PHARMACOVIGILANCE - FDIC NEWS

Vol. 5 no 2, 2012:

Editor's Note

The National Pharmacovigilance Centre (NPC) is committed to sending out quarterly newsletter to it's stakeholders. The objectives of the Newsletter are to disseminate information on Pharmacovigilance activities nationally and globally, to educate stakeholders on drug safety issues, to promote rational use of drugs and to promote spontaneous reporting. This second quarter issue of the newsletter focuses on the reported cases of Steven Johnson's Syndrome (SJS) attributable to the use of medicines in Nigeria.

Drug induced SJS constitutes 1.9% of Individual Case Safety Reports (ICSR) received by the Nigerian National Pharmacovigilance Centre (NPC), through spontaneous reporting system as at May, 2012. Other features in this edition include extracts of adverse drug reaction reports on Steven Johnson's Syndrome and Toxic Epidermal Necrolysis (TEN)as reported in "Reaction Weekly'', Communiqué of the recently concluded Pharmacovigilance Stakeholders Forum and public alert on use of banned drugs.

We encourage Health care Professionals and stakeholders to continue to report all adverse drug reactions. Also your valued comments and acknowledgement of receipt of this issue through our email (nafdac_npc@yahoo.com) would be most appreciated.

Pharm (Mrs) A.I Osakwe
National Coordinator, NPC

STEVENS JOHNSON SYNDROME

Overview

- Definition
- Aetiology
- Incidence And Risk Factors
- Classification
- Clinical Presentation
- Prevention

DEFINITION

Stevens - johnson syndrome is a rare, potentially life-threatening, immune- complex mediated disorder. It is characterized by a cutaneous reaction in which cell death causes the epidermis to separate from the dermis[1] and often It is a medical emergency that often requires hospitalization. It was first described in 1922 when 2 American pediatricians, Albert Mason Stevens and Frank Chambliss Johnson reported the cases of 2 boys ages 7 and 8 years who presented with 'an extraordinary generalized eruption with continued fever, inflamed buccal mucosa and severe purulent conjunctivitis'[2]

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[1] Medscape reference by C Stephen Foster, MD, FACS, FACR, FAAO , Rola Ba-Abbad, MBBS Fellow in Vitreoretinal Division, Department of Ophthalmology, Lund University Hospital, Sweden Sep 23, 2011.

[2] Clinical Classification of cases of Toxic Epidermal Necrolysis; Stevens - Johnson Syndrome and Erythema Multiforme: Batsugi-Garin. S, Stein R.S, Shear N.H, Naldi. L, Rojeau. J.C; Arch. Dermatol. 1993 Jan; 129(1): 92-6.

ETIOLOGY

SJS is an immune-reaction that can be triggered by a variety of factors including;

1. **Infections**- These are usually implicated in most paediatric cases of Stevens - Johnson Syndrome. Examples include Epstein Barr Virus, Mumps, Cat-scratch fever, Hepatitis, Mycoplasma pneumonia.
2. **Medicines-** This is often the most implicated cause. Medicines which can cause SJS include Antibiotics (such as Sulphonamides and Penicillins), Sedatives (such as Barbiturates), Anticonvulsants (such as Phenytoin, Carbamezipine and Valproic Acid), Anti-gout medication(Allopurinol) ,Non-Steroidal Anti-Inflammatory Drugs (NSAIDs including Piroxicam, Meloxicam, Tenoxicam and Ibuprofen), Antiretroviral (Non-nucleoside Reverse Transcriptase Inhibitors such as Nevirapine and certain Drug Combinations e.g. Lamotrigine and Sodium Valproates
3. **Malignancy**
4. **Idiopathic**- This accounts for 25-50% of cases.[3].

INCIDENCE AND RISK FACTORS

Stevens - Johnson Syndrome has a reported incidence of around 2.6 to 6.1 million people per year. Women are more affected than men at a 2:1 ratio.[4] It is more common in adults than in children. However in Nigeria, out of

[3] www.ncbi.nlm.nih.gov/pmc/articles/pmc2813820
The Natural History of Stevens - Johnson Syndrome: Patterns of Chronic Ocular disease and the role of Immunosuppressive therapy: De Rojas M.V, Dart J.K, Saw V.P; Journal Opthamol. Aug.2007; 91(8): 1048-53
[4] www.emedicine .medscape.com/article/1197450_overview

the 10,296 individual case safety reports received at the National Pharmacovigilance centre (NPC) as at May 2012, 200 cases of SJS were reported. This figure may not necessarily present a true picture of the occurrence of SJS locally due to under reporting as such the importance of adverse drug reaction reporting cannot be overemphasized as it gives a true picture or indicator of occurrence of any given ADR.

