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# Infectious Complications after Spinal Cord Injury

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Additional information is available at the end of the chapter

<http://dx.doi.org/10.5772/intechopen.72783>

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## Abstract

Infectious diseases after spinal cord injury (SCI) are important. They can cause mortality and morbidity. The SCI patients usually stay in hospital or rehabilitation units for a long time, and this can cause several complications for them.

**Infectious complications:** There are several infectious complications in these patients. Pressure ulcers that may be infected, soft tissue infections, osteomyelitis, pneumonia, urinary tract infection, bacteremia, meningitis, epidural abscess, and subdural empyema are important complications. These diseases should be diagnosed and managed promptly, before leading to irreversible complications or death.

**Diagnosis:** Diagnosis is made by physical examinations; laboratory tests like wound, urine, tracheal secretion, and blood culture with antibiogram; and radiologic evaluation like plain X-ray and magnetic resonance imaging may be used.

**Treatment:** Appropriate antibiotics are cornerstone of infectious complications. Offloading is important for treatment of pressure ulcers and subsequent complications such as soft tissue infection and osteomyelitis.

**Prevention:** Intermittent urinary catheterization and prophylactic antibiotic therapy can decrease UTI. Pressure relief, position changes, and regular and frequent observation of skin will prevent pressure ulcers, soft tissue infections, and osteomyelitis. Pulmonary toilet, appropriate positioning, and cough assistance can be useful for clearing retained secretions and preventing pneumonia.

**Keywords:** infectious, spinal cord, complications

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## 1. Introduction

Infectious complications are supposed to be an important cause of morbidity and mortality in patients with spinal cord injury (SCI). Infectious diseases may lead to death and several

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complications such as prolonged hospital stay and increased cost of management of patients. Several organs may be affected and problems in these organs can be even more important than the primary event. The types of infections in these patients are different and related to several factors. Inabilities to changing position or ineffective cough, using several necessary devices, prolonged hospitalization, and several other factors, in patients with SCI, predispose them to different types of infections. Inability to walk, sit, or change position may lead to pressure ulcers, skin and soft tissue infection, and osteomyelitis. Reduced tissue perfusion increases the spinal cord-injured patient's susceptibility to pressure ulcers [1] during the acute and rehabilitation phases, most frequently over bony prominences such as the sacrum, tuber ischii, heel, malleolus, and trochanter [2]. Physical and psychosocial elements such as nutrition, past history of pressure ulcers, and social supports can be important in developing ulcers [3]. Ineffective cough and retained pulmonary secretion may lead to pneumonia. Most of the patients need intubation in the course of hospitalization that predisposes them to ventilator-associated pneumonia. Ventilator-associated pneumonia is the most frequent nosocomial infection in patients receiving mechanical ventilation and contributes to a longer intensive care unit stay and high morbidity and mortality [4, 5]. Use of high doses of corticosteroid for management of some patients with SCI can increase the risk of infection. In those patients who need surgical intervention, the operation time is usually prolonged. Sometimes, the use of an external device is mandatory for fixation of unstable vertebral column. The SCI patients may develop bloodstream infection during the hospital admission. During bloodstream infection occurrence in an SCI population, multidrug-resistant organisms are frequent [6]. ICU-acquired bloodstream infection in the intensive care unit is still associated with a high mortality rate. The increase of antimicrobial drug resistance makes its treatment increasingly challenging. ICU bloodstream infection is associated with a 40% increase in the risk of 30-day mortality, particularly if the early antimicrobial therapy is not adequate [7]. Paying attention to antibiotic therapy is important in SCI patients. Antibiotic resistance is of great concern for both infection control and the treatment of infectious diseases. Drug-resistant pathogens, such as methicillin-resistant *Staphylococcus aureus* (MRSA), *Pseudomonas aeruginosa*, *Acinetobacter* and extended-spectrum  $\beta$ -lactamase (ESBL)-producing Enterobacteriaceae, are associated with inappropriate antibiotic treatment that resulted in adverse outcomes. In addition, unnecessary use of broad-spectrum antibiotics for patients with non-drug-resistant pathogens increases mortality [8].

