neglect should initially be positioned so that the right side faces the activity of the surroundings as a means of minimizing sensory deprivation. As soon as feasible, patients should be given cognitive tasks, both to maintain mental agility and as a form of interaction and recreation. Examples include puzzles, games, books, and models to build. Emotional support and psychological counseling need to be available to these patients, particularly if the period of immobility is to be prolonged or is associated with concomitant catastrophic illness.

Endocrine and Metabolic Systems

There are multiple endocrine and metabolic derangements that occur as a result of immobility.[56] Metabolic rate becomes reduced within days of immobilization and may persist for several weeks after remobilization.[6,11,98] Electrolyte homeostasis is altered in immobility such that there are increased losses of calcium, sodium, potassium, phosphorus, sulfur, and nitrogen.[98,99] The negative nitrogen balance reflects a state of increased protein catabolism that overtakes protein synthesis.[98]

Although profound hypercalcemia is rarely associated with immobilization, elevated parathyroid hormone levels have occurred in association with immobilization.[100] Henke and colleagues[101] reported a case of a 13-year-old boy who developed hypercalcemia 1 month after a femoral fracture and presented with progressive anorexia, nausea, vomiting, irritability, and respiratory arrest as a result. Weissman and colleagues[102] reported a case of unexplained intermittent hypercalcemia in a critically ill patient who was thought to be influenced by immobilization. Although the issue of immobilization was not specifically addressed, Forster and associates[103] reported a 15% incidence of hypercalcemia in 100 critically ill patients who had a longer than average length of stay (greater than 12 days) in the intensive care unit (ICU).

The mechanism of immobilization-induced hypercalcemia is a result of enhanced regional blood flow in the bone and increased osteoclastic activity.[63] Vico and colleagues[70] showed that in rats exposed to weightlessness for as little as 5 days, the number of osteoclasts per square millimeter in trabecular bone is significantly increased. Suppression of the increased osteoclastic activity with the resultant increased bone turnover and hypercalcemia is the rationale for treatment with calcitonin.

Treatment of severe hypercalcemia (> 13.0 mg/dL) consists of restricting dietary calcium and medications that might cause hypercalcemia (such as vitamin D and thiazide diuretics), administering intravenous isotonic saline (2.5 to 4.0 L/d) with simultaneous diuresis with furosemide or ethacrynic acid, and supplementing phosphate.[104] Mithramycin is sometimes used as well, especially for hypercalcemia associated with malignancy. Treatment with calcitonin, particularly when used in combination with glucocorticoids, may be of benefit, as both agents are inhibitors of bone resorption; calcitonin also enhances renal excretion of sodium.[105,106] Usual doses are 4 to 8 units per kilogram of body weight subcutaneously or intramuscularly every 6 to 12 hours. A major disadvantage of calcitonin is that it cannot be taken orally. Adverse effects may include mild nausea, abdominal cramps, flushing, and more rarely, an anaphylactic reaction.

Bisphosphonates, such as etidronate, bind to hydroxyapatite in bone and prevent dissolution of bone. They also inhibit osteoclast function. Etidronate and pamidronate have been approved for use in the United States.[107] Although available in oral preparation, their absorption from the gut is poor, so intravenous administration is preferable in acute hypercalcemia. The recommended dose of etidronate is 7.5 mg/kg of body weight intravenously over 4 hours daily for up to 7 days. Adverse reactions are fortunately mild and include altered taste perception, allergic reaction, transient temperature elevation, transient leukopenia, and slight serum phosphate reductions.[107]

Clodronate, an investigational bisphosphonate antiosteoclastic drug, has shown promise in a recent trial[82] comparing its efficacy in preventing demineralization and resorptive hypercalcemia to that of etidronate and calcitonin. Oral clodronate was found to be superior to etidronate and equally effective as calcitonin. The mineralization defects observed during prolonged treatment with etidronate were not observed with clodronate.

Potassium and magnesium depletion are to be expected as a consequence of therapy, so close monitoring of electrolytes, with replacement as needed, should be undertaken. The clinician should have a high index of suspicion for electrolyte perturbation in any immobilized patient who develops anorexia, nausea, vomiting, irritability, and mental status changes.

Insulin production remains normal during immobilization but glucose intolerance has been re-

ported.[108] This is believed to occur as a result of increased peripheral insulin resistance.[109] Further effects of immobilization include increased serum cholesterol levels with decreased low density lipoprotein levels.[56] Other reported endocrine effects of immobilization have been amenorrhea, and low levels of gonadotropin and estrogen.[63]

Urinary System

Urinary system management during immobilization is an often neglected part of patient care and usually only comes to attention when the patient becomes incontinent or oliguric. The major preventable complications are dehydration, renal lithiasis, and urinary tract infection.

Adequate fluid intake is simply assessed through use of intake and output monitoring as well as body weight measurements, skin turgor, and mucous membrane moisture. Unless there is a medical indication to restrict fluid intake, minimum water requirements for an adult are on the order of 2 to 2.5 L/d.[110] (This assumes no contraindications to free water administration such as renal failure, congestive heart failure, and syndrome of secretion of inappropriate antidiuretic hormone [SIADH], to name a few.)

Laboratory studies can also assist with assessment of hydration status. These include urine specific gravity, blood urea nitrogen (BUN), creatinine, and electrolytes (particularly sodium). Elevation of the BUN, especially in the face of a stable creatinine and rising urine specific gravity, and elevation of serum sodium can herald dehydration. If the patient cannot take free water orally, intravenous supplementation will be necessary. Maintenance of adequate fluid intake is of particular importance in the early stages of immobilization. Recumbent positioning initially increases the circulatory blood volume subsequent to resorption of extravascular fluid. The ensuing diuresis is accompanied by urinary excretion of sodium, potassium, calcium, and phosphorus.[9]

Hypercalcuria, particularly in the presence of urinary stasis, places the patient at risk of upper and lower urinary tract calculi. Up to 30% of immobilized patients develop lithiasis (Figure 12-1).[111] It is felt that bed rest itself increases the risk for the formation of calcium-containing renal stones. Hwang and associates[112] have shown that after 5 weeks of bed rest, the mean urinary calcium excretion rose during the first week of the 5 weeks of bed rest by 32% and remained elevated. Mean urinary phosphorus excretion increased by more than a factor of 10. Urinary excretion of sodium, urate, and magnesium rose slightly. Urinary pH, oxalate, and citrate changed very little. Urinary concentrations of calcium phosphate, calcium oxalate, and monosodium urate increased during the period of bed rest, showing that the propensity for crystallization of stone-forming salts is enhanced with bed rest. In fact, struvite and carbonate-apatite bladder calculi are most commonly encountered.[56] However, in the absence of hypercalcemia, it is not necessary to reduce dietary calcium intake.[113]

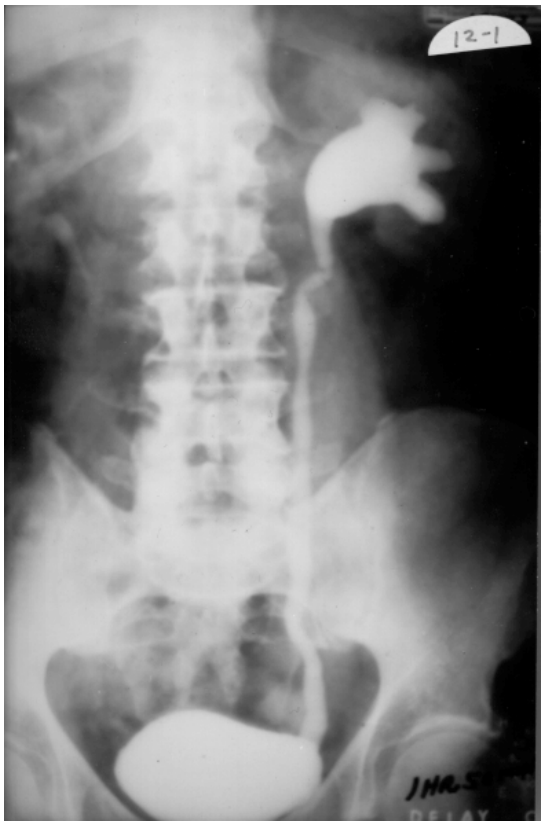


Fig. 12-1. Intravenous pyelogram showing left proximal urinary tract obstruction with hydronephrosis secondary to calculus. Reprinted from the Teaching File, Department of Radiology, Walter Reed Army Medical Center, Washington, DC.