It is a rare and unpredictable reaction. No test is available to help predict who is at risk. Some factors, however, may increase risk of developing SJS

- Immune-compromised Patients: Patients with viral infections, those undergoing radiotherapy and other diseases that decrease immunity such as HIV, Systemic Lupus Erythematosis (SLE) and chronic inflammatory diseases, have increased risk of developing S.J.S.[5]
- Genetics: Genetic predisposition to drug-induced S.J.S has been found in certain East-Asian populations including the Han Chinese and Thai. Carriage of certain Human Leukocyte Antigens (HLA) such as HLA-B12, HLA-B5801, HLA-B44, HLA-DR7, and HLA-A2 are associated with increased risk.[6]

CLASSIFICATION

Stevens - Johnson Syndrome and Toxic Epidermal Necrolysis (TEN) represent the same disease at different levels of severity. Stevens-Johnson Syndrome consists of epidermal detachment below 10% of the body surface area plus widespread macules or flat layers. It is a milder form of Toxic Epidermal Necrolysis. Toxic Epidermal

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5 www.mayoclinic.com/health/stevens -Johnson-syndrome/DSO0940

6 Stevens - Johnson Syndrome: An intriguing diagnosis.; Tigchelaar H., Kannikeswaran N., and Kamat D.; December 1, 2008

Necrolysis (TEN), on the other hand, consists of epidermal detachment of greater than 30% of Body Surface Area. Both forms of this disease can be very painful and very distressing. Stevens - Johnson Syndrome was previously confused with Erythema Multiforme, a skin disorder which can be caused by an allergic reaction or an infection. It can be also be caused by a reaction to a medication but is more often due to a type 3 hypersensitivity reaction to an infection (most often Herpes Simplex Virus). Erythema Multiforme also differs from SJS due to the character of skin lesions, lack of subjective symptoms, prolonged high fever and terminal heavy crusting.

CLINICAL PRESENTATION:

SJS often begins with a non-specific Upper Respiratory Tract Infection. There is a 1-14 day prodromal fever, sore throat, chills, headache, malaise and athralgia. Following the initial symptoms, patients usually develop a severe skin rash and blistering in the mucous membranes that, if allowed to progress, can become fatal. It is important for someone who has taken the medications, including NSAIDS, to understand the symptoms so they can detect it during the early stages to prevent a progression into a much more severe case.

Symptoms to look out for may include:

- Non-pruritic mucocutaneous lesions, Fever and Involvement of oral and/or mucous membranes may be so severe that patients may be unable to eat or drink.

- Ocular symptoms could also occur which include; Conjuctival hyperaemia (red eye), tearing, dry eye, pain, blephorospasm, itching, grittiness, foreign body sensation, decreased vision, photophobia, burning sensation in the eye, diplopia.[7]

- Stevens - Johnson Syndrome could involve the following sites in addition to the skin; Oral Mucosa ,Oesophagus, Pharynx, Larynx, Anus, Trachea, Vagina, Urethra, Eyes.

Prevention

- Obviously, the best form of prevention would be to avoid taking medicines that cause an allergic reaction, but someone cannot predict a first-time reaction to a medication. It is especially important to avoid taking that particular medicine in the future as a recurrence of an allergic reaction may be much more severe and fatal than the first time the reaction occurred.
- Alert your doctor and any other medical professionals to your drug allergy if you have already experienced an episode of Stevens - Johnson Syndrome.
- Keep a list of all medications known to cause Stevens - Johnson Syndrome. Discuss with your doctor the risks associated with taking these medications in the future.
- Understand the Signs and Symptoms ; It is important for people taking medications that have caused a bad reaction in the past to understand the signs and symptoms of Stevens - Johnson syndrome although there may not be a warning on the medicine's label. [8]

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[7] Episodic Conjuctival Inflammation after Stevens - Johnson Syndrome: Foster C.S, Fong L.P, Azar D., Kenyon K.R; Jour. Opthalmlogy. April 1988; 95 (4)

