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Management and Treatment of Pruritus

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ABSTRACT

Pruritus, or itch, is a common sensation that causes a person to want to scratch. It is a complex process that may negatively impact quality of life and commonly occurs with skin disorders such as atopic dermatitis and urticaria. It could also be a symptom related to an underlying disease process such as cholestasis or hyperthyroidism, or simply be caused by dry skin, especially in the cold, winter months. Therapy is often aimed at eliminating the underlying cause first, followed by the management of the itchy sensation. Treatment may include prescription and over-the-counter (OTC) medications, herbal remedies, hydrotherapy, phototherapy, and ultraviolet therapy. This overview provides information regarding the various management and treatment options for pruritus.

Key Words: *pruritus, itch, urticaria*

Pathophysiology of Pruritus

Pruritus is a complex process that involves the stimulation of free nerve endings found superficially in the skin. The sensation of pruritus is transmitted through the C-fibers in the skin to the dorsal horn of the spinal cord, and then, via the spinothalamic tract to the cerebral cortex for processing. Many chemicals have been found to be pruritogenic, therefore causing the itch sensation, including histamine, serotonin, cytokines, and opioids. There are six categories of pruritus: dermatologic, systemic, neurogenic, psychogenic, mixed, and other. Various treatment and management options exist depending on the category or cause.[1]

Treatment

Treatment of pruritus can be categorized in several ways. A common method of grouping the various options is causative vs. symptomatic treatment. Causative treatment involves finding the underlying disorder and then correcting it, thereby eliminating the itch sensation. Symptomatic treatment involves substituting another sensation for the itch, using methods such as cooling, heating, or counter irritation (e.g., scratching). Symptomatic treatment can be used in addition to treating the underlying disease process in order to provide earlier relief. Most of the available treatment options are categorized under symptomatic therapy and management.

Prescription Medications

Prescription medications include topical and systemic antihistamines, corticosteroids, local anesthetics, and topical immunomodulators, among others. Some lower concentration preparations of these medications are available OTC.

Antihistamines

Itching occurs when histamine is released, causing redness, swelling, warmth, and consequently itchiness. Antihistamines, or H1 antagonists, act by blocking the histamines, and are the most widely used medications for this condition. They take approximately 15–30 minutes to be effective and can be short- or long-acting.[2]

Topical antihistamines are available in prescription as well as nonprescription forms. Camphor (Caladryl®, Pfizer) is a common diphenhydramine preparation that has both antipruritic and anesthetic properties. This traditional therapy carries with it a small risk of contact dermatitis and allergic sensitization.[3]

Doxepin, a dibenzoxepin tricyclic compound, is a very active antihistamine that can be used for atopic dermatitis (AD) and also has a useful psychotherapeutic effect for pruritic patients. It acts by depressing cutaneous sensory receptors.[4] The starting dose is 25–50mg, taken orally at bedtime. Doxepin cream 5% may be applied q.i.d. Some side-effects of this medication include drowsiness and localized burning or stinging, which are usually transient. Findings in a placebo-controlled, double-blind trial have confirmed the effectiveness of doxepin in the relief of pruritus caused by AD.[5] In another study by Drake et al., topically applied doxepin was again found to be a safe and effective treatment for pruritus.[5] Berberian et al. conducted a double-blind, controlled study that yielded similar results in which topical doxepin was added to topical hydrocortisone or topical triamcinolone resulting in a significantly faster and more substantial reduction in itching than corticosteroid alone, and a more prompt resolution of underlying AD.[6]

Hydroxyzine hydrochloride 25mg, po, t.i.d. or q.i.d., or diphenhydramine 25–50mg, po, may be given at bedtime when pruritus is usually at its worst.

Systemic antihistamines are effective in treating some, but not all causes of pruritus, for example, their role in treating AD is limited. They can provide some level of sedation, which may assist sleep, but may also carry with it the adverse effects of unwanted sedation and other anticholinergic properties such as dry mouth, gastrointestinal upset, stomach pain, nausea, and headache. This can be prevented by using nonsedating antihistamines such as fexofenadine (Allegra®, Aventis Pharmaceuticals).

