Abstract: Non-steroidal anti-inflammatory drugs are commonly prescribed in dental practice after minor oral surgical procedures such as tooth extraction. Diclofenac sodium is one of the non-steroidal anti-inflammatory drugs widely used for pain relief in dentistry. Although adverse reactions to these drugs are rare, at times they can cause a life-threatening phenomenon. Stevens-Johnson syndrome is one such potentially lethal adverse drug reaction. Most reported cases of analgesic-induced Stevens-Johnson syndrome were due to oxicams or propionic acid derivatives. There are very few detailed reports of Stevens-Johnson syndrome due to use of diclofenac. We report here a case of Stevens-Johnson syndrome which occurred due to use of diclofenac sodium. The clinical features of this condition and multidisciplinary management of the patient are described in brief. (J Oral Sci 52, 343-346, 2010)

Keywords: adverse drug reactions; Stevens-Johnson syndrome; diclofenac sodium; corticosteroids.

Introduction
Modern day drug therapy for the control of postoperative pain has made great strides in the recent past. Nevertheless, adverse reactions, although rare, still remain a major threat to the patient welfare. Stevens-Johnson syndrome (SJS) is one such fatal drug reaction. A case of SJS secondary to use of diclofenac for control of post extraction pain is described because it is uncommon. We hope that this report will add to the existing meager body of literature and throw some light on the occurrence and manifestation of this condition.

Case Report
A 45-year-old female patient reported to our institution with complaints of toothache in relation to the left mandibular molar of 7 days duration. The pain was moderate, intermittent in nature, and aggravated on mastication. The patient had not taken any medication for the pain. This was the patient’s second dental visit. Five years earlier she had undergone uneventful extraction. The patient reported no systemic illness, prolonged drug intake, hospitalization or drug allergy. The patient’s family history was also non-contributory.

On examination, vital signs were within the normal limits and no extraoral abnormalities were detected. No abnormalities of the intraoral soft tissues were noted. Hard tissue examination revealed the presence of grossly decayed 36, which was tender on vertical percussion. The patient was therefore advised to undergo extraction of that tooth. Forceps extraction was performed under local anesthesia on a routine outpatient basis. Routine post-extraction instructions were given along with prescription of diclofenac sodium (50-mg tablets) b.i.d. for 3 days.

The patient reported back 6 days later with multiple ulcerations and burning sensation of the oral cavity. On examination, there were multiple ulcerations (Fig. 1) distributed on the right and left buccal mucosa, floor of the mouth and ventral surface of the tongue. These ulcers had a reddish base, irregular borders and measured approximately 5 mm in size. Along with the oral ulcers,
multiple ulcers accompanied by reddish-purple maculopapular and vesicular lesions were noted on the back, forearms (Fig. 2), legs (Fig. 3) and genital area. Ulcerated areas were also noted on the conjunctiva, nasal mucosa and lips. All these features favored a diagnosis of SJS secondary to diclofenac administration (since the patient was not under any other medication). Main differential diagnosis was toxic epidermal necrolysis (TEN), wherein the manifestations would be much more severe and over 30% of the skin surface area would be involved. Eruptions secondary to viral diseases could be ruled out due to the absence of typical prodromal symptoms. She was immediately asked to stop the analgesic and then managed on an inpatient basis. The following medications were subsequently administered: betamethasone (1 ml) intravenously every 12 h for the first 3 days and later pheniramine (2 ml) intramuscularly every 12 h and oral prednisolone (30 mg) for the next week. The patient was examined by a team of specialists including an otolaryngologist, a dermatologist and an ophthalmologist. Topical application of gentamicin drops (0.3%) over the eye and nasal lesions was prescribed. Fusidic acid cream (2%) was applied over the cutaneous lesions and triamcinolone acetonide gel (0.1%) was prescribed for the oral ulcers. Routine blood investigations revealed that the patient was anemic while the urine analysis revealed no abnormalities. The patient’s condition was reviewed on a daily basis and at the end of 1 week there was significant healing of the oral (Fig. 4), cutaneous (Figs. 5 and 6), genital, nasal and eye lesions. The patient was prescribed iron supplements along with oral corticosteroids and was discharged from the hospital. The steroid dose was tapered gradually over
the next 2 weeks.

By the end of the third week, there was no evidence of cutaneous or mucosal ulcers. The patient has since been under continuous surveillance for the past 2 years and has exhibited no signs of recurrence.