[8] www.mayoclinic.com/health/stevens -johnson-syndrome/DSO0940

REPORTED CASES OF STEVENS-JOHNSON-SYNDROME IN NPC DATABASE

Table 1: Showing the individual case safety reports received on SJS

DRUG	INDICATION	NO OF ICSRS	CONCOMMITANT	OUTCOME
Nevirapine	HIV	78	Combivir, Cotrimoxazole, Azithromycin, Septrin, lamivudine ,zidovudine, tenofovir , emtricitabine, ciprofloxacin,	Death (2) Life threatening () Hospitalized(2) Resolved(15) Resolving(4) Resolved with disability(2) Unknown(28) Recovered fully (18)
AZT+3TC+NVP	HIV	11	Cotrim Fersolate Multivite Ciprofloxacin Cimetidine protobex	Unknown(7) Resolved(3) Hospitalization (1)
TDF+FTC+NVP	HIV	1		Unknown
Aurobindo (CBV/NVP)	HIV	1	cotimoxaole	-
Efavirenz	HIV	2	Zidovudine 300mg Lamivudine150mg Cotrim	Unknown(2)
Lamivudine/ zidovudine	HIV	2	Flurbiprofen eyedrops Vancomycin	

			Activated methyl polysiloxane Combivir	
Zidovudine	HIV	1	Lamivudine 150mg Efavirenz 600mg Cotrimoxazole 960mg	Unknown
Cotrimoxazole	HIV COUGH Prophylaxis Infection Pneumonia	22 10 5 2 1	Nevirapine Amino fift	Death (5) Life threatening (4) Hospitalized Resolved (3) Resolving Resolving with disability Unknown (2)
Sulfadoxine Pyrimethamine(21)	Fever Malaria Febrile Illness	21	Paracetamol Septrin	Death (2) Life threatening (4) Resolved (3) Uknown (1) Hospitalization Ongoing
Artesunate	Malaria	3	Paracetamol , Piroxicam	Unknown (1) Resolved (1) Ungoing (1)
Artesunate/ Amodiaquine	Malaria	3	Fersolate Augmentin	Hospitalisation(1) Recovered(1)
Artemether/ lumefantrine	Malaise Malaria	1 3	Quinine injection	Unknown Death (2)
Ciprofloxacin	Fever Skin Rash Decompensated CLD	1 1 1	Metronidazole, Lactulose	Unknown (1) Death (1)
Clotrimazole	Prophylaxis	1		Uknown (1)

Tetracycline	Prophylaxis	1		Life threatening (1)
Ampiclox	 Infection Fever	1 1 1	 Seven keys	Resolved (1) Recovered Fully (2)
Cloxacillin	Osteomyelitis	5	Ferrous sulphate tablets, folic acid tablets, Paludrine	Recovered fully (5)
Crystalline Penicillin	Lobar Pneumonia	1	Chloramphenicol, ibuprofen , furosemide	Recovered fully
Erythromycin	Fever Cough Vaginal Discharge/Boil In The Vulvae	1 1	Tramadol piriton	Life threatening (1) Resolved (1) Unknown(1)
Cefuroxime	Fever	1	p-alaxin Septrin	Recovered
Spafloxacin	Cough	1	Vit B Co hematinics	Resolved
Amoxycillin	Malaria	1	Quinine	Hospitalisation
Rifampicin	Tuberculosis	1	Isoniazid, pyrizinamide, ethambutol	Ongoing
Amitryptiline/ Ceftriaxone	Gullain Barre	1	Hydrocortisone Diclofenac Diazepam	Unknown(1
Paracetamol	Pain relief	1	Routine drugs	Recovered with disability
Meloxicam	Lumbar spondylitis	1	Arthotec , Baclofen	Unknown
Tenoxicam	Myalgia	1	Lisinopril, Amlodipine	Recovered fully
Phenytoin	Seizures	2	IV Hydrocortisone	Death(1)

