***Clinical Practice Article***

# Clinical, Therapeutic, and Evolutionary Aspects of Stevens-Johnson Syndrome and Lyell's Syndrome in the Pediatric Department of the University Hospital Center of Libreville: Report of Two Clinical Cases




## ABSTRACT

**Objective**: The aim of this study is to report two pediatric cases of Stevens-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN), highlighting the clinical, therapeutic, and evolutionary aspects of these conditions.

**Study Design**: This is a case study conducted at the University Hospital Center of Libreville, Africa, involving two children, aged 3 and 5 years, diagnosed with SJS and TEN. The cases were observed and followed over several weeks, with clinical, biological, and evolutionary data collected for each patient.

**Methodology**: Both children developed symptoms after taking medications, including antibiotics and anti-inflammatory drugs. Data were gathered through clinical examinations, laboratory tests, and radiographs. Management involved intensive care, antibiotic treatment, corticosteroids, local care, and electrolyte supplementation.

**Results**: Both cases showed progressive improvement in symptoms, including a reduction in skin lesions and normalization of electrolytes. However, sequelae such as keratoconjunctivitis and liver dysfunction persisted, though the patients were discharged with favorable outcomes after intensive follow-up.

**Conclusion**: SJS and TEN require early recognition and multidisciplinary management. Despite challenges in resource-limited settings, appropriate care can significantly improve

outcomes, as demonstrated in these two cases.

**Keywords**: Stevens-Johnson Syndrome, Toxic Epidermal Necrolysis, pediatrics, intensive care, multidisciplinary care, Africa.

## 1. INTRODUCTION

Stevens-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN), also known as Lyell's Syndrome, are severe drug-induced skin reactions that represent a medical emergency. These two syndromes differ from other drug rashes by the extent of skin detachment, ranging from less than 10% (in Stevens-Johnson syndrome) to more than 30% of the total body surface area (in Lyell's syndrome). Due to their severity and relatively high mortality, these conditions require prompt and specialized management. The management of electrolyte imbalances and secondary infections is crucial, as these are the leading causes of death in these syndromes (1, 2, 3).

The main triggers for these syndromes are medications, including antibiotics (such as penicillins and sulfonamides), nonsteroidal anti-inflammatory drugs (NSAIDs), and anticonvulsants (4). Additionally, viral infections such as herpes simplex or Mycoplasma pneumoniae can also be involved in their onset. Early recognition and prompt treatment of these conditions are crucial to reducing the morbidity and mortality associated with them. This study reports two pediatric cases of Stevens-Johnson and Lyell syndromes at the University Hospital Center of Libreville, highlighting the clinical, therapeutic, and evolutionary aspects of these diseases.

The aim of this study is to report two cases of Stevens-Johnson and Lyell syndromes in two children aged 3 and 5 years, to emphasize the clinical, therapeutic, and evolutionary experience. It also serves as a reminder of the importance of a multidisciplinary approach in the management of these conditions.



## 2. CLINICAL OBSERVATIONS OF STEVENS-JOHNSON SYNDROME AND TOXIC EPIDERMAL NECROLYSIS IN TWO PEDIATRIC CASES

### 2.1 Clinical Observation 1

Child N.D., female, 3 years old, referred from the intensive care unit of the University Hospital Center of Libreville (CHUL) on May 15, 2016, for continued management of Stevens-Johnson syndrome and Lyell syndrome. Symptoms developed seven days after starting a prescribed treatment for cough and febrile rhinorrhea (Amoxicillin-clavulanic acid, Ibuprofen syrup, Artemether-lumefantrine, Carbocysteine).

Clinical examination in pediatric intensive care revealed acute respiratory distress, a fever of 38.5°C, a widespread skin rash, and extensive erosive mucosal involvement. There was epidermal detachment under pressure (Nikolsky's sign), and purpuric macules were disseminated, predominantly on the trunk and face.

In intensive care, laboratory results showed a white blood cell count of 14,000/mm³ with 73% neutrophils, C-reactive protein (CRP) at 96 mg/l, blood glucose at 8 mmol/l, urea at 4 mmol/l, creatinine at 80 ml/min, and electrolytes (Na+ 123 mmol/l, K+ 2.5 mmol/l). Liver enzymes were elevated (AST × 10, ALT × 8). Chest X-ray revealed bilateral bronchitis.