There is increased risk of urinary tract infection in immobilized patients, particularly when there is stasis of urine. Colonization in and of itself is not justification for treatment with antibiotics, as this merely increases the risk of producing antibiotic resistant organisms. The exception to this is urea-splitting bacteria such as *Proteus* species. Because of the increased risk of struvite stone formation, colonization with urea-splitting organisms should

be eradicated.[114,115] Otherwise, antibiotic treatment should be reserved for clinically apparent infection by observing white blood cells (WBCs) in the urinalysis (> 8 WBC per milliliter of midstream urine or > 20 WBC per high powered field of centrifuged urine) associated with proteinuria, bacteriuria and clinical signs of infection.[116,117] In this manner, if and when a urinary tract infection develops, the treated organism will be minimally resistant. Prophylactic measures include adequate urinary flow and frequent, complete drainage of urine from the bladder. If, however, the patient has a history of more than two urinary infections per year, prophylaxis with nitrofurantoin or trimethoprim-sulfamethoxazole may be prudent both from clinical and cost-effectiveness standpoints.[118]

It must be ascertained that the immobilized patient is voiding the bladder completely to minimize the risk of urinary tract infection and reflux of urine into the upper urinary tract. This is best confirmed by determining the postvoid residual volume, which involves placing a catheter into the bladder immediately after the patient has voided. Normally, the residual volume should be less than 75 mL. If it is more than 75 mL, there is incomplete emptying.[117,119] To ensure complete emptying of the bladder, a program of intermittent catheterization is recommended.

The frequency of catheterization in the continent patient is dependent on the volume of the postvoid residual. If the postvoid residual volume is between 75 and 150 mL, the patient should be catheterized once daily; if it is between 150 and 250 mL, the patient should be catheterized twice daily; if it is between 250 and 350 mL, the patient should be catheterized three times daily; and if it is between 350 and 450 mL, the patient should be catheterized four times daily. Postvoid residual volumes greater than 450 mL require more frequent catheterizations, up to every 4 hours.[117,119] Intermittent catheterizations more frequently than every 4 hours are not practical from a patient care standpoint and will not allow the patient adequate sleep. Also, the primary advantage of intermittent catheterization over an indwelling catheter is the reduced risk of urinary tract infection. More frequent intermittent catheterization will negate this advantage, and thus, indwelling catheterization may be preferable. Indwelling catheters are also preferable when urine volumes are fluctuating considerably due to changes in the patient's volume status.

The various etiologies of retained urine are beyond the scope of this chapter but may involve outlet obstruction, lower motor neuron disease, upper motor neuron disease, or intrinsic damage to the bladder wall. Differentiation of these etiologies requires urodynamic study. Fluoroscopy is recommended during the urodynamic study to determine if reflux of urine into the upper tract is present. If reflux is present, the risk of hydronephrosis and pyelonephritis is a concern.

In patients with retention of urine who are undergoing intermittent catheterization, use of urinary antiseptics has been advocated as a means of reducing the likelihood of infection.[120] However, the use of prophylactic antibiotics remains controversial.[121,122] Clinical advantage in instituting antibiotic treatment for prevention of urinary infections has not been conclusively demonstrated, and recent studies tend to indicate that prophylactic antibiotics do not have a long term effect in reducing bacteriuria.[121,122]

Gastrointestinal System

Nutrition

One of the often overlooked risks of immobilization is its effect on the gastrointestinal system. As indicated above, metabolic abnormalities caused by immobilization, particularly immobilization hypercalcemia, can present with gastrointestinal complaints including anorexia, nausea, and vomiting.[101] The anorexia associated with illness also places the bedridden patient at increased risk for malnutrition. Vigilance in the form of calorie counts; frequent weighing of the patient; and monitoring of serum albumin, protein, hematocrit, hemoglobin, and WBC count can serve as markers to evaluate the patient's nutritional status. If the patient is unable to maintain adequate intake, nutritional supplements in the form of enteral or parenteral support will be required to maintain adequate nutrition.[123] It must be remembered that during illness, the metabolic rate is increased, and without adequate nutrition, excessive catabolism will occur. And, as will be seen in the Integumentary System section, inadequate nutrition and increased catabolism are particular hindrances in the prevention of pressure sores.

Constipation

The most commonly encountered gastrointestinal complication of immobilization is constipation. Kinnunen[124] studied 439 patients and found the relative risk for constipation at 1.7 in patients who walk less than 0.5 km daily. The relative risk for bedbound

patients is nearly 16 times that for a person who walks more than 0.5 km per day. The prevalence of constipation was directly correlated with fecal incontinence. Decreased peristalsis secondary to increased adrenergic tone may play a role in the development of constipation in the immobilized patient. Decreased fluid and dietary fiber intake, which is common during illness, will also contribute to the development of constipation. Therefore, the best way to avoid this complication is to mobilize the patient. If this is not possible, an adequate bowel program is required.

The goals of a bowel program are to ensure regular and complete evacuation. Initially, this should be a daily routine at a specified time. To make optimum use of the gastrocolic reflex, the program should follow a meal by 30 to 60 minutes. Usually, this is following breakfast or the evening meal to minimize disruption of the daily diagnostic or rehabilitation program, or both. Once regularity is established, the frequency of the program can be reduced to an optimal evacuation pattern of three times per week. If the patient is incontinent of stool, the possibility of fecal impaction should be investigated, as this can hinder the establishment of a successful program. Impaction should especially be considered if the patient has been treated with medications that have a constipating effect, such as narcotics. If this is the case, disimpaction, treatment with laxatives, enemas, or any combination will be necessary to clear the lower gastrointestinal tract prior to initiating the bowel program. Objectives of the program are to provide adequate bulk and softness to the stools such that laxatives can generally be avoided.

Regular defecation can be stimulated reflexively through distention of the rectum. This can be achieved through use of a glycerin suppository or by digital stimulation by placing gloved digits into the rectum and sweeping in a circular pattern at the time desired for defecation. Adequate intake of dietary fiber greatly enhances the effectiveness of a bowel program by providing adequate stool bulk. Recommended dietary soluble fiber intake should exceed 10 g/d. If this is not possible from the diet, supplemental fiber should be prescribed. One such regimen is to consume 3 to 4 grams of psyllium hydrophilic mucilloid fiber (Metamucil [Procter and Gamble; Cincinati, Ohio]) in 250 mL of water three times per day. This will also help to maintain adequate free water intake to promote soft stools. (This assumes no contraindications to free water administration such as renal failure, congestive heart failure, or SIADH, to name a few.) Psyllium is contraindicated if fecal impaction or intestinal obstruction is present.

If softening of the stool is necessary, this can be accomplished through use of a nonabsorbable softening agent, such as docusate sodium (Colace [Mead Johnson Pharmaceuticals; Evansville, Indiana]) 100 mg by mouth twice a day. Digital stimulation or a glycerin suppository is then used to initiate defecation as desired. The recommended initial bowel program is as follows: (*a*) rule out impaction, (*b*) maintain adequate hydration (> 2 liters free water orally per day), (*c*) administer psyllium hydrophilic mucilloid (3 to 4 grams 3 times daily), (*d*) administer docusate sodium (100 grams 2 times daily), and (*e*) use a postprandial glycerin suppository or digital stimulation once daily. The dosage of soluble fiber and stool softener will likely need to be titrated to optimize consistency and to ease completeness of defecation; but the primary goal remains regular, controlled defecation.