Several low-sedating antihistamines have become available in the last decade. These newer antihistamines, such as loratadine (Claritin®, Schering Canada), block histamine receptors and prevent the activation of cells by histamine, thus preventing an allergic response. Unlike the traditional antihistamines, loratadine, desloratidine (Clarinex®, Schering-Plough; Aerius®, Schering Canada), and cetirizine (Zyrtec®, Pfizer) do not cross the blood-brain barrier and, therefore, do not cause drowsiness. However, these medications have had limited success in the treatment of pruritus.[4]

Corticosteroids

Corticosteroid medications are derivatives of the natural hormones produced by the adrenal glands and have many functions including the control of inflammatory responses. Topical formulations are applied to the skin and typically used for localized pruritus such as dermatitis. Low potency preparations are available without a prescription. This class of medications has proven to be successful in the treatment of pruritus for many years by reducing skin inflammation, thus reducing the itching. Corticosteroids seldom alleviate generalized pruritus without dermatitis, but may rarely be helpful if used with lubricants in elderly patients with dry skin. Corticosteroid creams or ointments applied t.i.d. as maintenance therapy are most effective, especially for AD. Emollients, such as white petrolatum, hydrogenated vegetable oil, or hydrophilic petrolatum may be used as a supplement between corticosteroid applications to help hydrate the skin. Corticosteroids should not be used for prolonged periods because of the risk for skin atrophy.[4]

Oral corticosteroids, such as prednisone, should be considered a last resort, but if given, are best used in 1–2 week courses. Alternate-day use of this drug at 20–40mg every other morning may help to reduce side-effects.[4]

Local Anesthetics

Topical anesthetics work by directly interfering with the transmission of impulses along the sensory nerve fibers or by depressing cutaneous sensory receptors. Those drugs that interfere with transmission include benzocaine, diperodon, and lidocaine.[7] Hercogova suggested that caine-based anesthetics should be avoided due to risk of sensitization, but lotions or creams containing 0.25% – 0.5% menthol can be useful.[4]

Pramoxine, another topical anesthetic, has a documented antipruritic effect and is most useful for mild-to-moderate pruritus. It may be combined with coolants, such as menthol, to increase its effectiveness.[8] One study demonstrated that both the magnitude and duration of histamine-induced itch were reduced by pramoxine.[9]

Capsaicin, the active ingredient in cayenne and red pepper, owes its antipruritic properties to the desensitization of nociceptive nerve endings responsible for transmitting the itch sensation. It is useful at concentrations of 0.025–0.075% in localized intractable pruritus,[10] but may cause localized burning and stinging which can limit its use and reduce compliance in patients. This irritation will subside with repeated use of the medication if the patient chooses to overcome the initial irritations.[8]

Calcineurin Inhibitors

Topical calcineurin inhibitors pimecrolimus (Elidel® Cream 1%, Novartis) and tacrolimus (Protopic® Ointment, Astellas) possess anti-itch properties and, similar to corticosteroids, they reduce skin inflammation. However, they have a different mechanism of action and, thus, are not associated with the same adverse effects. Calcineurin inhibitors prevent T-cell activation, inhibit inflammatory cytokine release, and down-regulate high affinity immunoglobulin E receptor expression on the Langerhans' cells.[11] They are second-line therapies indicated for short-term and non-continuous chronic treatment of mild-to-moderate AD in non-immunocompromised people ages 2 and older who have failed to respond adequately to other topical prescription treatments or when those treatments are not advisable.

Pimecrolimus is an ascomycin macrolactam. It shows activity not only against T-cell activation, but also against mast cells and pruritus. In a study of real-life usage by Lubbe et al., incorporation of 1% pimecrolimus cream into patients' standard treatment regimen was well tolerated and improved AD in approximately two-thirds of patients.[12]

Tacrolimus is a macrolide lactone isolated from Streptomyces tsukubaensis. The release of cytokines, such as interleukins 4 and 5, are inhibited by this drug.[13] A study by Drake, et al. demonstrated that topical tacrolimus ointment was associated with significant quality of life benefits in adult and pediatric patients with AD.[14]

There is concern about continuous long-term use of calcineurin inhibitors, because of the risk of cancer development. This is based on the FDA's public health advisory regarding information from animal studies, as well as case reports in a small number of patients. The FDA has received reports of lymphoma and skin cancer in children and adults treated with these drugs, however it has not been clearly established whether the reported cancers are associated with direct use of these products.[15] Based on these findings, we suggest caution in prescribing these drugs for long-term use. Application should be limited to areas of the skin affected by AD.