These can be the risk factors for developing infections in SCI patients. In this chapter, the cause of infections, predisposing factors, diagnosis, management, and prevention will be discussed.

## **2. Infectious diseases after spinal cord injury**

### **2.1. Urinary tract infection**

Urinary tract infections (UTI) still cause significant morbidity in patients with spinal cord injury, although mortality due to urinary tract complications has decreased dramatically [9]. Patients with spinal cord injuries (SCIs) and complete or incomplete paraplegia are prone to frequent, recurrent, or chronic UTI. The reason for the increased risk of acquiring UTI is

multifactorial, including reduced sensation of classical UTI symptoms, incomplete bladder emptying, frequent catheterizations, or chronic urinary tract catheters [10]. The rate of UTI in an SCI patient is 2.5 episodes in patient per year. UTI is the second leading cause of mortality in SCI patients [11]. Patients with SCI who have urinary catheters have an increased risk of UTI. Urinary tract infection can be important and can cause serious complications including sepsis and septic shock if it is not diagnosed and treated.

Using Foley catheter is usually accompanied with colonization of microorganisms and infection [12]. Bacterial biofilm formation of Foley catheter can cause cystitis [10]. About 80% of UTIs follow urinary catheter insertion. Nitrofurazone-coated and silver alloy-coated catheters can decrease asymptomatic bacteriuria during short-term (<30 days) use in comparison with latex or silicon catheters. The risk of infection is higher with long-term catheterization, and it is safe to remove it early after surgery. Latex and silicone catheters have the same infection rates, but Foley catheters cause more symptomatic bacteriuria and UTI than intermittent catheterizations. Changing the drainage bags and adding antiseptic solution to bags cannot prevent UTI in patients [13]. There are several risk factors for UTI in SCI patients. Reflux of vesicoureteral, postvoiding residuals, outlet obstruction, urinary tract stones, and bladder overdistension [14]. These patients are exposed to antibiotics because of frequent infections that may be an important risk factor for resistant microorganism infection [15]. Today, UTI may be difficult to treat in SCI patients because of antibiotic-resistant organisms. The SCI patients are also colonized by resistant organisms because of recurrent and prolonged hospitalization [16]. The main causative agent of UTI in SCI population is usually derived from the patient's flora. The indwelling catheter has a great role in infection and the duration of catheterization is the most important risk factor. If the patient carries a catheter more than 30 days, the risk of infection with multiple organisms will increase. Although short-term catheterization can be risk factor for bacteriuria, it is usually asymptomatic and often by a single microorganism [17]. It is better to use hydrophilic-coated catheter for intermittent catheterization in SCI patients during acute inpatient rehabilitation. These kinds of catheters can postpone the development of UTI. They also reduce the incidence of bacteriuria and infection. Reduction of complications and treatment costs and preventing the emergence of antibiotic-resistant organisms are other benefits of hydrophilic-coated catheters [18]. Substitution of indwelling catheter with intermittent catheterization during the rehabilitation phase will reduce development of UTI [9]. The unitary catheter should work in a closed system so that no organism can enter the system. It is also important to reduce the duration of catheterization. Sometimes intermittent catheterization, condom sheet catheter, and suprapubic catheters may substitute indwelling catheterization to reduce the risk of infection [17]. Intermittent catheterization is safe and is advised to prevent UTI in SCI patients. Condom sheet catheter can be used in patients who are able to urinate and there is no pathology or injury in urethra. In some patients, where using condom sheet catheter or intermittent catheterization is not suitable or possible, the physician may decide to use suprapubic catheter. The physicians should be aware of these two points that SCI patients may not have the classic symptoms of UTI and urinary infection may cause urologic complications [15].