Peptic Ulcer Disease

Patients facing physiological stress have long been known to be at risk for peptic ulcer disease.[125-127] Lev and colleagues[128] examined increased stress ulcer occurrence in the battle wounded during the Vietnam War. It has also been shown experimentally that immobility is a risk factor for ulceration.[129,130] Clinically, the incidence of stress ulcers due to immobility alone is not known, but in spinal cord injured patients who are physiologically stressed and presumably immobilized, the incidence of stress ulcers has been reported to be 4%.[131,132] In Kewalramani's[131] study, 42% of patients with gastric or duodenal ulceration developed perforation. Kuric et al[132] and Dietz et al[133] have indicated that adequate nutrition (meeting the patient's total energy requirements) will reduce the incidence of gastric ulceration by more than half. Anorexia and nausea are early symptoms.[134] Melena is the usual clinical presentation.[135]

The diagnosis is made by positive barium contrast upper gastrointestinal tract radiography or fiber optic endoscopy, or both (Figure 12-2). Of those patients with gastrointestinal bleeding, in the spinal cord injured population, 63% had duodenal ulcers; 21% had gastric ulcers; and approximately 5% each had gastritis, esophagitis, Mallory-Weiss tear, or gastric carcinoma.[135] Use of anticoagulants and steroids can further increase the risk of gastrointestinal bleeding.[136] In the spinal injured population, administration of decadron in the first 48 hours postinjury has not been shown to be associ-

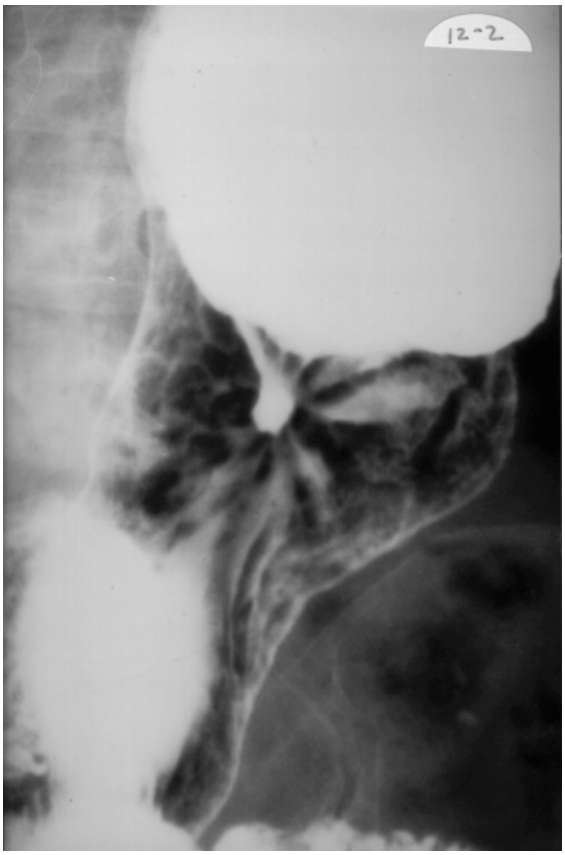


Fig. 12-2. Upper gastrointestinal series demonstrating an acute gastric ulcer. Reprinted from the Teaching File, Department of Radiology, Walter Reed Army Medical Center, Washington, DC.

ated with ulcers, but it has been associated with pancreatitis.[137]

As indicated above, the important preventive strategy for stress ulcers is adequate nutrition.[132,133] Additional suggested medical measures are administration of antacids, (H_2) Histamine$_2$-receptor antagonists, sucralfate (Carafate [Marion Merrill Dow; Kansas City, Missouri]), Omeprazole (Prilosec [Merck Sharp and Dohme; West Point, Pennsylvania]), and misoprostol (Cytotec [G.D. Searle and Co; Chicago, Illinois]).[138-142] H_2-receptor antagonists remain the mainstay of prevention and treatment. H_2-receptor antagonists inhibit the action of histamine at its receptor on the gastric parietal cell, resulting in decreased acid secretion.[143,144]

Antacids (magnesium hydroxide and aluminum hydroxide combinations) are comparable to H_2-receptor blockers in treatment of duodenal ulcers, but their use in prevention of gastric and duodenal ulcers and for treatment of gastric ulcers is not well established.[145] Their primary method of action is acid neutralization. Although sucralfate has been shown to be as effective as H_2-receptor blockers in the treatment of duodenal ulcers, it has not been approved by the Food and Drug Administration for treatment of gastric ulcers.[146] Its exact mechanism of action is not known, but it appears to have cytoprotective effects.[141] Omeprazole is a proton pump inhibitor that reduces the secretion of hydrogen ions from the parietal cell. MacLellan and colleagues[140] have shown that in spinal cord injured rats, omeprazole is more effective than antacids or H_2-blockers in preventing ulceration. In humans, omeprazole heals ulcers more rapidly and with fewer failures than H_2-receptor antagonists, but it is very expensive. It is best reserved for the treatment of refractory ulcers; the suggested regimen is 40 mg/d for 8 weeks.[147-149]

Prostaglandin analogues, such as misoprostol, inhibit acid secretion from the parietal cell and stimulate bicarbonate and mucus secretion from the gastric mucosa. In terms of healing peptic ulcers, misoprostol is less effective than H_2-receptor antagonists.[150] Misoprostol is indicated for the prevention of gastric ulcers for patients who are on chronic nonsteroidal antiinflammatory drugs.[151-154] Fabian and colleagues[142] completed a study of 278 ICU patients that indicates that both an H_2-receptor antagonist (cimetidine) and sucralfate are effective for stress ulcer prophylaxis in severely injured patients. A suggested regimen is presented in Table 12-1. With the exception of

TABLE 12-1

SUGGESTED ORAL REGIMEN FOR THE PREVENTION AND TREATMENT OF PEPTIC ULCERS

Medication	Dose/Frequency
H_2-receptor antagonists	
Cimetidine	800 mg once daily
Famotidine	40 mg once daily
Nizatidine	300 mg once daily
Ranitidine	300 mg once daily
Sucralfate	1 g four times daily
Anatacid	10 cm^3 four times daily
Omeprazole	40 mg once daily x 8 wk for refractory ulcer
Misoprostol	200 μg four times daily if patient is taking NSAIDs

NSAID: nonsteroidal antiinflammatory drug

antacids, all the medications listed in Table 12-1 should generally be avoided in pregnancy due to the lack of controlled data on their teratogenic effects on the human fetus. Misoprostol is contraindicated in pregnancy due to its abortifacient property.

Superior Mesenteric Artery Syndrome

A rare, but potentially life threatening, gastrointestinal complication concomitant with immobility is the superior mesenteric artery syndrome. This syndrome results from a loss of mesenteric fat coupled with bed rest (supine immobilization), which causes the superior mesenteric artery to obstruct the upper gastrointestinal tract by compressing the third part of the duodenum against the underlying aorta.[155] It tends to be more common in females than males, in younger ages (14 to 19 years), and in asthenic body habitus.[156]

The clinical presentation includes nausea and voluminous, bilious postprandial projectile vomiting. There may be periods of normal appetite and the presence of bowel sounds if the obstruction is intermittent.[156] Diagnosis is confirmed with an upper gastrointestinal cinefluoroscopy (Figure 12-3). The primary interventions are nasogastric drainage with intravenous hydration and nutrition. Eating in the left lateral decubitus or upright positions may help to alleviate symptoms. In the Hutchinson and Bassett report[156] on 14 patients, all responded to conservative management, with none requiring surgical decompression; although 50% had more than one episode that required treatment.

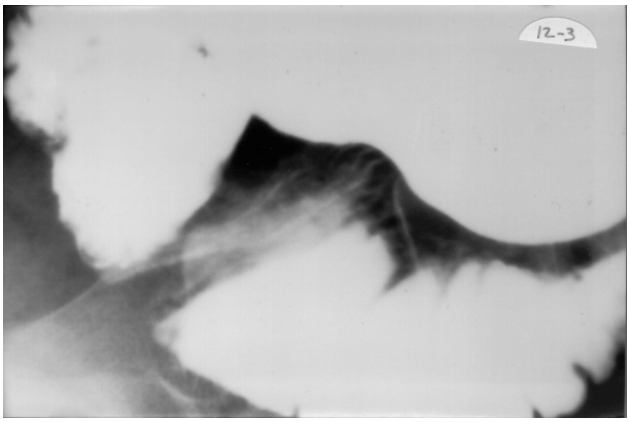


Fig. 12-3. Upper gastrointestinal series demonstrating the superior messenteric artery syndrome with partial obstruction of the inferior duodenum. Reprinted from the Teaching File, Department of Radiology, Walter Reed Army Medical Center, Washington, DC.

Less commonly, other potential gastrointestinal system emergencies that can complicate the recovery of the immobilized patient include pancreatitis and small-bowel obstruction, or ileus. Awareness is the primary means of prevention for all of the gastrointestinal complications of immobility.