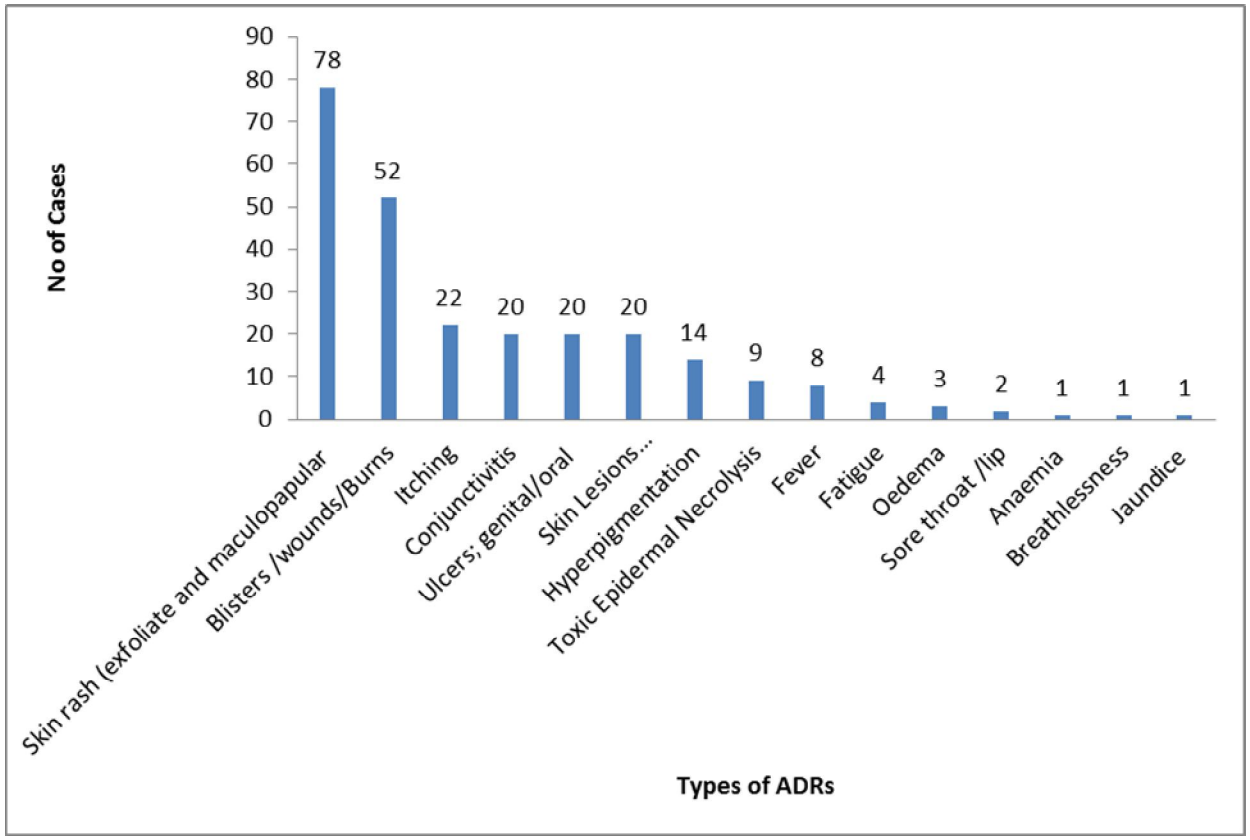
	Post- hernioraphy	1	Artemeter Amoxicillin/cloxacillin Calcium sandoz Methyl phenylate Metronidazole	Life threatening(1) Resolved(1)
Tetanus oxide	Anti-toxin	1	IV Xtaphen IV phenobarb chlorpromazine	Unknown
Herbal Concoction and analgesics	Body pain	1	-	-
Phenobarbitone + Vitamin k injection	Bleeding PV	1	Salbutamol, Paracetamol and diazepam	Hospitalization
Baclofen	Low Back pain	1	Norgesic, Nifedipine ,Vasoprin, Teneoretic	Ongoing
Analgin I.M	Fever and cough	1	Crystalline Penicillin	Recovered Fully
Carbamazepine	Hemifacial Spasm	1	Phenytoin , NA	Recovered

AZT –Zidovudine, 3TC- Lamivudine,NVP- Nevirapine

TDF-Tenofovir , FTC –Emtricitabine, CBV- Combivir

DESCRIPTION OF REPORTED STEVENS - JOHNSON SYNDROME

Of the 200 case reports of SJS , 59 cases were reported as Stevens - Johnson Syndrome without a detailed description of the reaction presented. The other cases were described as a combination of two or more of the signs listed in the fig 1 below:



*Nine cases of Toxic Epidermal Necrolysis (TEN) , 4 of which were reported as both SJS and TEN, were reported to the NPC.

