



Course Objectives

The goal of this program is to inform nurses about Stevens-Johnson syndrome and toxic epidermal necrolysis so that they can promptly recognize their symptoms and facilitate timely treatment. After studying the information presented here, you will be able to —

- Describe the difference between Stevens-Johnson syndrome and toxic epidermal necrolysis.
- Identify the signs and symptoms and clinical course of Stevens-Johnson syndrome and toxic epidermal necrolysis.
- List the treatment modalities and supportive interventions necessary to maximize recovery from Stevens-Johnson syndrome and toxic epidermal necrolysis.

Twenty-eight-year-old Sadie Williams* had been taking Bactrim (trimethoprim/sulfamethoxazole), a sulfa-based antibiotic, for a urinary tract infection. After a week, Ms. Williams developed influenzalike symptoms of malaise, headache, lowgrade fever, myalgia, and sore throat, which lasted for three days.

Thinking she had the flu, Ms. Williams did not seek further medical assistance. Two days later, however, she developed a rash with multiple lesions appearing as targets: a bright red inner ring, a light pink middle ring, and a darker pink outer ring. The lesions appeared over her entire trunk, down her arms, and on the palms and dorsum of both hands. The lesions began to blister and grow together, leaving large areas of painful denuded tissue.

Her oral cavity had also ulcerated, causing her such discomfort that she couldn't eat or drink. After a visit to the ED, Ms. Williams was admitted with combined Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN).

Most investigators and clinicians describe SJS/TENS as severe variations of erythema multiforme, a skin disorder caused by a reaction to a drug, infection, or illness. But erythema multiforme generally occurs after a bodily reaction to microbes (particularly the herpes virus)¹ while SJS and TEN tend to occur after a reaction to a medication.

SJS/TEN can cause severe mucosal erosions with widespread erythematous, cutaneous macules, or target lesions that merge together with subsequent epidermal detachment, i.e., detachment of the epidermis from the dermis.¹ With such skin involvement, especially if occurring on the face, some patients with SJS/TEN may experience the shock of their families' not recognizing them.

SJS epidermal detachment involves less than 10% of the total body skin area while TEN involves epidermal detachment of more than 30%. A further category of SJS/TEN has been proposed that includes patients with epidermal detachment between 10% and 30% of total body skin area.^{2,3,4} It's often difficult to diagnose what category a patient may fit in because the exact percentage of epidermal detachment is hard to estimate until all the blisters erupt. Clinicians generally estimate the percentage of epidermal detachment with the Rule of Nines, a method of calculating body surface area using a multiple of nine for body parts, e.g., each arm equals 9% of the body's surface area.⁵

The term Stevens-Johnson syndrome dates from 1922, when two U.S. pediatricians (Albert M. Stevens and Frank C. Johnson) documented dermatological eruptions, mucosal and buccal ulcerations, high fever, and conjunctivitis in two children.⁶ In 1969, another physician wrote about two pediatric cases with "scalded skin" and a massive loss of epidermis due to a staphylococcal infection and called it toxic epidermal necrolysis.⁷

Nurses in all settings should be familiar with SJS/TEN so they can recognize possible symptoms and promote early diagnosis and treatment.

How frequent?

The incidence of SJS has been estimated at one to six 6 cases per million people. The incidence of TEN is between 0.4 and 1.3 cases per million.⁸ Both SJS and TEN tend to occur more often in females, with a ratio of 2:1.^{9,10}

All races and ages appear to be affected. SJS/TEN occur more frequently in infants and children and increase even more significantly in the elderly.¹¹ The incidence may be higher in the elderly because they tend to use more medications.^{11,12}

What causes SJS/TEN?