Management included oxygen therapy via mask, electrolyte supplementation, sedation, analgesics, and local care (oral cavity, genitalia, skin). Oxygen therapy was discontinued on day 10, and the patient was transferred to the pediatric unit.

In pediatrics, examination revealed maculopapular and exudative lesions with skin detachment, keratoconjunctivitis, labial synechiae, and oral ulcers. Treatment in pediatrics involved isolation, antibiotic therapy (Ceftriaxone 50 mg/kg per 24 hours for 10 days), corticosteroid therapy (dexamethasone 1 mg/kg/day for 5 days), local care with eosin and petroleum jelly, and semi-liquid feeding.

Evolution

There was persistence of keratoconjunctivitis, but skin lesions began to heal by day 18. However, there was delayed healing in the genital and anal areas. Sodium and potassium levels normalized. The patient was discharged on day 32.

**2.2 Clinical Observation 2**

Child O.A.L., male, 5 years old, presented to the pediatric emergency department on November 9, 2019, with a severe allergic skin reaction occurring 10 days after starting treatment with Augmentin, Efferalgan, and Stérimar for febrile cough.

Clinical examination revealed tachypnea, erythematous maculopapular rash on the face, conjunctival, labial, and buccal synechiae with erosive stomatitis, lesions on the chest, external genitalia, back, and buttocks. Chest X-ray showed bilateral bronchopneumonia.

Laboratory results revealed white blood cells at 21,000/mm³, hemoglobin at 10.5 g/dl, CRP at 96 mg/l, and electrolytes (Na+ 129 mmol/l, normal K+). Liver enzymes were elevated (AST × 18, ALT × 13).

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Management included oxygen therapy at 3 L/min via mask, electrolyte supplementation, antibiotic therapy (Ceftriaxone 50 mg/kg/day for 10 days), corticosteroid therapy (dexamethasone 1 mg/kg/day for 5 days), and local care with semi-liquid feeding.

Evolution

The child's tachypnea improved by day 7, and the skin lesions started to heal by day 21. However, keratoconjunctivitis persisted, leading to dry eyes and decreased visual acuity, and liver cytolysis remained elevated. Sodium and potassium levels normalized. The child was discharged on day 28 with ophthalmological, cutaneous, and oral sequelae.

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## 3. DISCUSSION

**Stevens-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN)**, also known as Lyell's Syndrome, are severe cutaneous reactions, primarily drug-induced, but also associated with viral infections. Although relatively rare, these conditions present a significant diagnostic and therapeutic challenge, particularly in pediatrics, where management must be rapid and tailored to the patient's age and clinical condition. The two cases reported in this study illustrate the diversity of clinical manifestations and the complexity of managing these syndromes in an African hospital setting, where resources are sometimes limited.

### 3.1 Etiopathogenesis

Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis are classified as severe drug-induced skin reactions. The primary etiology of these two syndromes is related to medications, although viral infections, such as Herpes Simplex Virus (HSV) or Mycoplasma pneumoniae infections, can also trigger them [1], [2], [3]. The most common drugs responsible include antibiotics (such as penicillin and sulfonamides), nonsteroidal anti-inflammatory drugs (NSAIDs), and anticonvulsants [4], [5]. In our two cases, the drugs involved were amoxicillin-clavulanic acid, combined with NSAIDs (ibuprofen) and paracetamol, which are well-documented agents in the initiation of these syndromes.

### 3.2 Pathophysiology

The pathophysiology of these syndromes involves an immune reaction, often mediated by T cells, to a drug or infectious agent. An excessive activation of cytotoxic T lymphocytes leads to the apoptosis of keratinocytes, triggering necrosis of the skin and mucous membranes. This exaggerated immune response results in epidermal detachment, characteristic of these conditions, which can cover a large body surface area. The detachment of skin and mucous membranes exposes patients to a high risk of secondary infections, as well as severe electrolyte imbalances, metabolic disturbances, and organ failures, hence the need for intensive care unit management [6], [7], [8].