Table 2.0 Showing Number of SJS case reports attributable to individual Medicines as reported in NPC Database

DRUG NAME	NUMBER OF REPORT	PERCENTAGE OF OCCURENCE (N=200)
Nevirapine	91	45.5
Aurobindo	1	0.50

Efavirenz	2	1.00
Lamivudine/Zidovudine	3	1.50
Cotrimoxazole	33	16.50
Sulphadoxine /Pyrimethamine	21	10.50
Artesunate	3	1.50
Artesunate/Amodiaquine	2	1.00
Artemether/Lumefantrine	3	1.50
Ciprofloxacin	3	1.50
Clotrimazole	1	0.50
Tetracycline	1	0.50
Ampiclox	3	1.50
Cloxacillin	5	2.50
Crystalline Penicillin	1	0.50
Erythromycin	2	1.00
Cefuroxime	1	0.50
Spafloxacin	1	0.50
Amoxycillin	1	0.50
Rifampicin	1	0.50
Amityptilline/Ceftriaxone	1	0.50
Paracetamol	1	0.50
Meloxicam	1	0.50
Tenoxicam	1	0.50
Phenytoin	3	1.50
Tetanus Oxide	1	0.50
Herbal Concoction And analgesics	1	0.50
Phenobarbitone+Vitamin K Injection	1	0.50
Baclofen	1	0.50
Analgin I.M	1	0.50
Carbamazipine	1	0.50

Extracts OF SJS/TEN CASE REPORTS AS PUBLISHED IN REACTONS WEEKLY FROM THE UPPSALA MONITORING CENTRE

Amoxicillin/Antiepileptic drugs/ Sulphonamides

Stevens Johnson syndrome: 5 case reports

In a retrospective study, five patients developed Stevens Johnson syndrome (SJS) during treatment with antiepileptic drugs, amoxicillin or sulphonamides *[routes, dosages, therapeutic indications and durations of treatment to reaction onset not stated]*. All patients received supportive care [outcomes not stated]. A summary of the cases is as presented below:

- An 8.4-year-old boy developed SJS during treatment with a Sulphonamide *[specific drug not stated]*. He experienced another episode of SJS 4.6 years later due to a *Mycoplasma* infection, followed by a third episode of unknown etiology 2.3 years later.
- A 14- year old girl developed SJS during treatment with phenytoin. After 1.3-years, she developed a second episode due to lamotrigine.
- A 15-year old boy was receiving treatment with carbamazepine when he developed SJS. Six years later at the age of 21years, he experienced a second episode of SJS during zonisamide therapy.
- An 11.8 year old boy developed SJS during treatment with amoxicillin. After 0.7 years, he developed a second episode due to *Mycoplasma* infection.
- A 14.5 year old girl was receiving treatment with lamotrigine when she developed SJS. A second episode of unknown etiology occurred 0.3 years later.

Author comment: *"Recurrence, especially multiple episodes, of such a rare event… is unlikely coincidental and strongly suggests long-lasting vulnerability and potential genetic predisposition".*

Finkelstein Y, et al. Recurrence and outcomes of Stevens Johnson syndrome and toxic epidermal necrolysis in children. Pediatrics 128:723-728, No. 4, Oct2011. Available from: URL: http://dx.doi.org/10.1542/peds.2010-3322- Canada 803064081

Allopurinol/amoxicillin/clavulanic acid

Toxic epidermal necrolysis treated with ciclosporine: 3 case reports

One man and one woman developed toxic epidermal necrolysis (TEN) during treatment with allopurinol, and a second woman developed TEN while receiving amoxicillin/ clavulanic acid *[dosages not stated; not all routes and times to reaction onset stated]*. All three patients were successfully treated with ciclosporin 3 mg/kg/day in two split doses; ciclosporin was first administered IV, followed by enteral administration after resolution of oropharyngeal lesions.

A 56 year old woman, who had been receiving allopurinol for hyperuricaemia for one month was admitted to an ICU with suspected TEN. She had presented to an emergency room with dyspnoeic crisis and rash on multiple occasions over the preceding 10 days. Her symptoms had initially been treated with corticosteroids, antihistamine and aerosols, but had not resolved. At the time of ICU admission, an erythematous, maculopapular blistering rash affected 70% of her total body surface area (TBSA), including her oropharyngeal mucosa and she also exhibited respiratory failure, renal failure and a tendency for hypotension; Nikolsky's sign was positive. Ciclosporin was started, and she received supportive care. Her condition improved and her skin lesions had re-epithelialized 21 days after ICU admission; she was then returned to a ward.

A 42-year old man was admitted for possible interstitial lung disease 14 days after he started receiving allopurinol for an unknown indication. While in hospital, he developed a rash presenting as polymorphous erythema, and was treated with methylprednisolone. However, his skin lesions worsened and the predominantly squamous lesions affected 65%TBSA, including his oropharyngeal and ocular mucosae. He then developed renal dysfunction, tachycardia and a tendency for hypotension. TEN was suspected and he was admitted to an ICU. Ciclosporin was

administered with good clinical response, and he was discharged 7 days after admission. At that time most of the initial lesions had re-epithelialized, and his mucous membranes had improved.