Integumentary System

Pressure ulcers are among the most costly complications of immobility in terms of added morbidity and cost. Prevalence in the acute care setting is estimated to be between 3% and 28%; with an incidence of 1% to 8% during hospitalization.[157] In spinal cord injured patients, development of a pressure ulcer is associated with a doubling of inpatient hospital days and an increased cost of up to $40,000 per occurrence.[158] Cost estimates in the non–spinal-injured population during acute hospitalization are nearly $4,000 per occurrence.[159] Not surprisingly, the associated costs are lower in the chronic care setting.[160] Therefore, the prevention of pressure ulcers is of great importance in minimizing the morbidity of immobilization and in the conservation of healthcare dollars.[161,162] Up to $14 billion can be saved if pressure ulcers are prevented.[16]

Pressure ulcers are localized areas of cellular necrosis due primarily to increased pressure over a focal area of soft tissue for a sufficient length of time to result in ischemia.[163] Sustained pressures (as low as 32 mm Hg), shear forces, friction, moisture, increased skin temperature, hypoproteinemia, and anemia have all been found to be important in the pathogenesis of pressure ulcers.[164-172] Tissue subjected to pressures of more than 32 mm Hg for extended periods of time will cause capillaries to collapse, resulting in tissue ischemia, thrombosis, cell death, and ulceration.[172] Pressures of 70 mm Hg applied to the skin for only 2 hours can result in irreversible tissue injury.[173]

Pressure distributions over healthy skin is dependent on the patient's position in bed. Figure 12-4 illustrates the varying pressure gradients in the supine and prone positions.[174] The areas exhibiting the highest pressures are at the greatest risk for ulceration. In the supine position, pressures sufficient enough to cause tissue ischemia are found over the occiput, spine, sacrum, and heels. In the sitting position, pressure over the ischial tuberosities can approach 300 mm Hg.[163,166,174] Patients with insensate skin, impaired mental status, or inability to perform pressure relief are at even greater risk for development of pressure ulcers.[172,175] These ulcers can develop over any bony prominence but are most com-

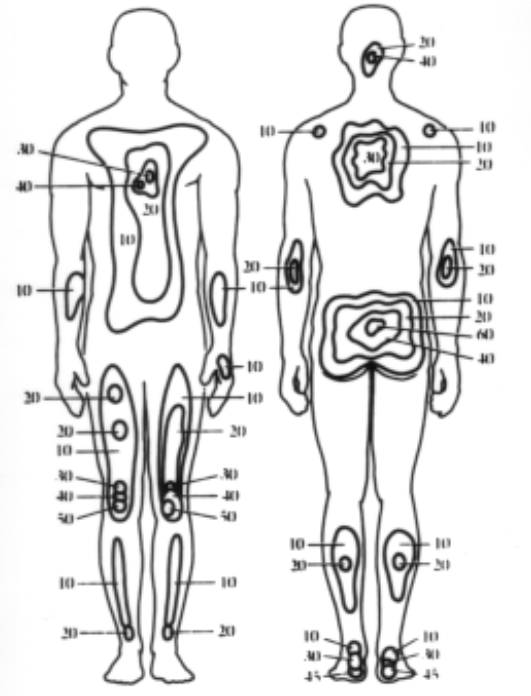


Fig. 12-4. Pressure distributions in recumbent healthy adult male (mm Hg). Left: Prone. Right: Supine. Adapted with permission from Lindan O, Greenway RM, Piazza JM. Pressure distribution on the surface of the human body: 1. Evaluation in lying and sitting position using a "bed of springs and nails." *Arch Phys Med Rehabil.* 1965;46:378.

TABLE 12-2

SITES OF PRESSURE SORES IN PARAPLEGIC PATIENTS

Site	Percentage
Ischial tuberosity	28
Trochanter	19
Sacrum	17
Heel	9
Malleolus	5
Pretibial	5
Patella	4
Foot	3
Anterosuperior spine	3
Elbow	2
Other (including occiput and costal margin)	6

Source: Dansereau JG, Conway H. Closure of decubiti in paraplegics. *Plast Reconstr Surg.* 1964;33:474-480.

mon over the ischial tuberosity, greater trochanter, sacrum, heel, malleolus, and tibia (Table 12-2).[176]

In Persian Gulf War casualties, the prevalence of lower extremity pressure ulcers was 3%.[14] This compares favorably to the reported incidences of up to 8%.[157] Upper extremity and torso ulcers were even less frequent, at 2% each. Still, pressure ulcers are completely avoidable, and the mainstay of management is prevention.

Several tools have been developed to assist in identification of patients at risk.[177-179] An example of an instrument for identification of patients at risk for pressure sores is presented in Exhibit 12-1.[177]

EXHIBIT 12-1

INSTRUMENT FOR IDENTIFICATION OF PATIENTS AT RISK FOR PRESSURE SORES

A. Mental Status
- 5 Alert
- 4 Apathetic
- 3 Confused
- 2 Stuporous
- 1 Unconscious

B. Continence
- 4 Fully controlled
- 3 Usually continent
- 2 Minimally continent
- 1 Uncontrolled

C. Bed Mobility
- 4 Full
- 3 Slightly limited (requires minimal assistance)
- 2 Very limited (requires moderate assistance)
- 1 Immobile

D. Activity
- 4 Ambulatory without assistance
- 3 Walks with assistance
- 2 Chairfast
- 1 Bedfast

E. Nutrition
- 3 Good: eats a balanced diet
- 2 Fair: occasionally refuses meal
- 1 Poor: seldom eats complete meal/dehydrated

Maximum score = 20; Minimum score = 5. High risk of pressure sore if score ≤ 11. Reprinted with permission from Gosnell DJ. An Assessment Tool to Identify Pressure Sores. *Nurs Res.* 1973;22:55-59.

Normally, a person changes bed position as frequently as four times an hour, and, ideally, patients should relieve areas of pressure for 5 seconds every 15 minutes, although this may be impractical.[180] For bedridden patients, a practical minimum is to turn them at least once every 2 hours.[181,182] For the patient using a wheelchair, pressure relief (particularly over the ischial tuberosities, sacrum, and trochanters) should be initiated at least every 30 minutes for a duration of 15 seconds.[183] Proper positioning of the patient at bed rest will help minimize the development of pressure ulcers and will assist with contracture prevention.[15,47,184] The basic positioning strategies are described in the section on contractures.

Use of pressure relieving devices such as seat cushions, special beds, mattresses, and bolsters can be of assistance in redistributing pressure.[185] Maklebust and associates[186,187] found that the air-fluidized bed (Clinitron [Hill-Rom Company, Inc.]), low-air-loss bed (Flexicare [Hill-Rom Company, Inc.]), and three-layered air cushion (Sof-Care [Gaymer Industries, Inc.]) all reduced tissue interface pressures below 32 mm Hg. Use of therapeutic air suspension beds has been shown to reduce the incidence of pressure ulcers in the intensive care unit setting by 79%.[16] Several of these devices are illustrated in Figures 12-5, 12-6, and 12-7. However, none of these measures affords complete pressure relief, particularly beneath the heels, and are not substitutes for frequent skin checks and regular pressure releases.[186] Inspection of susceptible areas (see Figure 12-4 and Table 12-2), meticulous attention to skin hygiene, and adequate nutrition are of utmost importance.[15,172] Maintenance of adequate hydration and nutrition is essential both for prevention of ulceration and for healing, should a pressure sore develop. Increased tissue pressure and shear, combined with skin atrophy from poor nutrition, accelerate the development of decubiti.

Although preventable, pressure ulcers do occur. The classification of pressure ulcers is dependent

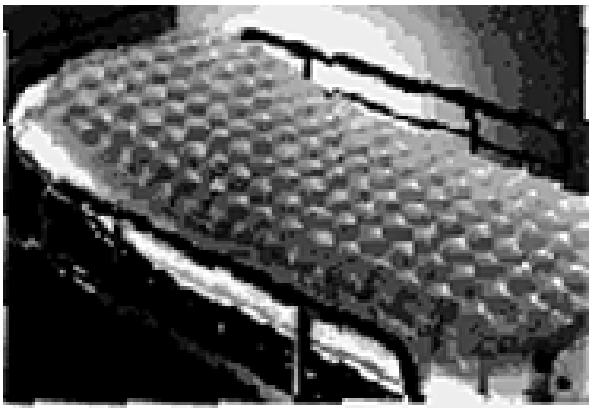


Fig. 12-6. Sof-Care alternating pressure mattress. Designed to relieve pressure in the recumbent patient. Except at the heels, reduces tissue interface pressures below 32 mm Hg.[185,186] Reprinted with permission from Gaymar Industries, Inc., Orchard Park, New York.