Calcineurin inhibitors are not indicated for use in children <2 years of age, and for tacrolimus, only 0.03% b.i.d. should be used in 2–15 year olds. In adults, tacrolimus ointment should be applied to the skin as a 0.03% or 0.1% ointment b.i.d., and discontinued following resolution of symptoms. If symptoms persist beyond 6 weeks, the patient should be re-examined and the diagnosis confirmed.[4]

Cholestyramine

Pruritus is a common and sometimes disabling manifestation of cholestasis. Cholestyramine is a nonabsorbable, basic polystyrene that serves as an anion exchange resin binding bile salts in the gut lumen. It is effective in a large proportion of cases of cholestasis-related pruritus. The resin depletes the serum bile salt pool, and has a greater affinity for dihydroxy bile salts than for trihydroxy bile salts. Cholestyramine also has complex effects on absorption of a variety of compounds other than bile salts, and it has been reported to improve pruritus in polycythemia rubra vera and uremia. Side-effects are mild, but common, and include constipation, fat malabsorption, and an unpleasant taste. These side-effects may make compliance an issue.[16]

Rifampicin

Rifampicin is an antibiotic that has also been shown to lower hepatocyte bile salt concentrations by competing for the uptake of these salts into the hepatocyte. In one study, pruritus disappeared in 11 of 14 subjects receiving rifampicin 600mg/day and three experienced partial improvement.[16]

Naltrexone

Naltrexone, an opiate receptor antagonist, was studied in a randomized, double-blind, placebo-controlled trial to assess the antipruritic effects in patients with chronic cholestatic liver disease. The investigators found that oral naltrexone may be an effective and well-tolerated alternative for pruritus, refractory to regular antipruritic therapy. In this study, five of eight patients treated had considerably less itching.[17] In another study, nine out of 20 patients receiving naltrexone had >50% improvement of pruritus. Side-effects in this study, including dizziness, nausea, vomiting, headache, drowsiness, dry mouth, and cramps, were transient and did not require specific treatment.[18]

Ultraviolet (UV) Light Therapy

UV phototherapy is used to treat various pruritic conditions including chronic renal failure; AD; HIV; aquagenic pruritus; solar, chronic, and idiopathic urticaria; urticaria pigmentosa; polycythemia vera; pruritic folliculitis of pregnancy; breast carcinoma skin infiltration; Hodgkin's lymphoma; chronic liver disease; and acquired perforating dermatoses, among others. It is often undertaken after multiple attempts to treat stubborn itch, and can offer relief without many of the side-effects and risks of systemic medications. UV-based therapy utilizes UVB and UVA in both broadband and narrowband, as well as PUVA (psoralen UVA). Cost and side-effects can be a prohibitive factor for patients. Erythema is common in UVB, as is premature aging and photocarcinogenesis with both UVA and UVB. Side-effects associated with PUVA include redness, burning, headache, and nausea.[16,19]

UVA, UVB, and PUVA light therapies have been especially useful in the treatment of pruritus in HIV patients, as well as in those patients with systemic mastocytosis and cutaneous T-cell lymphoma. It localizes the effect on the

superficial nerve endings, sparing the remaining helper cells, and relieving the pruritus. Because of its more superficial penetration, UVB is believed to be safer than UVA. UVB also spares the remaining helper cells in HIV patients and may localize the effect on the superficial nerve endings, thus relieving pruritus. Systemic mastocytosis and cutaneous T-cell lymphoma also respond to UV therapy and because destruction of the proliferating CD4 clone is desirable, UVA is usually the preferred modality over UVB, although Millikan suggests that the relief of pruritus is more predictable with UVB than with UVA.[3]

Cutaneous Field Stimulation (CFS)