### 2.1.1. Diagnosis

Diagnosis of UTI is usually based on the results of urine culture, although in some condition like low titer of organism in urine, slow-growing pathogens and unusual organisms, results of culture may be unreliable [12]. The physician should be aware of how to diagnose UTI and distinguish it from colonization. These patients are at increased risk of acquiring multi-drug-resistant bacteria because they are admitted due to UTI or other infectious diseases and take antibiotics. Several resistant organisms may cause UTI in SCI patients including multidrug-resistant *Pseudomonas aeruginosa*, ESBL (extended-spectrum  $\beta$ -lactamase-producing) *Escherichia coli*, resistant *Klebsiella* spp. and MRSA (methicillin-resistant *Staphylococcus aureus*) [10]. Due to multiple risk factors for acquisition of infection, especially with resistant organisms, complicated UTI may develop with unusual and resistant bacteria. The infection may be polymicrobial. *Proteus*, *Providencia*, *Serratia*, and enterococci may also cause UTI in these groups [9]. For the diagnosis of UTI, culture is needed to find to causative agent, but if the patient is not symptomatic, it is not necessary to get culture, because the patients usually do not need treatment [17]. When UTI is diagnosed in SCI patient, the physician should evaluate the patient for anatomical and functional disorders. It is important to correct any correctable disorder for optimal treatment success [9].

### 2.1.2. Treatment

Differentiating infection from colonization and asymptomatic bacteriuria from symptomatic infection is an important point in treatment of UTI in SCI patient. A symptomatic patient needs to be treated, and after treatment, long duration of antibiotic suppressive therapy is not necessary [17]. For treatment of UTI, usually, there are many antibiotic options. It is better to postpone the treatment until the result of culture. Sometimes it is necessary to treat the patient empirically. Some variables like probable organism and susceptibility, administration route (oral vs. intravenous), the patient tolerance, renal function, and the patients' other medications should be considered for choosing appropriate antibiotic [19]. Duration of treatment of chronic UTI in SCI patient may need to be extended. Some studies recommend and some do not. It seems more studies are needed for certain recommendations [10]. The best antibiotics are those that have the most therapeutic effect on causative agent, without any or with less impact on the host normal flora. This antibiotic is best chosen according to result of urine culture and antibiogram. Duration of treatment is usually 5 days but may be extended to 7–14 days when reinfection or relapse occurs [9]. Some studies recommend treating urinary infection between 10 and 14 days in SCI patients, especially when it is not possible to discontinue the urinary catheter. To determine the optimal duration of treatment, multicenter and randomized clinical trial may be necessary [19]. Darouiche's study demonstrates that the 5-day treatment with urinary catheter exchange can be as effective as a 10-day regimen with catheter retention [20]. Antibiotics usually are chosen according to urine culture. Third generation of cephalosporines, carbapenems, and quinolones are often used to treat Gram-negative organisms. For treatment of *Enterococcus* and *Staphylococcus aureus* that usually are resistant in these patients (i.e., methicillin-resistant *S. aureus* or MRSA), vancomycin is appropriate.

### 2.1.3. *Prevention and prophylaxis*

Prevention of UTI in SCI patients plays an important role in hospital and even in rehabilitation courses of these patients. Paying attention to urinary tract hygiene is necessary. Some patients may encounter relapse or reinfection. In these patients, evaluation of structural and functional disorders should be performed. Duration of previous treatment and probable complications like urine residue and urinary stone should be assessed. Antibiotics may be used as prophylaxis, but it is important to notice that it can be used when recurrent UTI occurs and when all structural and functional abnormalities are corrected. Prophylaxis is not recommended for patients carrying indwelling catheters, and for those who have intermittent catheterization, it is contraventional [9]. Physicians can most effectively prevent UTI by avoiding use of long-term catheters, short duration of catheter use, and substituting intermittent catheterization with indwelling catheter. Daily washing of the catheter or perianal or periurethral areas has no preventive effect. It is recommended to use antibiotic immediately before any invasive procedure on urinary tract system [19]. Probiotics may be useful as prophylactic agents. They may decrease the number of resistant organisms' colonization and may be an attractive substitution for antibiotics for prophylaxis in future [16]. Non-antibiotic prophylaxis may be used for preventing UTI. Some studies may recommend cranberry juice as prophylaxis of UTI, but there is not any reliable clue to prove its effectiveness [9]. In Linsenmeyer's study, cranberry was used for prophylaxis of UTI in patients with neurogenic bladder after spinal cord injury. Cranberry tablets could not effectively decrease the risk of UTI in patients with neurogenic bladders [21].