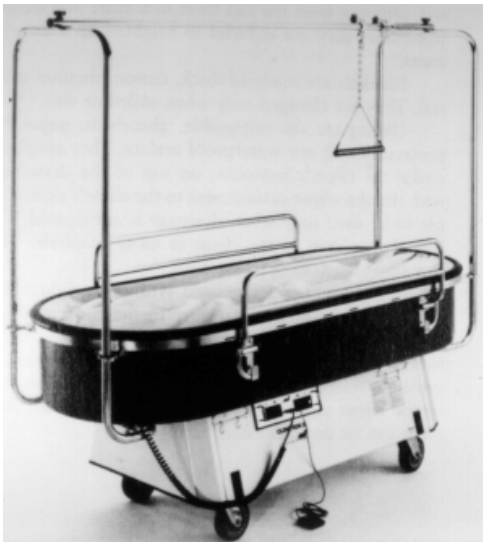


Fig. 12-5. Clinitron air-fluidized therapy bed. Designed to relieve pressure in the recumbent patient. Except at the heels, reduces tissue interface pressures below 32 mm Hg.[185,186] Reprinted with permission from Hill-Rom Company, Inc., Batesville, Indiana.

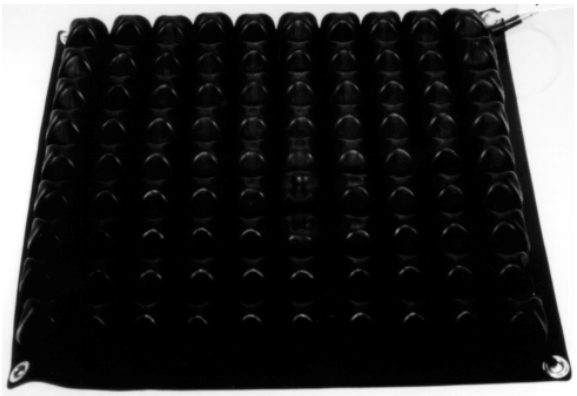


Fig. 12-7. ROHO low profile dry flotation cushion. Designed to relieve pressure in the sitting patient. Reprinted with permission from ROHO Incorporated, Belleville, Illinois.

TABLE 12-3

GRADING OF PRESSURE SORES

Classification	Description
Grade 1	Skin erythema that persists > 24 h and does not blanch to digital pressure
Grade 2	Ulceration of dermis
Grade 3	Ulceration into subcutaneous fat
Grade 4	Ulceration of muscle
Grade 5	Ulceration into body cavity (including bursae and bone)

Adapted with permission from Daniel RK, Hall EJ, MacLeod MK. Pressure sores-a reappraisal. *Ann Plast Surg*. 1979;3(1):53-63.

on the depth of tissue injury.[188] The grading of pressure sores is summarized in Table 12-3. In the earlier stages of ulceration (grades 1 and 2), conservative management can be effective.[189] Blanchable erythematous skin should return to normal in 1 day if pressure is relieved. Nonblanchable erythematous skin should heal in 1 to 3 weeks if corrective action is taken. Bullae may require 1 month or more to heal.[172] It is therefore important that the developing decubitus ulcer be addressed. The most obvious reason is that the more superficial the ulcer, the less morbidity and cost will be encountered. The risk of bacterial superinfection will be minimized as well.

Malignant degeneration has also been reported to occur in long-standing ulcers.[190] As with ulcer prevention, relief of pressure and friction over the injured area is the primary treatment. Nutrition and hydration should be optimized to hasten wound healing. Necrotic tissue should be debrided. Frantz and colleagues[191] have conducted a 5-year retrospective trial that revealed over 70 different treatments used to treat pressure ulcers. Approximately 40% involved open-air or dry gauze treatments and in 60%, an antiseptic solution was used. A subsequent clinical trial has indicated that moist dressings applied three to four times daily are the conservative treatment of choice.[191]

Wounds of grades 3 through 5 will usually require surgical attention. Surgical management includes skin grafts, skin flaps, muscle flaps, musculocutaneous flaps, and free flaps in progressing order from superficial to extensive treatment. The reader is referred to surgical literature for a detailed discussion of these options.[192] Postoperative complications to be wary of include hematoma, seroma, and wound infection. It should be noted that recurrence of ulceration in the same region is as high as 67%.[193] The roles of patient education and prevention along with meticulous postoperative care cannot be overstated.

Respiratory System

A major adverse effect of immobilization on the respiratory system is of a restrictive nature.[17] This stems from two of the processes discussed above: (1) muscular weakness (disuse atrophy) and (2) contracture. As with the limb muscles, the muscles of respiration undergo atrophy with lack of use. This is especially true of the accessory muscles of respiration, including the intercostals. The ensuing weakness results in a loss of chest wall expansion. Lack of mobility also predisposes to loss of range of motion of the costovertebral and sternocostal joints through the process of contracture. Both the weakness of respiration muscles and the loss of mobility of the thorax lead to a restrictive reduction in pulmonary function. In addition, supine patients tend to hypoventilate.[194] Restriction of respiration gives rise to an elevated risk of atelectasis with a concomitant increase in arterial-venous shunting; this results in a perfusion of poorly ventilated regions,[195] leading to impaired oxygenation and fall in partial pressure of oxygen (P_{O_2}) and rises in partial pressure of carbon dioxide (P_{CO_2}) and pH. Immobilization has also been implicated in reduced ciliary activity in the upper respiratory tract, which impairs clearance of respiratory pathogens and increases the risk of pneumonia.[195]

Pulmonary Function Tests

The pulmonary function tests (PFTs) most directly affected by immobility are the vital capacity, tidal volume, minute volume, and maximal voluntary ventilation. This is not surprising, given the restrictive impairment caused by immobilization. Vital capacity and maximal voluntary ventilation can be reduced by more than one third from normal values.[17] Should such restrictive impairment be encountered, Hintzelmann has demonstrated that application of ultrasound diathermy to costovertebral joints followed by deep breathing exercises, result in improved PFTs in patients with ankylosing spondylitis.[196] This same technique can be applied to the patient who suffers unfavorable pulmonary effects due to immobilization. Therefore, PFTs

should be performed at least once per week on patients at bed rest. Treatments included in pulmonary management of the immobilized patient are: (*a*) turn every 2 hours; (*b*) incentive spirometry every 4 hours while awake; (*c*) weekly PFTs; (*d*) assisted cough every 4 hours; (*e*) airway suctioning, if needed, every 4 hours; (*f*) percussion and postural drainage every 4 hours; (*g*) humidified air and mucolytic (acetylcysteine) inhalation for obstipated secretions four times daily; and (*h*) bronchodilators, if clinically indicated.

Lower Respiratory Tract Infection

The adverse effects of prolonged immobility are due primarily to gravitational effects on blood flow and ventilation, impairment of the normal mucociliary escalator, and possibly, an increase in extravascular lung water. The sequence of events that culminate in nosocomial pneumonia is unclear; however, low tidal volumes, increased extravascular lung water, and the accumulation of bronchopulmonary secretions may lead to atelectasis, a well-known precursor of pneumonia. Theoretically, continuous lateral rotational therapy should reverse these abnormalities.

In a randomized, prospective trial of 106 ICU patients, Fink and associates[197] tested the hypothesis that the incidence of lower respiratory tract infections in critically ill, blunt trauma victims can be significantly reduced by employing continuous postural oscillation. Among 48 patients in the control group, 47 met criteria for lower respiratory tract infection or pneumonia. By comparison, out of 51 patients in the treatment group, only 20 developed lower respiratory tract infection or pneumonia. It was concluded that continuous postural oscillation through a 40° to side arc for 10 to 16 hours per day decreases the risk of pulmonary sepsis in victims of major blunt trauma.

The efficacy of using lateral rotational treatment to prevent or reduce pulmonary complications in severely head-injured patients is unclear. Clemmer and colleagues[198] undertook a prospective, randomized trial which compared the kinetic treatment table to conventional bed care in severely head-injured patients. They found that there was no significant difference in mortality, CNS morbidity, length of stay, or rate of pulmonary complications between the two groups; this indicated that the efficacy of the kinetic treatment table in reducing pulmonary complications in head-injured patients remains unclear.