CFS, which electrically stimulates thin afferent fibers, including nocireceptive C-fibers, was reported to inhibit histamine-induced itching. The reduction in itching is accompanied by degeneration of the epidermal nerve fibers. In one open trial, localized itching responded to CFS treatment, and pruritus was reduced by 49% at the end of 5 weeks. Itch relapsed gradually after the discontinuation of CFS, which led the researchers to conclude that nerve fibers regenerated into the epidermis.[20]

Over-the-Counter Treatments

In addition to the nonprescription medications mentioned above, there are other OTC treatments that can be helpful for treating and managing pruritus. Moisturizing after a bath is extremely important, and emollients such as white petrolatum, or petrolatum depositing moisturizing body washes, and in-shower moisturizers (e.g., Olay® Ribbons®, Procter & Gamble; emulsifying ointment USP) can be helpful when applied while the skin is still wet.[21]

There is new evidence to show that moisturizers containing niacinamide and glycerin (e.g., Olay® Quench®, Procter & Gamble) not only hydrate the skin, but improve the skin's resistance to external factors and improve the barrier function. Glycerin is required for moisturizers to work quickly and add moisture to the skin, but the niacinamide helps to sustain that benefit over a longer period of time.[21]

Alternative Therapies

Several alternatives to traditional treatment of pruritus have been proposed. Often these therapies can be used in conjunction with prescribed or OTC medications to relieve symptoms quickly. Compounds that have been found to be effective for pruritus by depressing cutaneous sensory receptors include menthol, camphor, and phenol.[7] Some other alternative therapies that have been suggested include herbal remedies, nutritional therapy, reflex therapy, and hydrotherapy.[3]

Location	Potential Causes of Itch
Eyes, eyelids	• Allergic blepharitis • Allergic conjunctivitis • Atopic dermatitis • Allergic contact dermatitis
Nose	• Allergic rhinitis
Arm	• Brachioradial pruritus (lateral) • Xerotic eczema • Eczematous dermatitis (antecubital)
Trunk	• Scabies • Allergic contact dermatitis
Hands	• Dyshidrotic eczema (pompholyx) • Allergic contact dermatitis • Scabies (web spaces)
Groin	• Tinea cruris • Erythrasma • Allergic contact dermatitis • Intertrigo • Pediculosis • Scabies
Feet	• Tinea pedis • Eczematous dermatitis • Allergic contact dermatitis • Scabies
Legs	• Xerotic eczema (shin) • Neurodermatitis • Stasis dermatitis • Atopic dermatitis (popliteal fossa) • Lichen simplex (lateral malleolus) • Dermatitis herpetiformis (knee)
Scalp	• Pediculosis • Psoriasis • Seborrheic dermatitis • Allergic contact dermatitis • Folliculitis
Ear Canal	• Otomycosis • Otitis externa (early) • Allergic contact dermatitis • Seborrheic dermatitis • Psoriasis
Back	• Notalgia paresthetica • Xerosis • Psoriasis • Folliculitis
Anus	• Pruritus ani • Anal fissure • Condyloma acuminatum • Pinworms

Table 1: Causes and Location of Pruritus [22]

Herbal Remedies

Several herbs have been proposed as corticosteroid-sparing agents and may provide a viable alternative to topical steroids and their side-effects. Oatmeal baths appear to be most useful because of its colloidal protein and high mucilaginous content. Other herbs have been suggested because of their high mucilage content as well, including flax, fenugreek, English plantain, hearts ease, marshmallow, mulberry, mullein, and slippery elm.[3] More extensive research needs to be conducted regarding their possible use and effectiveness for the treatment of pruritus.

Tannins, also derived from herbs, may be helpful as well. The exact mechanism of action is unclear, but may perhaps be related to the coagulation of proteins in the skin. The most common tannin-containing herb is witch hazel, but others include oak bar, English walnut leaf, goldenrod, Labrador tea, lady's mantel, lavender, and St. John's wort.