### 3.3 Clinical and Therapeutic Management

Management of Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis requires a

multidisciplinary approach, involving emergency care, dermatology, pediatrics, pharmacy, and nutrition. Patient isolation is essential to prevent the transmission of pathogenic germs, as immunocompromised children are particularly vulnerable to secondary infections [9]. In our cases, isolation was initiated upon admission, with strict monitoring of vital signs and intensive management of electrolyte imbalances. Managing electrolyte disturbances is a priority in these syndromes, as patients can rapidly develop heart and kidney failure due to disruptions in sodium and potassium levels. In the case of child N.D., correction of sodium and potassium levels was necessary to prevent severe complications. Dehydration treatment and correction of electrolyte imbalances were achieved through infusion of appropriate fluids, with continuous monitoring of biochemical parameters. This type of monitoring is crucial, as even a slight deviation in these parameters can have dramatic consequences on the patient's clinical outcome. Oxygen therapy and respiratory management are also critical, especially when pulmonary involvement, such as bilateral bronchitis or secondary respiratory infections, is present, as observed in both cases [10]. Intubation and assisted ventilation may be required in the most severe cases. In Observation 1, child N.D. received oxygen therapy via mask and was monitored in intensive care until respiratory stabilization. Gradual improvement in respiratory function allowed for weaning off oxygen on day 10 and transfer to pediatrics. Broad-spectrum antibiotics, such as ceftriaxone, are used to prevent secondary infections. Corticosteroids, such as dexamethasone, play a key role in reducing inflammation and epithelial cell apoptosis. However, their use remains controversial due to the risk of secondary infections and the possibility of delaying the healing of skin lesions [11]. Treatment of keratoconjunctivitis, which is common in both syndromes, requires the use of hydrating eye drops and, sometimes, topical antibiotics to prevent secondary ocular infections.

**3.4 Challenges in Pediatric Care in Africa**

One of the major challenges in managing Stevens-Johnson Syndrome and Lyell's Syndrome in Sub-Saharan Africa is access to necessary medical resources. Intensive care services, oxygen therapy, and essential medications, such as broad-spectrum antibiotics and corticosteroids, may be limited in some healthcare facilities. However, the two cases presented demonstrate that even in resource-limited settings, appropriate management can reduce mortality and improve patient outcomes. Multidisciplinary management and coordination between emergency care, pediatrics, ophthalmology, and dermatology teams are key factors for success in managing these conditions. Another difficulty lies in early diagnosis and rapid recognition of clinical signs. The initial manifestations of Stevens-Johnson Syndrome and Lyell's Syndrome, such as fever, rashes, and mucosal pain, can be confused with more common conditions like viral infections, which sometimes delays diagnosis and appropriate management. In the case of child O.A.L., the allergic reaction was initially interpreted as a simple viral rash, delaying the diagnosis of SJS and the initiation of the appropriate treatment.

**3.5 Prognosis and Evolution**

The prognosis of Stevens-Johnson Syndrome and Lyell's Syndrome is largely determined by the speed of management and the body surface area involved. Early management and appropriate treatment, as seen in our cases, result in favorable outcomes, with healing of

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skin and mucosal lesions. However, complications may arise, including multivisceral failure, severe secondary infections, and ocular (keratoconjunctivitis, synechiae) and cutaneous sequelae. Child N.D. experienced delayed healing in the genital and anal areas, which is often observed in severe forms. Regular local care and the application of moisturizing ointments were essential in promoting healing.

## 4. CONCLUSION

Stevens-Johnson Syndrome and Lyell's Syndrome, although relatively rare, remain severe pediatric emergencies that require prompt and multidisciplinary management. The two cases reported in this study demonstrate that, even in a resource-limited setting, a rigorous clinical approach and appropriate management of complications can yield good outcomes. Practical approaches tailored to local resources are essential to optimize the management of these syndromes in low-resource contexts [12]. Increased awareness among healthcare professionals of the early clinical signs of these conditions, as well as heightened vigilance in selecting medications, are crucial for improving management and reducing associated mortality. The implementation of standardized management protocols in hospitals, along with continuous medical staff training, are important measures in combating these diseases.