However, three prospective, randomized studies,[199-201] that evaluated patients with acute head trauma, stroke orthopedic injuries requiring traction, and blunt chest trauma, all showed a decreased incidence of nosocomial pneumonia with continuous lateral rotational therapy compared to those treated in a conventional bed and turned every 2 hours by the nursing staff. A fourth study,[202] performed in an ICU with a heterogeneous group of patients, showed no difference in incidence of nosocomial pneumonia between those treated with continuous lateral rotational therapy and those in a conventional bed, but it did show a decreased length of ICU stay for pneumonia patients treated with continuous lateral rotational therapy. It, therefore, appears that for continuous lateral rotational therapy to be effective, it needs to be instituted early in the patient's illness.[203]

The length of time that continuous lateral rotational therapy should be utilized is unknown. It is also unclear whether continuous lateral rotational therapy should be started at full rotation immediately or begun at lesser degrees of rotation and advanced serially over several hours. In the studies cited above, rotations from 40° to 62° in each direction were used. Another unknown is the minimum time that continuous lateral rotational therapy should be administered per day. In the studies discussed, most patients were rotated for 10 to 16 hours per day. Based on the current data, the early use of continuous lateral rotational therapy in comatose or otherwise immobile patients decreases the incidence of pneumonia over the first 7 to 14 days of ICU care.

Although the use of continuous lateral rotational therapy appears to be advantageous in the prevention of lower respiratory tract infections, its availability may be limited. If it is not available, the following is recommended: In addition to the every-2-hour turning program discussed above, aggressive pulmonary toilet should be performed at least every 4 hours. This includes assisted cough (diaphragmatic thrust in patients without abdominal or thoracic wounds), airway suctioning when necessary, chest physical therapy (percussion), and postural drainage. Incentive spirometry at least four times daily can help expand atelectasis and prevent costovertebral and costochondral contracure (Figure 12-8).[204] Humidified air and mucolytic medication such as acetylcysteine (Mucomist [Apothecon; Princeton, NJ]) will also be of benefit with opstipated secretions. If bronchospasm is present, use of broncho-dilators may be of additional benefit.

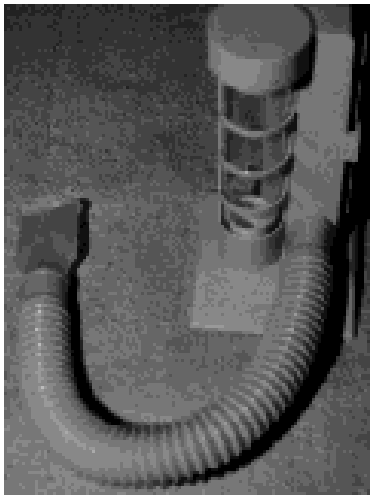


Fig. 12-8. Incentive spirometer for prevention of atelectasis. Maximum inspiratory effort should be performed every 4 hours while awake.

TABLE 12-4

CRITERIA FOR THE CLINICAL DIAGNOSIS OF PULMONARY EMBOLISM

	Likelihood of Pulmonary Embolism	
Clinical Findings	**High**	**Low**
Reasonable precipitating cause	Yes	No
Typical symptoms and signs	Several	Few
Pa_{O_2} < 80 mm Hg	Yes	No
FDP and SFC	Both positive	Both negative
Chest roentgenogram	Abnormal	Normal

FDP: fibrin degredation products
SFC: soluble fibrin complexes
Pa_{O_2}: partial pressure of oxygen, arterial
Source: Wilson JE. Pulmonary embolism. In: Wyngaarden JB, Smith LH, Bennett JC, eds. *Cecil Textbook of Medicine*. 17th ed. Philadelphia, Pa: WB Saunders; 1985:426-431.

Pulmonary Embolism

Pulmonary embolism is a serious medical complication with life threatening consequences. Up to 20% of all deaths occurring in hospitals are a result of pulmonary embolism.[205] The immobilized patient is at particular risk. Xue and Zhang used rabbits to develop an experimental model for inducing pulmonary fat embolism by forced immobilization.[206] Forced immobilization for 5 hours was found to induce pulmonary embolism. The results suggest that the disorder of homeostasis caused by immobilization alone may bring about pulmonary embolism. In one autopsy study,[207,208] pulmonary embolism was shown to be present in 50% of patients who die in hospital; but less than 50% of the patients who died were suspected of having pulmonary embolism prior to death.

The origin of pulmonary embolism results from thrombi that migrate and pass through the right atrium and ventricle and lodge in the pulmonary arteries. (The reader is referred to the section on venous thrombosis for its etiology.) Approximately 50% of patients with diagnosed pulmonary embolism have no clinical sign of deep venous thrombosis.[209] Yet, between 85% to 95% of all pulmonary emboli are believed to arise from lower extremity thrombi.[210] The resulting ventilation-perfusion mismatch results in reduced PO_2 with resulting complaints of dyspnea. Substernal crushing pleuritic chest pain and hemoptysis may or may not be present. Tachycardia and tachypnea are often observed. Cyanosis may also be noted if the hypoxia is significant. Differential diagnosis includes pulmonary infection (pneumonia), atelectasis, congestive heart failure, acute myocardial infarction, dissecting aortic aneurysm, ruptured esophagus, bronchospasm, and mucous plugging. Table 12-4 lists criteria for the clinical diagnosis of pulmonary embolism.[205]

Chest roentgenograms remain useful in diagnosis, particularly if infarction has resulted in a wedge-shaped infiltrate, but the diagnosis can be suspected from roentgenograms in only about 50% of patients with pulmonary embolism (Figure 12-9).[211] Use of radioisotope ventilation-perfusion scanning can further assist with diagnosing suspected pulmonary embolism, although the diagnosis is definitively made through pulmonary angiography (Figures 12-10, 12-11, and 12-12).[212] It must be noted that there is a 4% to 10% risk of morbidity associated with pulmonary angiography. The acceptable diagnostic endpoints for diagnosis of pulmonary embolism without angiography are as follows[205]:

1. Pulmonary embolism is excluded
   - normal perfusion scan
   - low probability perfusion scan with:
     - low estimate of clinical likelihood of pulmonary embolisms, or
     - normal chest x-ray
2. Pulmonary embolism is confirmed
   - high probability perfusion scan with:
     - high clinical likelihood, or

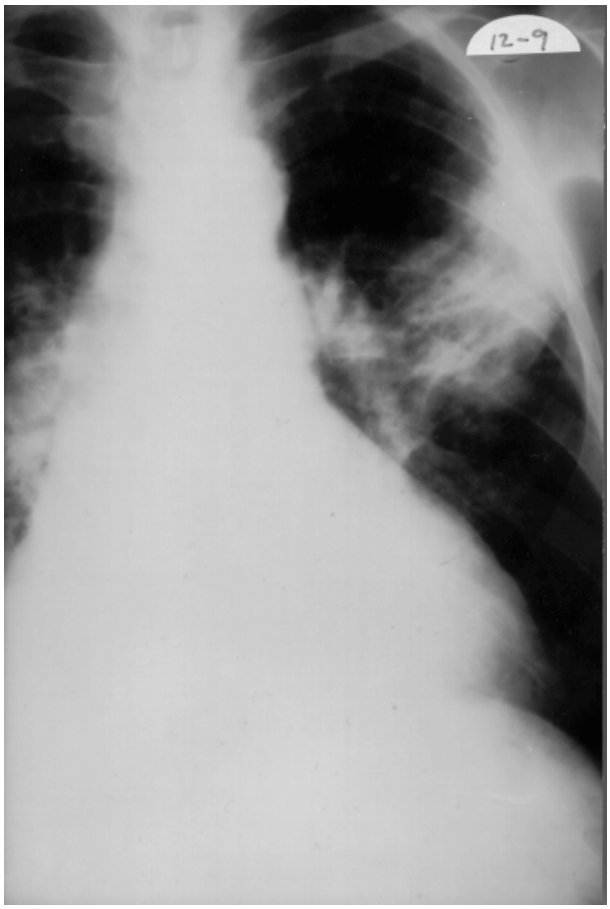


Fig. 12-9. Chest radiograph showing a left wedge-shaped pulmonary infiltrate in pulmonary embolism. Reprinted from the Teaching File, Department of Radiology, Walter Reed Army Medical Center, Washington, DC.

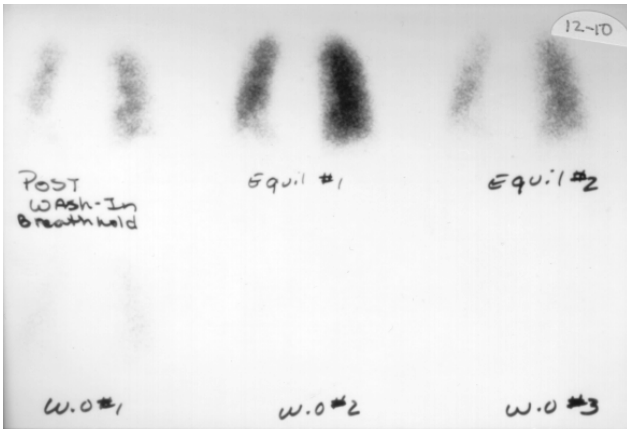


Fig. 12-10. Complete ventilation of all lung fields. Reprinted from the Teaching File, Department of Radiology, Walter Reed Army Medical Center, Washington, DC.