Other possible herbs that may be advantageous include chamomile, which has shown to be equivalent to low concentrations of hydrocortisone, aloe vera, and capsaicin.[3] Some side-effects may include irritant or allergic contact dermatitis. Some herbals can be toxic if ingested as well. Some of the oldest group of medications used to soothe and cool pruritic skin is menthol and camphor, which are both considered low risk and safe to use topically. [3,4]

Nutritional Therapy

Nutritional therapy, despite not being sufficiently researched as a monotherapy for pruritus, may be helpful in combination with other anti-itch treatments. Vitamins D and E, and linolenic acid have shown some efficacy in the treatment of psoriasis and atopic eczema.[3]

Reflex Therapy, Acupuncture, and Hydrotherapy

While they are not traditionally used, reflex therapy, acupuncture, and hydrotherapy are three treatments that may be beneficial as adjunctive therapy, however further research is needed. There is little research available regarding the effectiveness of reflex therapy and hydrotherapy. These options may be considered in difficult-to-treat patients where traditional approaches have been unsuccessful. Acupuncture is based on the gate theory of neurotransmission, however it is infrequently used in the Western world, and therefore has insufficient evidence to fully support its use. [3]

Management

The management of symptoms is paramount in the treatment of pruritus. Patients should be educated regarding the self-care aspects of this condition. Eliminating the use of irritating or tight clothing is recommended, as well as maintaining a cool environment. Patients should avoid the frequent use of soap, topical irritants in clothing, dry environments, and vasodilators such as caffeine, alcohol, and hot water. Patients should be advised to take brief, tepid or lukewarm baths using mild cleansers with a low pH. Soap film should be rinsed off completely and skin should be patted lightly, followed by the generous application of a moisturizing lotion or cream.[4,7,22]

Conclusion

Pruritus is a common complaint, but one that can often be a challenge to treat. It can be a major quality of life issue for patients, so it is important that both the underlying disease and associated symptoms are treated as quickly and effectively as possible. Health teaching regarding the prevention and management of pruritus should be included in the overall treatment of the cause and symptoms.

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IVIG for the Treatment of Toxic Epidermal Necrolysis

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ABSTRACT

Intravenous immunoglobulin (IVIG) has been proposed as a treatment for toxic epidermal necrolysis (TEN) and Stevens-Johnson Syndrome (SJS). A number of retrospective and prospective studies have been conducted, with varying levels of evidence for the efficacy of IVIG. Recent publications provide opposing conclusions. A multi-center, comparative, long-term analysis needs to be conducted to determine the role of IVIG in the management of patients with SJS/TEN.

Key Words: *Intravenous immunoglobulin, IVIG, toxic epidermal necrolysis, TEN, Stevens-Johnson Syndrome, SJS*

The terms erythema multiforme (EM), Stevens-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN) have become entangled and confusing over time. Current concepts support EM as a specific disease that is different from the SJS/TEN spectrum. SJS and TEN represent different degrees of a severe, acute mucocutaneous reaction that often can be caused by drugs.[1] TEN or SJS is diagnosed objectively according to a consensus-derived definition.[2] The differentiation between SJS and TEN is determined based on the percentage of body surface area (BSA) affected: SJS is characterized by mucous membrane erosions and blisters on less than 10% of the total BSA, whereas TEN involves more than 30% of the total BSA.[2] Important prognostic factors for SJS/TEN include the percentage loss of BSA, age, heart rate, cancer/hematologic malignancy, urea, bicarbonate, and glucose serum levels.[3]

Clinical Features

SJS/TEN is most commonly characterized by skin changes (scattered 2-ring target-like lesions with a dark red centre and lighter red halo, red macules with central blistering that can coalesce to larger areas of denuded skin), hemorrhagic mucositis (mouth, eyes, genitals, and respiratory tract), and systemic symptoms (fever, malaise, possible internal organ involvement).[1] In severe TEN cases, fingernails and toenails, eyebrows and cilia may be lost as well. There may be extensive involvement of the gastrointestinal tract and respiratory tract. Sepsis and respiratory distress are the most common complications and ultimately the direct causes of death.