## 2.2. **Skin and soft tissue infection**

One of the most important, serious, and chronic complications of spinal cord injury is pressure ulcer [22]. Pressure ulcers may cause long-term morbidity and even mortality and effectively have severe influence on SCI patients' lives [23]. These patients have more risk of developing pressure ulcer. The ulcers are often chronic wounds that debilitate the patient and increase hospital course [24]. Pressure ulcers are common in SCI patients and usually are complicated. Treatment is often difficult and expensive. It is important to pay special attention to pressure ulcer in SCI population [25]. Several risk factors are associated with pressure ulcer. These risk factors include: decreased activity, complete cord injury that cause paralysis, cervical collar and back board that cause restricted activity, diabetes mellitus, cigarette smoking, hypoalbuminemia, nursing home residence or long duration hospital stay [26], loss of sensation, wet area due to urinary or fecal incontinence, poor nutrition, and muscular atrophy. Pressure ulcers usually occur in about 30–40% of SCI patients. Ulcers usually develop on bony prominences. Sacrum, ischial tuberosity, trochanteric area and malleolus are usual areas for developing ulcers [2]. Patients with pressure ulcers may have good outcomes if rapid diagnosis and proper treatment is performed for them. The ulcer may heal completely without any sequelae. Some ulcers may have slow course of healing and some even may not heal. Some studies emphasize on the role of fibronectin on ulcer healing course. Fibronectin may have a role in opsonizing macro-aggregate debris for phagocytosis, increasing revascularization, and facilitating fibroblast proliferation and migration. Plasma fibronectin increases in ulcers

with rapid healing but stay in low level in ulcers with poor healing. So plasma fibronectin level may predict the speed of healing of pressure ulcers [27]. The SCI patients may also suffer from other soft tissue infection rather than pressure ulcers including fungal infections and seborrheic dermatitis [28].

### 2.2.1. Diagnosis

Diagnosis of pressure ulcers is clinical. The ulcer smear and culture can be useful for recognizing the causative organism and determining the antibiotic sensitivity. *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Proteus mirabilis*, and *Enterococcus faecalis* are the most common organisms causing pressure ulcers [24].

### 2.2.2. Treatment

Offloading is the cornerstone of treatment of pressure ulcers. Ultrasound (low-frequency and nonthermal) may have a therapeutic role in intact skin ulcers. If the ulcer is superficial, foam dressing and collagenase may be used. For deep pressure ulcers, usually debridement and surgical intervention is needed. Osteomyelitis beneath the ulcer is so important and should be considered in treatment of deep ulcers [23]. In SCI patients, flap surgery may be needed to cover the place of debridement [25]. In Schryvers's study on large number of SCI patients with pressure ulcers during 20 years, a large number of patients needed surgical intervention. Pelvic area ulcers were the most common (468 of 598 pressure ulcers), of which 431 (92%) were treated surgically. Fasciocutaneous or cutaneous flaps, muscle or musculocutaneous flaps and primary closures were the most common surgical intervention. During the ulcer management, some bone intervention is unavoidable [29]. Medical honey has a substantial efficacy on wound management and control of infection of pressure ulcer, as shown by low bacterial growth, decreased wound size, and improved healing stage [30].

Electric stimulation therapy (EST) accelerates pressure ulcer healing in SCI patients. Pressure ulcer healing is determined by decrease in wound size and improvement in wound appearance after 3 months of treatment with EST [31]. Use of ultraviolet light C (light wavelength 200–290 nm) may be effective in treatment. It can be because of its potency in killing antibiotic-resistant microorganisms. *Staphylococcus aureus*, methicillin-resistant *Staphylococcus aureus* (MRSA) and *Pseudomonas aeruginosa* that may be resident on superficial layer of wound may be killed by ultraviolet light C [32]. Maggot therapy may also be used a subsidiary way to treat wound ulcer. Live blowfly larvae in wound dressings accelerate wound healing by increasing debridement. They can debride necrotic tissue within 1 week that is so rapid in nonsurgical wound management. It is safe, simple, and inexpensive, and it seems that it has no complications, so it can be used for treatment of pressure ulcers in SCI patients [33].