Drugs are a major etiological factor in both SJS and TEN. The drugs frequently associated with the conditions include:^{10,12-14}

- Sulfonamide antibiotics, e.g., trimethoprim/sulfamethoxazole (Bactrim)
- Other antibiotics, such as the aminopenicillins — amoxicillin (Amoxil) and ampicillin (Omnipen or Principen), and cephalosporins, such as cephalexin (Keflex) and cefazolin (Ancef)
- Anticonvulsants, e.g., phenobarbital (Luminal), phenytoin (Dilantin), and carbamazepine (Tegretol)
- Corticosteroids (Prednisone)
- Nonsteroidal antiinflammatory drugs, e.g., ibuprofen (Advil, Motrin)
- Quinolones, e.g., ciprofloxacin (Cipro)
- Antiretroviral drugs, e.g., nevirapine (Viramune), acyclovir (Zovirax)
- Anti-cancer agents, e.g., topical nitrogen mustard (Mustargen)
- Allopurinol (Aloprim, Zyloprim)
- Cocaine
- Cyclooxygenase-2 inhibitors

Infectious agents have also been reported as a contributing factor in SJS/TEN. The following microorganisms have been associated with SJS/TEN: herpes simplex and influenza viruses, Rickettsia, poxvirus variola, group A beta streptococcus, Corynebacterium diphtheriae, and Salmonella enterica.⁹ In children, the Epstein-Barr virus and enteroviruses — such as coxsackieviruses, hand-foot-and-mouth disease, hepatitis A, and other viruses that live in the intestinal tract that cause nonspecific viral complaints — have been reported as causative agents. In children, SJS often occurs as a result of infections. Adult cases are usually due to drug reactions. In 25% to 50% of cases of SJS/TEN, no cause may be identified.⁹

Patients who undergo organ or bone marrow transplants may also develop SJS/TEN attributable to graft-vs.-host disease and to the many drugs they may have to take. Studies have also found that patients with HIV and systemic lupus erythematosus have an increased susceptibility to SJS/TEN.^{9,14}

The exact pathogenetic mechanism that causes SJS/TEN is unclear. Altered patterns of drug metabolism as well as cell-mediated immunity (overactive immune response) have been suggested as causative factors.⁵ Research has identified the presence of circulating immune complexes (attached antibodies and antigens) that become trapped in the microvasculature of the skin, resulting in massive epidermal damage.¹⁵

What happens when

If the result of an adverse drug reaction, SJS/TEN typically occurs one to three weeks after a patient begins to take the causative drug.¹² A prodromal period of flulike symptoms usually occurs one to three days before the outbreak of the rash. Patients may complain of malaise, sore throat, headache, cough, myalgia, fever, fatigue, rhinitis, nausea, and diarrhea.^{5,12,13} Typically these prodromal flulike symptoms last for two or three days, but they can last up to 14 days.^{12,13} A rash then develops that consists of erythematous macular eruptions, which are often painful and can cause a burning sensation. The eruption begins on the face and upper trunk and quickly spreads to the entire trunk and limbs. The lesions are macular with a dark or dusky center, a raised edematous middle ring, and pale pink outer edges — giving them the appearance of a target.^{2,9,16} The lesions tend to coalesce, creating large blisters.

A hallmark of Stevens-Johnson syndrome and toxic epidermal necrolysis is a positive “Nikolsky’s sign,” in which the epidermis detaches from the dermis in large sheets.^{3,12} The denuded area can look like an extensive burn. The hair follicles tend to be spared from this process; therefore, the scalp is often unaffected.⁴

Mucous membranes (the oral cavity, conjunctiva, and anogenital areas) also become affected early, and 40% of all cases involve all three areas. Ocular damage can be one of the more serious sequelae of Stevens-Johnson syndrome and toxic epidermal necrolysis. Damage can range from dryness and corneal sloughing to permanent blindness in 3% to 10% of patients.⁹ Inflammation, blistering, and ulceration may occur in the oral cavity, vagina, and lower GI tract. Sloughing of the tracheobronchial mucosa may cause respiratory failure. Patients with genitourinary involvement may complain of dysuria and may, in fact, be unable to void.^{9,10,17}