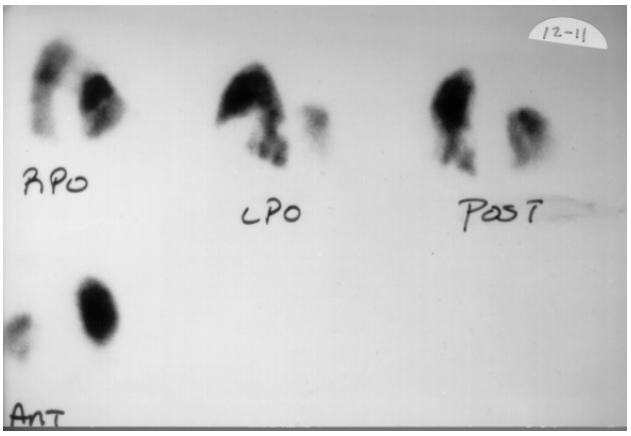


Fig. 12-11. Impaired perfusion of the left lobe of lung. Reprinted from the Teaching File, Department of Radiology, Walter Reed Army Medical Center, Washington, DC.

Fig. 12-12. Pulmonary angiogram demonstrating massive left pulmonary embolism. The lower lobe artery is totally occluded, and there is a large filling defect in the artery to the upper two segments. Reprinted from the Teaching File, Department of Radiology, Walter Reed Army Medical Center, Washington, DC.

- normal ventilation scan, or
- positive venogram, or
- impedance plethysmography.

Thirty-three percent of deaths from pulmonary embolism occur within the first hour of the embolism lodging in the pulmonary arteries, thus making prevention the most important management strategy. Prevention of pulmonary embolism has been investigated through institution of early heparin therapy, including patients with spontaneous intracerebral hemorrhage.[213] In 68 patients with spontaneous intracerebral hemorrhage, the effect of low-dose heparin treatment beginning on the 2nd, 4th, or 10th day was investigated. Early (day 2) low-dose heparin medication significantly lowered the incidence of pulmonary embolism. An increase in the number of patients with rebleeding was not observed. The results indicate that the early use of heparin in these patients is safe and can be recommended for the prevention of thromboembolic complications. The recommended dose is 5,000 units, subcutaneously, twice daily.[205] For additional preventive measures, the reader is referred to the section on venous thrombosis.

For confirmed pulmonary embolism, anticoagulation is necessary.[214] The duration of treatment should be at least 3 months.[205] Fibrinolytic therapy has also been used to dissolve emboli. The use of thrombolytic therapy is reserved for life-threatening situations.[205,215] If anticoagulation therapy is inadequate or contraindicated, partial venous interruption may be indicated and accomplished through placement of an intraluminal filter in the inferior vena cava.[216] Heroic measures include pulmonary embolectomy.[217]

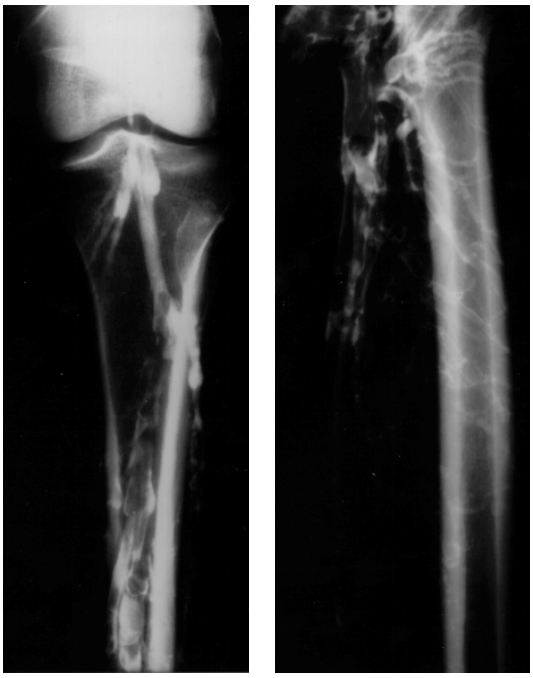
Early mobilization reduces the risks of all pulmonary complications, including pulmonary embolism. When immobilization is necessary, following the guidelines set forth above should help minimize these risks.

Cardiovascular System

Thromboembolism

It is estimated that there are nearly 20 million cases of lower extremity deep venous thrombosis in the United States annually.[218] Thromboembolism is known to occur in the immobilized patient.[219] One study[220] has attributed up to 25% of acute iliofemoral venous thrombi directly to immobilization. If additional risk factors are present, the danger is magnified. The risk factors for lower extremity deep venous thrombosis include prolonged inactivity, trauma (including long bone fractures), paralysis or paresis, dehydration, advanced age, obesity, malignancy, hypercoagulable states, pregnancy, premenopausal estrogen use, polycythemia, and congestive heart failure.[209]

In a study of immobilized multiple trauma patients, 60% had clinically silent, deep venous thrombosis, with half of these extending above the knee.[221] Venous thrombosis develops when the components of Virchow's triad are present: stasis of blood flow, hypercoagulable state, and endothelial damage. In the immobilized patient all three of these are possible. Most venous thrombi seem to originate in regions of slowed blood flow, particularly in the veins of the calf and thigh (Figures 12-13 and 12-14). Decreased blood flow, or even stasis due to lack of the pumping action of immobilized muscles, is undoubtedly a major factor. As blood pools, activation products of the coagulation system accumulate and lead to local hypercoagulability. Activation products of clotting and fibrinolysis can induce



Figs. 12-13 and 12-14. (**12-13,** left) Venogram demonstrating a popliteal deep venous thrombosis. Reprinted from the Teaching File, Department of Radiology, Walter Reed Army Medical Center, Washington, DC. (**12-14,** right) Venogram demonstrating a femoral deep venous thrombosis. Reprinted from the Teaching File, Department of Radiology, Walter Reed Army Medical Center, Washington, DC.

endothelial damage, which, in turn, leads to further activation of the hemostasis system. Endothelial damage may also result from distension of the vessel walls by the pooling blood. Blood flow is further decreased by hyperviscosity due to elevated fibrinogen levels and dehydration.[222]

Deep venous thrombosis in the popliteal vein, or proximally, are felt to be more dangerous than distal thrombosis due to the higher risk of pulmonary embolism.[210] More than half of all patients with a documented deep venous thrombosis will have at least a clinically silent pulmonary embolism.[223] The percentage for calf deep venous thrombosis is less, but still in excess of 15%.

Clinical suspicion should be high for any patient at bed rest for more than a few days. Signs of possible thrombosis include unilateral edema of an extremity, pain, erythema, palpable cords in the calf, or Homan's sign. Homan's sign is calf pain with passive dorsiflexion of the foot with the knee slightly flexed (to relax the gastocnemii). Of these indicators, only unilateral swelling of the leg, either above or below the knee, is a reliable discriminatory sign of venous thrombosis.[210] Therefore, regular measures of calf and thigh circumference are essential in monitoring the immobilized patient for venous thrombosis. Unfortunately, Homan's sign is present in only 10% of documented cases of deep venous thrombosis.[209] It is also nonspecific when present, as it can be present in any cause of calf inflammation or herniated low lumbosacral intervertebral disk.[224]

Although the differential diagnosis of deep venous thrombosis is extensive, it can be organized into general categories.[225] These include soft tissue inflammatory disorders (cellulitis, myositis, tendonitis), popliteal (Baker's) cyst, trauma, neoplasm, other venous disorders (varicose veins, superficial thrombophlebitis, extrinsic venous compression), bone disorders (fracture, heterotopic ossification, osteomyelitis), peripheral arterial disease, arthritis, peripheral nerve disorders (including radiculopathy), systemic edema (congestive heart failure, cirrhosis, malnutrition, pregnancy), and lymphedema. A detailed listing of the differential diagnosis is available in a text devoted to venous thrombotic disorders.[226]