A 43-year old woman, who had previously been diagnosed with pustular psoriasis and associated erythroderma, ampullary lesions and dysphagia, received an Amoxicillin/Clavulanic acid tablet, and developed erythroderma six hours later; previous psoriasis treatment had included antibiotics, steroids and Ciclosporin. Erythroderma subsequently progressed to generalized ampullary lesions affecting 85%TBSA (including her oropharyngeal and ocular mucosae), and ciclosporin was initiated. Her erythroderma resolved 48 hours after admission, and the affected skin was de-epithelialized. Subtotal re-epithelialization of the initial lesions was observed after 7 days, and she was transferred to a ward.

Carmona AF, et al. Toxic epidermal necrolysis treated with cyclosporin A. Medicina Intensiva 35:442-445, No. 7, Oct2011. Available from: URL: http://dx.doi.org/10.1016/j.medin.2010.09.012 [Spanish; summarised from a translation.] Spain 803062892

Nimesulide

Stevens Johnson syndrome, leading to fatal bronchiolitis obliterans in a child: Case Report

A 5-year old boy developed Stevens-Johnson syndrome (SJS), leading to fatal bronchiolitis obliterans while receiving Nimesulide.

The boy was prescribed oral Nimesulide for a mild upper respiratory illness *[dosage not stated].* Two days later, he developed red eyes and generalised maculopapular rash, associated with a burning sensation. Over the following 2 days, the lesions became vesiculobullous, with a "target lesion" appearance. He was diagnosed with SJS and admitted. He developed a cough and respiratory distress 2 weeks later.

The boy received antibacterials; however, his respiratory distress persisted. Three months after the reaction onset, he was referred to another hospital with an oxygen saturation of 94% on room air. Chest examination revealed bilateral biphasic wheezing and crackles. Imaging analysis led to a diagnosis of bronchiolitis obliterans. He received oxygen, beta-adrenergic receptor agonists, budesonide, prednisolone and azathioprine. However, his respiratory distress persisted and he died 1 year later.

Dogra S, et al. Fatal bronchiolitis obliterans complicating Stevens Johnson syndrome following treatment with nimesulide. A case report. Annuals of Tropical Paediatrics 31:259-261, N0 3, Aug 2011. Available from: URL: http://dx.doi.org/10.1179/1465328111y.0000000019- India
803060789

Oxcarbazepine

Stevens Johnsons Syndrome; case report

A 38-year old woman developed Stevens-Johnsons syndrome (SJS) following treatment with oxcarbazepine for brochial seizure.

The woman was hospitalized with pyrexia, fatigue and sore throat. She was receiving oxcarbazepine 600 mg/day *[route not stated]*, during the first week, to treat bronchial seizure due to parasagittal mass lesion; after three days, her dose was increased to 900 mg/day. Ulcers and lesions located to the mouth, lips and genital area ensued after 10 days of therapy. Two days later, pyrexia in addition to multiple maculopapular rashes affecting her face and neck developed. Blisters subseguently appeared, on her thigh, followed by oral ulcers in addition to hyperaemic conjunctivae. A presumed diagnosis of SJS was made. Tests revealed leucocytosis (WBC count 14 660/µL) with a CRP level of 59.30µg/mL. The results of a skin biopsy were consistent with SJS.

Dexamethasone and antihistamines were initiated. The woman's condition improved and she subsequently returned home. Tests revealed a HLA genotype of HLA-B*1518/B*4001.

Wal P, et al. genetic predisposition to oxcarbazepine induced Stevens - Johnsons syndrome. Indian journal of critical care medicine 15: 173-175, No. 3, Jul - Sep 2011. Available from: http://dx.doi.org/10.4103/0972-5229.84904- India 803063394

Docetaxel

Stevens-Johnson syndrome and atypical keratinocytes: case report

A 56-year old woman developed Stevens-Johnson syndrome while receiving docetaxel. The regenerating epidermis was found to be composed of atypical keratinocytes. The woman, who had been receiving metoclopramide and famotidine, received her first cycle of docetaxel 60mg/m^2 for metastatic breast cancer. She developed a severe skin eruption [*time to reaction onset not stated*]. Examination revealed erythematous and erosive lesions on her trunk and extremities as well as severe erosions on her oral and perianal mucosae. She had

a decreased leucocyte count, a low number of neutrophils and a CRP level of 12.37 mg/dL. Biopsy of a non-erosive lesion showed her epidermis in a regenerating state presumably after a bullous change. Her epidermis consisted of numerous atypical keratinocytes, some of which had a clumping appearance; a moderate lymphocytic perivascular infiltrate and vascular endothelial cell proliferation were observed in the upper dermis. Drug eruption was tentatively diagnosed.