Hypophosphoremia (decreased serum phosphorous) is frequent in SJS/TEN because of fluid losses and can cause altered

glycemic levels and muscular dysfunction if not corrected.⁴ If large areas of the body's surface are involved and the patient is immobile for long periods, thromboembolism can be a risk. The patient may receive heparin while hospitalized.¹⁰ Slight bleeding may occur from the denuded tissues, but it's usually limited.⁴ Patients may receive antacids to reduce the risk of gastric bleeding.¹⁰

A tricky diagnosis

Diagnosing SJS/TEN can be difficult, particularly in milder cases. A skin biopsy and immunofluorescent study (during which antibodies linked to a fluorescent dye are used to study antigens in the tissue) can be helpful if epidermal separation occurs. Subepidermal bullae, infiltration of lymphocytes in the perivascular areas, and epidermal cell necrosis may also occur.^{2,9} Even though a skin biopsy is helpful in determining whether the condition is SJS/TEN, it cannot determine whether it's drug related.

The prognosis of SJS/TEN is largely influenced by the overall body surface involved, the age of the patient (the elderly having a poorer prognosis), the blood urea nitrogen level, and the presence of any comorbidities or visceral involvement.^{4,12} The mortality rate for adults is less than 5% for SJS and about 30% for TEN. Children seem to do better, with a mortality rate of 5% for SJS or TEN.¹¹

Taking action

One of the essential first interventions is to withdraw the offending drug.^{4,11,16} Elimination of any drugs with short half lives significantly reduces the mortality rate, particularly if they are withdrawn before blisters occur.^{4,11} But if drugs are to be stopped at this point, adverse drug reactions must be recognized early.

Nurses often are the first to recognize a cutaneous reaction in patients and must be vigilant in reporting the reaction and ensuring that any new drugs are stopped. Generally, any drug started within the previous month should be withdrawn if a cutaneous reaction occurs.⁸

Treatment must be started swiftly to reduce mortality and morbidity. Many experts maintain that patients with SJS/TEN should receive treatment at burn centers^{4,5} and that early referral to a burn unit can significantly reduce the overall mortality rate.¹⁸

No definite treatment for SJS/TEN exists; treatment tends to be aimed at supportive interventions. However, immediate treatment should involve fluid, nutritional, and airway management and ocular support. Environmental temperature control, aseptic handling, and maintenance of venous access are crucial. Management of pain and anxiety with analgesia and antianxiety agents remains an important adjunct in the overall management.

Even though widespread skin damage may occur, generally only the epidermal surface is destroyed, unlike the process that may occur with burns. Subcutaneous edema tends to be less in Stevens-Johnson syndrome and toxic epidermal necrolysis than in burns, probably because in Stevens-Johnson syndrome and toxic epidermal necrolysis damage is confined to the blood vessels in the epidermal layer.

Even though patients with SJS/TEN may need less fluid replacement than patients with burns do, fluid and electrolyte therapy must be maintained during SJS/TEN management, particularly if large areas are involved. Many patients (particularly children) with oral and GI involvement cannot tolerate an adequate oral intake and can quickly become dehydrated or malnourished. Parenteral or nasogastric supplementation may be necessary for one or two weeks to replace any protein losses and promote cutaneous healing. Oral antiseptic and anaesthetic rinses and analgesia may also help with any discomfort. Viscous lidocaine gels should be applied to oral lesions frequently. Oral and nasal crusting should be gently cleansed daily with normal saline/warm water and soft gauze or cotton-tipped applicators. Saline compresses can also be soothing to edematous eyelids, lips, and nares.⁹

Bronchial involvement is generally associated with a much poorer prognosis as respiratory failure frequently occurs.^{18,19} If severe ulceration of the respiratory tract occurs, mechanical ventilation and intubation may be necessary. Adequate oxygenation, frequent respiratory assessments, postural drainage, and careful suctioning are part of the respiratory care.¹³