Contrast venography has been the standard on which all noninvasive techniques for detecting deep venous thrombosis are compared (see Figures 12-13 and 12-14). Although this technology is extremely sensitive and specific, its disadvantages include discomfort, contrast reactions, and relative expense.[210] Visualization of the iliac veins can be problematic because of rapid dilution of contrast in the these large veins.[227] Of note, venography itself can cause deep venous thrombosis in up to 3% of patients undergoing the test.[228] Impedence plethysmography, a noninvasive test which measures blood volume in the leg by changes in electrical impedence, is sensitive and specific for detecting proximal lower extremity deep venous thrombosis. It is quick to perform and relatively less expensive than contrast venography. It is, however, inaccurate for detecting distal (calf) deep venous thrombosis.[210]

Color-flow Doppler ultrasonography is a recent advance in using ultrasound in the evaluation of deep venous thrombosis. Blood flow away from the transducer appears blue, while flow toward it is red. The intensity of the color is proportional to the flow rate. Stationary structures, such as vessel walls, appear gray. Compared to venography, the sensitivity and specificity of this test approaches 100% for proximal deep venous thrombosis and shows promise for the noninvasive diagnosis of distal (calf only) deep venous thrombosis.[210,229,230] A diagnostic algorithm is presented in Figure 12-15.[227]

Thrombosis prophylaxis should reduce the incidence of this potentially life-threatening complication. Simple steps that can be taken include elevation of the legs and use of thigh-high graduated-compression elastic stockings while the patient is at bed rest.[225,231] Intermittent pneumatic calf compression may be a useful treatment to substitute for the reduced venous pumping in the lower extremities.[231,232] Isometric exercise of the lower extremities will serve the same purpose. A further recommended prophylactic measure is 5,000 units of heparin subcutaneously twice daily until the patient is remobilized. If a deep venous thrombosis is diagnosed, then anticoagulation is indicated. Traditionally, this has meant intravenous heparinization to achieve an activated partial thromboplastin time of between 1.5 and 2.5 times the control value, and initiation of warfarin sodium by the second treatment day.[233] When the prothrombin time (PT) reaches two times control, the heparin is discontinued (typically 5 days), and warfarin is maintained for 3 months with a PT between 1.5 and 2.0 times control.[234-238] PT should be checked three times a week during the first week of therapy, twice weekly for the next 2 weeks or until a stable dose of warfarin is achieved, then weekly thereafter.[236,237]

A clinical trial[239] has found that replacing continuous intravenous heparin with subcutaneously administered low molecular weight heparin, dosed at 175 international factor Xa inhibitory units per kilogram of body weight once daily is an equally

Fig. 12-15. Diagnostic algorithm for the diagnosis of deep venous thrombosis (DVT). Reprinted with permission from Satiani B, Rustin R, Biggers K, Bordner L. Noninvasive diagnosis of deep venous thrombosis. *Am Fam Physician*. 1991;44(2):569–574.

effective treatment for proximal vein thrombosis and allows outpatient treatment of uncomplicated thrombi. Thrombolytic treatments have also shown promise, especially in preventing symptoms of postphlebitic venous insufficiency.[215] Inferior vena cava interruption is reserved for patients who develop pulmonary emboli despite adequate anticoagulation or for those who cannot be anticoagulated.[240]

Cardiovascular Deconditioning

Among the major cardiovascular changes that occur with immobilization are fluid shift, negative fluid balance, orthostatic instability, decreased exercise tolerance, and loss of blood volume.[241,242] With bed rest, there is a redistribution of body fluids from the lower extremities to the central circulation. This fluid shift can be in excess of 0.5 L,[6,243] and affect homeostasis. This has two major consequences:

1. The heart rate decreases in response to increased central venous pressure, increased left ventricular end diastolic volume, and increased stroke volume. Initially, this results in up to a 40% increase in cardiac output in the supine position.[244] Cardiac output is reduced toward baseline levels through reduced heart rate, and blood pressure is controlled through reduced peripheral resistance.[241-243] With prolonged bed rest, there is a gradual increase in the resting heart rate of an average of 1 beat per minute every 2 days up to an overall increase of up to 15 beats per minute above basal.[241,242]

2. The central venous pressure is reduced through negative fluid balance, or excretion. During the first week of bed rest there is a corresponding plasma volume loss of approximately 7%.[245] There is a parallel loss of blood volume, with a resultant 8% decrease in red blood cell mass.[245] Although these losses stabilize, the result is relative dehydration.

The impact of these hemodynamic changes becomes apparent when, after weeks of bed rest, the immobilized subject stands. On standing, the heart rate increases by nearly 30% of that of a mobile subject. Despite the increased pulse, cardiac output falls by a similar degree.[245] And although peripheral vascular resistance does increase, it is not sufficient to compensate for the reduced stroke volume and the blood pressure falls on standing. This orthostatic

intolerance is manifested clinically by tachycardia, diaphoresis, nausea, and possible syncope.[242] Postural hypotension occurs when the pulse increases by 20 beats per minute and the systolic blood pressure falls by more than 20 mm Hg on rising from a supine position.

Another major consequence of prolonged bed rest is reduced aerobic capacity, or exercise tolerance, as a result of decreased volume of maximum oxygen consumption (VO_2max). VO_2max is a function of the body to deliver oxygen to the tissues and is a product of maximal cardiac output and maximum arteriovenous oxygen difference. Because cardiac output does not increase in response to exercise to the same degree as it does in the nonrested subject, reductions of up to 46% in VO_2max have been reported following 4 weeks of bed rest.[241] Decrease in VO_2max occurs whether the patient is at complete bed rest or is allowed to exercise in bed.[246] However, this loss of VO_2max can be minimized by performing isometric exercise.[247] Finally, it has been recently observed that left ventricular atrophy occurs in bedridden elderly patients.[248]

In attempting to mobilize a patient who has been at bed rest for more than 3 to 5 days, it is important to monitor blood pressure and pulse to observe if hypotension is occurring. The signs of orthostasis mentioned above should be looked for. It may be necessary to use a passive tilt table, starting with only a small angle of incline for relatively short periods of time, to reacclimate the patient to the nonhorizontal position. The rapidity of progress is dependent on the patient's tolerance. The longer he or she has been at bed rest, the longer this process will take.

Vallbona[17] has suggested a regimen that starts with the table at 30° of incline from the horizontal, for 1 minute, twice a day and builds tolerance at that angle gradually until this angle can be tolerated for 30 minutes twice a day. Once this is accomplished, the angle can be advanced 5° to 10° per week until an angle of 70° is reached, which approximates 1G of force. At 1G of force the body experiences the normal acceleration force of gravity in the upright position (approximately 9.8 m/s^2).[249] From this point, progressive ambulation can begin.

While on the tilt table the patient will need to be monitored closely for signs of orthostatic hypotension. Several measures can be added to assist in mobilizing the patient and prevent orthostasis. To prevent venous pooling of blood in the lower extremities, thigh-high graduated-compression elastic stockings should be applied. An abdominal binder can also assist in maintaining venous return to the heart. Should either of these measures prove ineffective, adrenergic support in the form of ephedrine, 25 mg by mouth, 20 to 30 minutes before therapy, can be of assistance.

Once the patient is able to tolerate the upright position, a program of cardiac reconditioning can begin. Initially, exercise activity should be limited to 70% of the maximal heart rate (roughly 70% of 220 minus age) or an elevation in resting pulse of 20 beats per minute to begin aerobic conditioning.[56] The duration of the exercise and how rapidly it can be advanced will depend on patient tolerance. Maximum gains in endurance and aerobic capacity will be on the order of 20% to 40% per week. The program should include both warm-up and cool-down exercises to prevent exercise induced ST segment depression and postexercise hypotension.[56]

CONCLUSION

The era in medical history of employing complete bed rest as a primary treatment has passed. The complications of immobility generate staggering costs in healthcare dollars and resources, and lost productivity can be substantial.

Implications for extended loss of personnel in a combat situation, given the multisystem physiologic effects and complications of immobilization, are not inconsequential, but prevention of these complications can have a substantial impact on the practice of military medicine.

All the complications described in this chapter can be minimized, if not prevented, by avoiding the use of immobilization and bed rest as much as is practical. When necessary, immobilization should be for as small a region as possible, for the shortest amount of time possible. There are very limited uses for prolonged immobility. When a patient is prescribed bed rest, it is the responsibility of the care providers to be vigilant and aggressive with interventions to prevent the complications that will inevitably result from the altered homeostasis. Physical medicine services can be of great assistance in evaluating, educating, managing, reconditioning, and preventing the ill effects that can befall the immobilized patient.

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