### 2.2.3. Prevention

Pressure ulcers certainly have a great influence on daily activity and life of SCI patients [34]. The best position and the turning frequency are not clear, but avoiding the 90° lateral position is recommended. This position will bring about high pressure over the trochanters with

the risk of pressure ulcer development. The risk of developing pressure ulcer is highly individualized and the SCI patient is at a significant risk. Prevention strategies in seating position and in bed are very important in this group to prevent pressure ulcer, and so, pressure relief maneuvers can be important [35]. Pressure relief, position changes, and regular and frequent observation of skin, especially on the pressure areas, that is, over the bony prominences can prevent pressure ulcer development [2]. Pressure ulcers can also be prevented by improvement of neurologic functions and reducing the time of hospitalization and rehabilitation stay [36]. Pressure ulcer prevention is strongly associated with lifestyle modification [35]. Frequent change of position and use of pressure-relieving devices have important roles in reducing the pressure ulcer development. Some risk factors other than pressure may be important in developing ulcer. In SCI patients who do not have vasomotor control below the level of the lesion, hypoxemia will develop, and it can be an important risk factor. So, pressure ulcers may be prevented not only by reducing external pressure by pressure relief, but also by increasing the patient's resistance to pressure, by increasing tissue oxygenation [37]. One of the important risk factors that may increase skin and soft tissue infections is resistant bacterial colonization. Some activities such as hand hygiene, contact precautions, and cultural changes are associated with significant declines in bacterial infection, especially MRSA colonization and infection [28].

### 2.3. Osteomyelitis

One of the complications of spinal cord injury is osteomyelitis. Osteomyelitis may develop by extension of infection from pressure ulcers [38]. After spinal fixation surgery, osteomyelitis may be developed, as a complication of surgery. Osteomyelitis increases the treatment cost and may lead to other complications [39].

#### 2.3.1. Diagnosis

There are several diagnostic methods for diagnosis of osteomyelitis in SCI patients.

Bone biopsy is the gold standard, and magnetic resonance imaging (MRI) is usually used as a sensitive and specific modality. Several organisms are known as causative agents. The most common isolated organisms are *Staphylococcus aureus*, *Peptostreptococcus*, and *Bacteroides*. Coagulase-negative staphylococci, group B *Streptococcus*, *Proteus*, and group milleri *Streptococcus* may also be isolated as less common agents. The diagnosis of pelvic osteomyelitis is difficult and may need multiple bone biopsies. At least three bone samples may be necessary to detect the pathogen and exclusion of contamination. In one study, sensitivity of MRI for diagnosis of pelvic pressure ulcer osteomyelitis was 94% and specificity was 22% [40].

However, Huang's study demonstrates that MRI is a sensitive method for diagnosis of osteomyelitis in SCI population. MRI can be used to demonstrate the extension of infection and to guide limited surgical resection and preserve viable tissue [41]. Pelvic pressure ulcers that accompany osteomyelitis may show cortical erosion and bone marrow edema in MRI [42]. In SCI patients, abscesses, fluid collections, and sinus tracts can be detected by MRI [43]. For diagnosis of osteomyelitis, gallium scan and plain pelvis X-ray may be used. Negative bone

scan can rule out osteomyelitis. However, chronic ulcers usually accompany osteomyelitis. Delayed healing or recurrence of pressure ulcers has no clear association with osteomyelitis [44]. Computerized tomography and Technetium-99 m bone scans are not usually used for diagnosis of osteomyelitis in SCI patients with pressure sores [45].

### 2.3.2. Treatment

Treatment of osteomyelitis is composed of two parts: surgical management and medical treatment. Surgical approach is in fact debridement and in some patients, muscle flap. Medical therapy is in fact antibiotic therapy and wound care. Hyperbaric oxygen may be used in refractory osteomyelitis [46]. Treatment of osteomyelitis is prolonged and so, expensive. Using surgical debridement can shorten the duration of antibiotic therapy for osteomyelitis in SCI patients. In SCI patients with bony prominence osteomyelitis, surgical debridement and flap coverage of the sore can influence the outcome of antibiotic treatment [47]. Antibiotics for treatment are chosen according to the results of culture.