Focus on the eyes

Preventing ocular sequelae is critical. Patients should undergo an ophthalmology examination and receive saline or antibiotic eye drops frequently. Some experts suggest gas-permeable contact lenses (rigid contact lenses that allow oxygen to flow through) to help with severe photophobia.⁸ Avoiding direct sunlight and bright room lights and using dark eye patches can

also reduce the discomfort of photophobia.⁵

The use of corticosteroids to treat SJS/TEN is controversial because corticosteroids are among the drugs that can cause the disorders. Corticosteroids may prolong wound healing and increase the risk of infection and GI bleeding.^{4,8,20}

The administration of IV immunoglobulin (IVIG) and immunosuppressive drugs, such as cyclophosphamide (Cytoxan, Neosar) and cyclosporine (Neoral, Sandimmune, Gengraf), also remains controversial although some researchers report favorable outcomes using IVIG. However, reports generally remain highly anecdotal, with few well-randomized control studies so far.^{3,4,10}

The goals for local skin care are prevention of infection and sepsis, moist wound healing, and reduction of pain. Because large areas of skin loss can occur, meticulous, gentle, and aseptic skin care is a must. Gentle saline rinses should be used. Local bacterial and fungal cultures should be taken two or three times per week to closely monitor any pathogenic growth.⁴ Patients also need to be monitored closely for signs and symptoms of sepsis.

Different opinions

The value of debriding, or removing, tissue that is sloughing off remains unclear. Many experts recommend peeling the loose epidermis off.^{17,19} Others maintain it's beneficial to leave the loose epidermis in place to minimize exposed dermis.^{2-4,13} Some clinicians recommend the use of biologic dressings, such as porcine cutaneous xenografts, cryopreserved cutaneous allografts, or collagen-based skin substitutes.¹⁰

Continual moist wound healing is essential, however, to achieve a positive outcome. Gently bathing and removing any crusted material are required, as well. Clinicians differ significantly on what is considered an appropriate solution to cover the denuded areas. Some recommend saline compresses⁹ while others recommend 0.5% silver nitrate compresses¹⁹ or dilute chlorhexidine compresses.¹⁰ But all agree that silver sulphadiazine (Flamazine) should be avoided because its sulpha component is a causative agent of SJS/TEN.²

Dressings should be nonadherent. Other factors to consider when selecting a dressing include the size of the wound and the presence of any exudate. Also check whether the dressing allows cooling to occur, which can cause a chilling effect.

Other comfort measures to consider:

- Minimize time during dressing changes; use assistance, have equipment ready.
- Avoid chilling that may occur when large areas of tissue are exposed. Maintain a slightly elevated temperature in the room; use warm solutions on tissue soaks.
- Use pressure-relief surfaces such as a low-air-loss or air-fluidized mattresses and overlays. Low-air-loss surfaces allow for temperature and moisture control and low interface pressure on damaged tissue. Fluidized surfaces reduce pressure on damaged tissue, but because of high volumes of warm air, they may dry out tissues and dressings.²¹ Fluidized surfaces are particularly helpful if large areas on the back or buttocks are involved.²²
- Provide adequate analgesia before dressing changes.
- Use distraction techniques during dressing changes, such as music or imagery.
- Use silicone dressings, the only true nonstick dressings available. Hydrogel sheet dressings can be used, but caution must be taken because they can have a cooling effect.²³
- Do not place tape on the skin or wrap circumferentially; use tubular net bandages to hold dressings in place.
- Be prepared to secure tubes with items other than typical taping, such as fine mesh gauze tied around an extremity.

With meticulous care, skin lesions should heal within three weeks if there are no secondary sequelae, such as infection.

Nurses cannot ignore the significant and frightening impact Stevens-Johnson syndrome and toxic epidermal necrolysis have on patients and their families. Often rapid deterioration is evident, with patients feeling a spiraling sense of loss of control. Added to the physical pain and discomfort of skin loss, patients may face the emotional pain of not being recognized by their families, particularly if the face is involved. Nurses need to be aware of this and offer reassurance to the patient and family. Postepisodic education about avoiding the causative agent, if known, is also an essential part of care.

**Patient's name has been changed.*

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