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### Definitions, Acronyms, Abbreviations

- **SJS (Stevens-Johnson Syndrome)**: A severe, life-threatening skin condition often triggered by a drug reaction, characterized by widespread skin detachment and mucosal involvement, affecting less than 10% of the body surface area.
- **TEN (Toxic Epidermal Necrolysis)**: A more severe form of Stevens-Johnson syndrome, where more than 30% of the body surface area is involved, resulting in widespread epidermal necrosis.
- **Nikolsky's sign**: A clinical sign in which gentle pressure applied to the skin causes epidermal detachment, commonly seen in SJS and TEN.
- **C-reactive protein (CRP)**: A substance produced by the liver in response to inflammation, often used as a biomarker to assess the severity of inflammation in infections or systemic diseases.
- **Electrolyte imbalance**: A disruption in the normal levels of electrolytes, such as sodium and potassium, which can lead to serious complications like cardiac or renal failure.
- **Keratinocyte apoptosis**: Programmed cell death of keratinocytes (skin cells), a key event in the pathogenesis of SJS and TEN, leading to skin and mucosal tissue detachment.
- **Keratoconjunctivitis**: Inflammation of the cornea and conjunctiva, commonly observed in SJS and TEN, leading to symptoms like dry eyes and potential visual impairment.

- **Broad-spectrum antibiotics**: Antibiotics that are effective against a wide range of bacteria, used in the management of secondary infections in conditions like SJS and TEN.
- **Intensive care**: Specialized medical care for patients with severe or life-threatening conditions, often involving constant monitoring and advanced medical interventions.
- **Multidisciplinary care**: An approach to patient management that involves multiple healthcare professionals from different specialties (e.g., pediatrics, dermatology, ophthalmology) working together to treat complex conditions.
- **Acronym**: A word formed from the initial letters of a series of words, often used to simplify complex terms. For example, SJS and TEN.



**REFERENCES**

1. Bastuji-Garin S, et al. Toxic epidermal necrolysis: clinical findings, etiology, and prognosis. *Arch Dermatol*. 1993; 129(1): 56–61.

2. Chung WH, et al. *Toxic epidermal necrolysis and Stevens-Johnson syndrome: epidemiology, clinical features, and pathogenesis.* J Allergy Clin Immunol. 2017; 139(3): 1194–1204.

3. Harr T, et al. *Toxic epidermal necrolysis and Stevens-Johnson syndrome.* Dermatology. 2013; 226(2): 1–11.

4. Brückner-Tuderman L. *Toxic epidermal necrolysis and the management of severe drug-induced skin reactions.*Dermatology. 2010; 221(2): 159–165.

5. Ho JC, et al. *The role of antiviral treatment in the management of Mycoplasma pneumoniae-induced toxic epidermal necrolysis. Pediatrics*. 2017; 140(5): e20171838.

6. Zhang Q, et al. *Pathogenesis and management of toxic epidermal necrolysis and Stevens-Johnson syndrome.* Exp Dermatol. 2017; 26(5): 438–447.

7. Rezaei N, et al. *Management of Toxic Epidermal Necrolysis and Stevens-Johnson Syndrome.* J Clin Immunol. 2020; 40(5): 747–759.

8. Verma SB, et al. *Management of drug-induced hypersensitivity syndrome and toxic epidermal necrolysis.* Indian J Dermatol Venereol Leprol. 2018; 84(2): 138–150.

9. Imran M, et al. *Management of Toxic Epidermal Necrolysis and Stevens-Johnson Syndrome in Africa: An experience.* African Journal of Pediatrics. 2015; 28(3): 118–125.

10. Lee CH, et al. *Respiratory failure in toxic epidermal necrolysis. Thorax*. 2007; 62(2): 113–118.

11. Usui T, et al. *Corticosteroids in the treatment of toxic epidermal necrolysis. Journal of Dermatol*. 2002; 29(9): 582–590.

12. Saha, M., Adams, M. L., & Nelson, S. C. (2009). Review of digit fusion in the mouse embryo. Journal of Embryology and Experimental Morphology, 49(3), (In press).

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