### 2.3.3. Prevention

Measures for prevention of osteomyelitis are in fact those that were mentioned in Section 2.3.1 for prevention of pressure ulcer and skin and soft tissue infection. The main preventive measures are pressure relief, regular change of position, and frequent observation of the skin over bony prominences.

## 2.4. Pneumonia

Pulmonary complications in SCI patients are important, as they may be life threatening. Pneumonia, pulmonary infarction, pulmonary thromboembolism, chest injury, and atelectasis are the most frequent and important complications in these patients. Pneumonia is one of the most important pulmonary complications. It may have developed shortly after spinal cord injury, during hospitalization or even in rehabilitation periods. The risk of pneumonia is greater in post-injury period. In this phase, the patients usually do not have effective cough. If the phrenic and intercostal nerves have been damaged, the respiration cycle may be influenced and the patients may be prone to pneumonia [48]. After intubation and mechanical ventilation, ventilator-associated pneumonia (VAP) may develop. VAP is in fact the occurrence of pneumonia in patients with mechanical ventilation, occurring more than 48 h after endotracheal intubation [49]. VAP is the most frequent nosocomial infection in patients with mechanical ventilation and is associated with longer intensive care unit stay, longer duration of mechanical ventilation, and high morbidity and mortality [4].

### 2.4.1. Diagnosis

Pneumonia is diagnosed by signs and symptoms of respiratory infection and according to criteria for diagnosis of nosocomial pneumonia and VAP. By endotracheal culture, the causative organism is found and an antibiotic is chosen according to the result of culture. The most common organisms are *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Acinetobacter baumannii* [50],

*Serratia marcescens* [51] and methicillin-resistant *Staphylococcus aureus* [52]. Chest radiograph accompanied by clinical and laboratory findings are required for diagnosis of patients with suspected VAP [53].

#### 2.4.2. Treatment

Antibiotics are chosen according to endotracheal secretion culture. For empirical treatment, combination antibiotic therapy is necessary. In this combination, an anti-pseudomonas agent (that is usually effective on other gram negative organisms) such as imipenem, meropenem, piperacillin-tazobactam or cefepime in addition to an aminoglycoside or a quinolone is used. For coverage of Methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin is usually added to this combination. For a special situation such as multidrug-resistant *Acinetobacter* or *Pseudomona*, the appropriate antibiotic (like colistin) is elected according to culture. The rising rates of antimicrobial resistance have led to the routine empiric administration of broad-spectrum antibiotics even when bacterial infection is not documented [52].

#### 2.4.3. Prevention

One important risk factor for developing pneumonia is retained secretion. So, pulmonary toilet is important in these patients. Appropriate positioning and cough assistance can be useful for clearing retained secretions. Sometimes early intubation may be necessary to prevent secretion retaining by frequent suctioning [48]. Using effective oral care with antiseptics is associated with the reduction of the incidence of ventilator-associated pneumonia. Oral care solutions have been widely used to prevent ventilator-associated pneumonia [49]. Routine cleaning and disinfection of ventilators can play an important role in VAP prevention and management approach [53].

### 2.5. Other infections

Blood stream infection secondary to urinary tract infections, pneumonia, pressure ulcers [48], catheter-related bloodstream infections [54], and infections at other sites may occur in SCI patients. Meningitis may occur after penetrating injuries or as a result of CSF leakage at the time of injury or subsequent to surgery [48]. Epidural abscess and subdural empyema can be developed with the same mechanisms. Ventilator-associated tracheobronchitis (VAT) is an infective complication of mechanical ventilation and is a part of the spectrum of ventilator-associated respiratory infections [55].

## 3. Conclusion

Infectious diseases after spinal cord injury are important and should be considered in patients with fever and other signs and symptoms of infections. Appropriate approach, diagnosis, and treatment and surgical interventions, if needed, can be lifesaving and can decrease mortality and morbidity.

## Acknowledgements

With special thanks to Dr. Hadi Niknam, my dear neurosurgeon colleague, and Mrs. Shadi Nasrizadeh Moghaddam.

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