Docetaxel, famotidine and metoclopramide were discontinued, and the woman received Clobetasol and Triamcinolone. Within 7 days, her skin eruption gradually improved; therapy was discontinued. Metoclopramide and Famotidine were restarted without recurrence of her skin eruption. Subsequently, Docetaxel was thought to be causative, and Stevens Johnsons-syndrome caused by docetaxel was diagnosed.

Sawada Y. Docetaxel-induced Stevens Johnson syndrome with regenerating epidermis composed of atypical keratinocytes. Journal of European Academy of Dermatology and Venereology 23: 1333-1335, No.11, Nov 2009 – Japan 801158328

COMMUNIQUE OF THE PHARMACOVIGILANCE STAKEHOLDERS' FORUM HELD AT 3J'S HOTEL, UTAKO, ABUJA ON 23RD APRIL, 2012.

The meeting of pharmacovigilance stakeholders organized by the National Agency for Food and Drugs Administration & Control (NAFDAC) in collaboration with National Malaria Control Programme (NMCP) commenced with an opening ceremony at 9.40 am.

Remarks/ addresses were taken from the Hon. Minister of Health, Prof. Onyebuchi Chukwu, represented by Pharm. (Mrs) Mary Okpeseyi, Chairman Senate Committee on Health, Senator Gyang Daylop Dantong represented by Senator Danladi Zankara, Director General of NAFDAC, Dr Paul Orhii, Pharmaceutical Advisor WHO Nigeria, Dr. Ogori Taylor, Chairman Pharmaceutical Manufacturing Group – Manufacturers'Association of Nigeria (PMG-MAN), Pharm. Bunmi Olaopa, The Ag. Registrar, Pharmacists Council of Nigeria, Mrs Gloria Abumere and DG Consumer Protection Council, Mrs. Ify Umenyi.

Other participants included Chairman and members National Drug Safety Advisory Committee (NDSAC), National President NMA, Dr. Omede Idris and President West African Postgraduate College of Pharmacists (WAPCP), Prof. Fola Tayo. Representatives of professional associations and regulatory councils present included; Nigerian Medical Association(NMA), Pharmaceutical Society of Nigeria (PSN), Association of Medical Laboratory Scientists of Nigeria(AMLSN) and Nursing and Midwifery Council of Nigeria (NMCN) .

Following presentations made, participants agreed that Adverse Drug Reactions (ADR) and other medicine related problems are important issues that should be adequately prioritized in the health care delivery system. Consequently, there is a need for a robust Pharmacovigilance (PV) system to monitor drug safety, detect and manage drug related problems. They also committed themselves to support pharmacovigilance activities in Nigeria in their various capacities.

After extensive deliberations during plenary, the forum resolved as follows:

1. Capacity building programs should be sustained through institutional ownership. This should involve both capacity building and strengthening in pharmacovigilance with knowledge, skills and attitude as objectives.
2. The National Pharmacovigilance Centre (NPC) should ensure adequate feedback to reporters as this is important in sustaining enthusiasm of practitioners to continue reporting.
3. Reporters should ensure that the Individual Case Safety Report (ICSR) tool is adequately completed to meet the specified minimum requirements of the NPC.
4. Institutions are encouraged to establish pharmacovigilance centres with operational committees.
5. Pharmacovigilance messages should be reconfigured to include drama, jingles etc for effective communication to the target audience.

6. Prescribing and dispensing should be done in compliance with existing drug laws with regards to drug identity and appropriate labelling. Also, there should be full disclosure of possible Adverse Drug Reactions (ADRs) as this would go a long way to encourage patients' compliance.
7. Patent and Proprietary Medicine Vendors (PPMVs) are to be encouraged to adequately key into the pharmacovigilance system in Nigeria.
8. There is need for curriculum revision to incorporate pharmacovigilance in health training programs at university and professional levels. Also, pharmacovigilance should be incorporated into continuing professional education programs of all relevant health care professions.
9. Internet based information technology should be used to send pharmacovigilance messages to the public.
10. The forum called upon NAFDAC to strengthen regulation of production, advertisement and distribution of herbal medicine and related products. Also, the use of herbal medicines should be put into cognisance by health care providers when monitoring for adverse drug reactions.
11. The Forum advocated regular stakeholders meeting to address emerging issues.
12. The pharmaceutical industry should be proactive on Pharmacovigilance issues.