**Discussion**

Numerous studies have shown that adverse drug reaction-related hospital admissions comprise up to 10% of the total number of admissions (1). Fortunately, only about 2% of adverse cutaneous reactions are severe and very few are fatal (2).

SJS is a severe adverse drug reaction characterized by widespread lesions affecting the mouth, eyes, pharynx, larynx, esophagus, skin and genitals. It almost invariably involves the oral mucosa. The spectrum of severe cutaneous adverse drug reactions includes SJS or TEN, hypersensitivity syndrome (HSS), anaphylaxis and angioedema, serum sickness, and cutaneous vasculitis (3).

In 1922, Stevens and Johnson described 2 patients, boys aged 7 and 8 years, who had an extraordinary, generalized eruption with continued fever and inflamed buccal mucosa (4). SJS had for years been considered an extreme variant of erythema multiforme (EM), with TEN being a different entity. In 1993, a group of experts proposed a new classification in which SJS was separated from the EM spectrum and added to TEN, thereby creating a new spectrum of severe drug-related diseases (5). The criteria for diagnosis of SJS are epithelial detachment less than 10% of body surface area (BSA) and widespread erythematous or purpuric macules of flat atypical targets. The same criteria were used for the diagnosis of the lesions in the present case. The lesions in our patient had an atypical appearance and epithelial detachment did not exceed 10% BSA.

More than 100 drugs have been associated with the development of SJS/TEN in single case reports or retrospective studies. In a rare prospective case control study, sulfonamides were the most strongly associated with TEN, followed by antibiotic drugs (in descending order of frequency: cephalosporins, quinolones, aminopenicillins, tetracyclines, macrolides), imidazole antifungals, anti-convulsants (phenobarbital, phenytoin, valproic acid, carbamazepine, and lamotrigine), and then non-steroidal anti-inflammatory drugs (especially oxicam), allopurinol, and others (6). Analgesic diclofenac sodium was the causative agent in our case since there was no evidence of intake of any other drug. Diclofenac sodium (50-mg tablets) was administered orally twice daily.

In the oral cavity, SJS causes widespread ulcerative lesions. A prodrome occurs in about 30% of cases and may begin within 1 to 3 weeks of starting a new drug and lasts 1 to 2 weeks before the onset of mucocutaneous manifestations, presenting with flu-like symptoms, sore throat, headache, arthralgias, myalgias, fever, bullous and other rashes, pneumonia, nephritis or myocarditis (7). Ocular changes such as dry eyes and symblepharon that resemble those of mucous membrane pemphigoid may be noted in certain cases. Balanitis, urethritis and vulval ulcers may occur. Our patient did not report any prodrome, but eye and genital ulcerations were present, along with skin and mouth ulcers. Drug-induced SJS is characterized by mucosal erosions plus widespread distribution of atypical targets or purpuric macules and epithelial detachment involving less than 10% BSA on the trunk, face and extremities (8).
SJS has to be clinically differentiated from viral stomatitis, pemphigus, EM, TEN and the sub-epithelial immune blistering disorders like pemphigoid. There are no specific diagnostic tests for SJS (7).

Early diagnosis with the prompt recognition and withdrawal of all potential causative drugs is essential for a favorable outcome. Intravenous fluid replacement must be initiated immediately upon admission using saline solution. Early initiation of massive oral nutrition by nasogastric tube to minimize protein loss promotes healing and decreases the risk of stress-induced ulcers. Corticosteroids have for years been the mainstay therapy for SJS in most cases, as in our case. The popular belief is that they suppress the intensity of reaction, control the extension of the necrolytic process, decrease the involved area, reduce fever and discomfort, and prevent damage to internal organs when given at an early stage and at a sufficiently high dosage (9). Antiseptic or antibiotic eye drops and eye ointments should be liberally used on ocular lesions. Lid-globe adhesions should be cautiously removed with a glass rod twice daily to avoid occlusion of the fornices, taking care not to strip pseudomembranes, which may lead to bleeding and increased conjunctival scarring (10). Topical antiseptics like 0.5% silver nitrate or 0.05% chlorhexidine are usually used for skin lesions to prevent secondary infections. The same treatment protocol was followed in our case with successful results. In severe cases, the patient must be transferred to burn units and measures such as environmental temperature control, careful and aseptic handling, and sterile field creation must be taken. Complications such as thromboembolism and disseminated intravascular coagulation and damage to vital organs such as the kidney deteriorate the prognosis. In our case, no such complications have been reported in a 2-year follow-up period.

References