Survivors of SJS/TEN may experience numerous long-term sequelae; the most disabling are those involving the eyes. Cicatrization of conjunctival erosions may lead to inverted eyelashes, photophobia, burning sensation in the eyes, watery eyes, a siccalike syndrome, and corneal and conjunctival neovascularization. As many as 40% of survivors of TEN have residual, potentially disabling lesions on the eye and/or surrounding area, that may cause blindness.

Epidemiology

TEN affects between 0.4–1.2 cases per million people every year.[4-7] SJS is seen more frequently, affecting 1–6 cases per million people every year.[5,7] SJS may prove fatal in approximately 5% of patients. Prognosis is worse in TEN, where there is more epidermal sloughing which increases the severity of the condition with mortality rates ranging from 20%–40% for extensive sloughing.

Pathogenesis

The pathogenesis of drug-induced SJS/TEN is unknown, although several theories have been developed. Reactive metabolites of oxidative drug metabolism have been shown to lead to covalent binding that can stimulate an immune response. For some drugs there have been clear associations with HLA-B haplotypes in specific populations.[8,9] Epidermal death is due in part to apoptosis that is triggered by a death signal (Fas-ligand) and *in vitro* antibodies to Fas-ligand can block the process.

Drug-related SJS/TEN

Many cases of SJS/TEN are related to drug exposure. The drugs most frequently cited as causes of SJS and TEN are anticonvulsants, antibiotics (especially sulfonamides), allopurinol, and NSAIDs (e.g., piroxicam).[4] Other causes, especially for SJS, include infections, neoplasia, and autoimmune diseases.

Treatment of SJS/TEN

There is currently no specific treatment for TEN and SJS.[10] Discontinuation of the suspected drug is the first step in the management of these patients, with supportive care

(e.g., wound care, hydration, and nutritional support) forming the basis of treatment. Immunosuppressives (e.g., cyclosporin, cyclophosphamide) are often recommended,[10] although the use of corticosteroids in SJS and TEN remains controversial. Other therapeutic modalities that have been attempted include hyperbaric oxygen,[11] granulocyte colony stimulating factor,[12-14] and plasmapheresis.[15]

Intravenous immunoglobulin therapy (IVIG) may improve outcomes and reduce mortality and morbidity in this population. Considered by many clinicians as a treatment option, it is produced from the plasma of thousands of healthy blood donors. The pooled plasma is fractionated and purified to produce a final product containing predominantly IgG (90%–98%) as well as traces of IgA, IgM, CD4, CD8, HLA molecules and cytokines.[16] Albumin also appears in IVIG in quantities ranging from trace amounts to 3000µg/mL.[17-19]

A number of retrospective and prospective studies have been conducted to examine the efficacy and safety of IVIG in SJS/TEN patients. A recent review of IVIG use in TEN and SJS examined studies with sample sizes of 10 or more patients.[20] Nine studies were included consisting of 134 TEN or SJS/TEN overlap patients and 22 SJS patients. The overall mortality rate of all the studies reviewed was 20.5%, and 22.4% for TEN-specific studies. In a subanalysis of these controlled trials, mortality rate for patients receiving IVIG were 27% compared with 30% for the predicted/control group. Further subanalyses revealed significantly higher average IVIG dose in studies with a positive "effect" conclusion than studies with an "ineffective" conclusion. The authors concluded that there was not strong enough evidence to support IVIG use in TEN or SJS patients. Seven of the nine publications analyzed did not report adverse effects with IVIG treatment. Of the two studies that did report adverse effects, one reported higher complications in the IVIG group. In the other report, there were higher plasma creatinine levels in IVIG patients, especially in elderly patients and in patients with past kidney function impairment.[20]

An updated review stratified results according to TEN and SJS and examined more studies.[21] In total, 14 studies in patients with TEN and 3 in patients with SJS were evaluated. The majority of studies reported positive results (11 out of 14),[9,22-31] while three cohort studies did not observe statistically significant improvement with IVIG administration.[32-34] For SJS, two of the three studies reported positive results.[23,35] The remaining study showed no significant differences in mortality, progression of detachment or speed of re-epidermalization.[32] In the pediatric population there were also positive results for IVIG response and adverse events.[9,25,28,32,35] Because of the heterogeneity of the studies, a meta-analysis could not be conducted for IVIG in TEN or SJS.