In conclusion, participants generally commended NAFDAC for her present role in ensuring the safe use of medicines in Nigeria and advocated for strengthened post marketing surveillance system in the country.

Signed:

Dr Paul Orhii	**Prof. A. O. Isah**	**Prof. Fola Tayo**
DG-NAFDAC	Chairman, NDSAC	Chairman, Technical Session

Active Substance	Product Name	Description of Action Taken, Grounds for Decision	Year Action Taken in Nigeria

PUBLIC ALERT ON THE CONTINUED USE OF BANNED PRODUCTS

It has come to the attention of the National Agency for Food and Drug Administration and Control, NAFDAC that some hospitals and practitioners continue to stock and use Gentamycin 280mg which was banned in 2009. This action was as result of documented safety data associating the use of high dose, single unit Gentamycin 280mg injection with ototoxicity, impaired hearing, deafness, nephrotoxicity, increase incidence of endotoxin reactions (anaphylactic shock), haemorrhage, fibrinolysis, hypotension, inflammation, vascular coagulation and deaths.

We hereby use this medium to "**Alert**" the general public on the continued use and distribution of Gentamycin 280mg and other banned products and request that anyone with useful information on their source and distribution in Nigeria should report to the nearest NAFDAC office.

Hospitals, Pharmacies and other outlets still stocking these banned products are hereby advised to surrender them to the nearest NAFDAC office for destruction. Furthermore, the general public is advised to patronise registered hospitals/ pharmacies and also encouraged to report any adverse drug reaction to their source of the medicine and NAFDAC promptly.

We appeal to healthcare providers to desist from the unethical practice of stocking, distributing, prescribing and administering banned medicinal products. We intend to collaborate with professional regulatory councils of healthcare providers in meting out sanctions to persons or groups found contravening these directives including prosecution in accordance with the dictates of the law.

For avoidance of doubt, the Agency wishes to bring to the attention of the healthcare providers and the general public the list of other banned products in the country.

Rosiglitazone	All Brands	NAFDAC directed Marketing Authorization Holder in Nigeria to voluntarily withdraw product from circulation in Nigeria within 6 months. Total recall to be effected by June 2012. Agency to carryout mop up of products remaining in circulation by June 2012. Risk of congestive Heart failure	2011
Gentamycin 280mg	All Brands	Deregistration of 280mg and mop up from circulation. Public Alert on action taken. Increased risk of ototoxicity and nephrotoxicity and increased risk of endotoxin reactions	2010
Teething mixture	All Brands	Deregistration and ban of all teething mixture in circulation in Nigeria. Low benefit/risk ratio	2009
Nimesulide	All brands	Restriction of registration of product due to report on liver toxicity. Product had no obvious advantage over existing NSAID that are already in the market.	2005
Dipyrone	All brands	Ban due to serious ADR's reported. E.g. tense (Toxic epidermal necrolysis).	2005
Chlorproguanil-Dapsone	(Lapdap®)	Voluntary withdrawal by NAFDAC and GSK. Haemolytic Anaemia	2005
Phenylpropanolamine	All brands	Ban of cough and cold remedies containing this active, directives from the agency for replacement of actives with the sympathomimetic agents.	2003
Mercury Containing Creams and Soap	All Brands	Ban on creams and soap containing mercury. Cause dermatitis, cumulative toxicity causes damage to kidneys which could manifest as hypertension and fatal kidney failure.	2002
Creams Containing Hydroquinone >2%	All Brands	Ban on creams containing Hydroquinone >2%. Exogenous ochronosis which manifests as a dirty brown pigmentation on sun exposed areas, loss of skin elasticity.	2002
Cosmetic Products Containing Corticosteroids	All Brands	Ban on cosmetic products containing corticosteroids. Prolonged use on the skin causes recalcitrant acne, red straie, excessive hairiness, proneness to infections (bacterial, fungal and parasitic). Absorption through the skin could manifest as severe hypertension, diabetes and cataract.	2002
Potassium Bromate as Dough Improvers/Ingredients in flour & Bread Improvers	All Brands	Banned and removed from the list of permitted food additives. Decomposes Vit A, B, B_2 and E. Implicated in kidney failure and hearing loss.	2002
Phenylbutazone	All Brands	Ban on use in human due to agranulocytosis	2002

Signed: Management

NAFDAC: Safeguarding the Health of the Nation

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