It is important to note that all IVIG studies have examined clinical outcomes based on treatment in adults with doses ranging from 0.2g/kg/day to 2g/kg/day for 1–5 days' duration. There is no information available on the impact of multiple dosing strategies.

The Toxic Epidermal Necrolysis Website Registry

Recently, a website for TEN and SJS has been launched (www.tenregistry.org) in Canada. At present, this new website is a pilot initiative that was created as an online resource to provide up-to-date information on SJS/TEN to clinicians, patients, and the public. The overall future objective of the website is to create a prospective, longitudinal database or registry of SJS/TEN patients across Canada and globally. At present, cases of suspected TEN or SJS should be reported to the adverse drug reaction monitoring agency. Reports to the adverse drug reaction monitoring centre may provide a signal for drugs that may cause SJS/TEN. Submitted reports of SJS/TEN will aid in determining the epidemiology, prognosis, and the possible causes, and will help plan health policy, especially for newly marketed drugs.

Conclusion

Based on the available data, IVIG may have a positive impact on the treatment of individuals with TEN and SJS. A large, multi-center, long-term analysis needs to be conducted to determine the role of IVIG in the management of these patients.

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Class	Name/Company	Approval Dates and Comments
Antiacne Agent	**Clindamycin Phosphate 1.2%/ Tretinoin 0.025%** *Ziana™ Gel* Medicis/ Dow Pharmaceuticals	The US FDA approved this gel formulation in November 2006 for once daily use for the topical treatment of acne vulgaris in patients 12 years or older.
Monoclonal Antibody	**Adalimumab** *Humira®* Abbott Pharmaceuticals	The US FDA approved an expanded indication in November 2006 that includes inhibiting structural joint damage and improving physical function in patients with psoriatic arthritis. This expanded indication is in addition to the psoriatic arthritis approval granted in October 2005.
Photodynamic Therapy	**Aminolevulinic Acid/ Light** *Levulan® Kerastick®* DUSA Pharmaceuticals/Stiefel Laboratories	The Brazilian drug regulatory authority, ANVISA, approved this product in October 2006 for the treatment of precancerous actinic keratoses.
Oncologic Agent	**Oblimersen Sodium Injection** *Genasense™* Genta	The Australian drug regulatory authority, the Therapeutic Goods Administration, granted Orphan Drug designation in October 2006 for the use of this anticancer drug as treatment for patients with Stage IV malignant melanoma.
Monoclonal Antibody	**Epratuzumab** *LymphoCide™* UCB/ Immunomedics	In November 2006, the US FDA lifted the clinical hold on existing trials with this monoclonal antibody in patients with lupus. Protocol amendments will be submitted to Institutional Review Boards to seek approval to treat patients who remain on the currently suspended studies and who are in need of retreatment.

Drug News

Drug Warning	The US FDA is alerting health care professionals and patients treated with rituximab (Rituxan®, Genentech/ biogen idec) to reports of an emerging risk of a serious side-effect in patients receiving, or who have used rituximab. Two patients who were treated with this drug for systemic lupus erythematosus (SLE) developed progressive multifocal leukoencephalopathy, a fatal viral infection of the central nervous system. This side-effect has been reported in patients as late as 12 months after their last dose. SLE is not an approved indication for rituximab; it is approved only for the treatment of patients with non-Hodgkin's lymphoma and patients with rheumatoid arthritis whose disease no longer responds to other common treatments. Health care professionals should report any serious adverse events possibly associated with the use of rituximab to the FDA's MedWatch Adverse Event Reporting program online at www.fda.gov/MedWatch/report.htm, or by phone at 1-800-FDA-1088.
Psoriasis and Myocardial Infarction	In an article recently published in JAMA*, Gelfand, et al. report that psoriasis is an independent risk factor for myocardial infarction, and this risk is greatest in young patients with severe psoriasis. The authors conducted a large, prospective population-based cohort study to determine the risk of heart attack in patients aged 20-90 years with psoriasis while controlling for major cardiovascular risk factors. *Gelfand JM, et al. JAMA 296(14):1735-41 (2006 Oct).

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