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Chapter 5

Role of Corticosteroids in Oral Lesions

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1. Introduction

Glucocorticoids were first introduced in the 1940s and have become a widely prescribed class of drugs. Corticosteroids are a class of chemicals that includes steroid hormones naturally produced in the adrenal cortex of vertebrates and analogues of these hormones that are synthesized in laboratories. Corticosteroids are involved in a wide range of physiologic processes, including stress response, immune response, and regulation of inflammation, carbohydrate metabolism, protein catabolism, blood electrolyte levels, and behavior. They are some of the most common drugs for management of patients undergoing stressful situations such as surgery and dentstry (Gibson 2004).

It has thus become common for standard textbooks in dentistry to recommend the administration of oral or intravenous steroids in the management of oral lesions.

Steroids have different effects on different tissues, which are dose dependent. The reason for varied effect of steroids lies in its mechanism of action (Grover 2007).

Glucocorticoids have potent anti-inflammatory actions, including the reduction in the number and function of various immune cells, such as T and B lymphocytes, monocytes, neutrophils, and eosinophils, at sites of inflammation. Glucocorticoids decrease the production of cytokines, chemokines, and eicosanoids and enhances the production of macrophage migration inhibitory factor (Gibson 2004).

Corticosteroid drugs are widely used in oral medicine such as in vesiculobullous diseases, orofacial granulomatosis, temporal arteritis and other oral mucosal disorders. Topical corticosteroids should be considered the treatment of choice unless the disease is very extensive. Systemic therapy is reserved for those with severe, refractory disease.

2. Mucosal ulceration and inflammation

2.1. Recurrent Aphthous Stomatitis

Recurrent Aphthous Stomatitis (RAS) are among the most common oral lesions in the general population, with a frequency of 5–25% and three month recurrence rates as high as 50%. Aphthous ulcers are often quite painful; may lead to difficulty in speaking, eating, and swallowing; and may negatively affect patients' quality of life (Ship 1996).

RAS is classified as minor, major, and herpetiform. Minor RAS involves the presence of one to five ulcers at a time, with each ulcer less than 1 cm in diameter.

Major aphthae are a cause of significant dysphagia and often result in extensive scarring. In herpetiform RAU there are 10–100 ulcers at a time, ulcer size is usually 1–3 cm, and the ulcers form clustersthat coalesce into widespread areas of ulceration lasting 7–10 days (Rees, Woo 1996).

The use of topical and systemic steroids in an attempt to manage apthous stomatitis is based on the presumption that the aphthae are the result of a noninfectious inflammatory process. Corticosteroids may act directly on T lymphocytes or alter the response of effect or cells to precipitants of immunopathogenesis (Vincent 1992).

2.1.1. Topical corticosteroids

Topical corticosteroid use in patients with RAS is intended to limit the inflammatory process associated with the formation of aphthae.

There are two double-blind, placebo-controlled trials have evaluated the efficacy of topical corticosteroids for RAS (Merchant 1978; Thompson 1989). The patients enrolled in one trial had minor RAS. Classification of ulcers was not available for the other trial. Both trials assessed patients for immuno -competence through laboratory studies. One trial excluded other medications used in RAS (Thompson 1989). In both trials there were significant reductions, compared with placebo, in ulcer duration and pain severity and no changes in the frequency of RAS in patients who applied betamethasone gel or beclomethasone aerosol spray to ulcers four times daily for six days to four weeks (Vincent 1992; Thompson 1989).

Two non-placebo controlled trials found no significant differences between triamcinolone ointment or betamethasone tablets and adhesive vehicles and Orabase in the frequency and duration of severe RAS. Subjective improvement tended to be greater with corticosteroids than with adhesive vehicle (Orabase), although the difference was not statistically significant (MacPhee 1968). A single blind, placebo-controlled trial involving fluocinonide ointment was performed in patients with minor and major RAS. Fluocinonide ointment significantly reduced ulcer duration, but ulcer frequency and subjective improvement were the same as for adhesive vehicle (Orabase). In the latter three trials, study design, ulcer severity, and vehicle activity may have contributed to findings inconsistent with those in the doubleblind, placebo-controlled studies (Pimlott 1983).

The drugs most commonly adopted for local oral application in RAS are hydrocortisone hemisuccinate (as pellets of 2. 5 mg) and triamcinolone acetonide (in an adhesive paste containing 0. 1% of the steroid). There is little risk of adrenal suppression provided that the recommended dose (fourtimes daily) is adhered to (Field 2003).

In severe RAS may be necessary to use a more potent steroid preparation. High potency topical steroid preparation such as fluocinonide, betamethasone or clobetasol placed directly on the lesions shortens healing time and reduces the size of lesion. The gel can be carefully applied directly to the lesion after meals and at bedtime 2-3 times a day or mixed with an adhesive such as orabase prior to application. Recently, Lo Muzio et al. treated oral aphthous lesions by applying clobetasol propionate with a bioadhesive system, which resulted insurprisingly good outcomes (Lo Muzio 2001).

Larger lesions can be treated by placing a gauge sponge containing the topical steroid on the ulcer and leaving it in place for 15-30 min to allow for longer contact of the medication. Ulcerations located in the areas that make them difficult to see or reach can be controlled by topical dexamethasone elixir, 0. 5 mg / 5 ml held over the area or applied with a saturated gauge pad to the ulcers, four times per day for 15 min (Lo Muzio 2001) and betamethasone sodium phosphate rinse (dissolve 0. 5 mg in 5 mL of water and rinse for 2–3 min), steroid aerosol (e. g. beclometasone diproprionate, 100 lg/puff) , or a high-potency topical corticosteroid, such as clobetasol 0. 05% in orabase or fluocinonide 0. 05% in orabase (Natah 2004).

2.1.2. Systemic corticosteroids

Major apthous ulcers often require systemic treatment as an initial approach. Therapy with prednisone 40 mg/day for one week is usually adequate to control the presenting outbreak. Systemically, oral prednisone is most commonly employed. Systemic prednisone therapy should be started at 1. 0 mg/kg a day as a single dose in patients with severe RAS and should be tapered after 1-2 weeks. Intralesional steroids can be used to treat large indolent major RAS lesions (Field 2003).

2.2. Behcet's disease

Behcet's disease is a multisystem, chronic relapsing inflammatory disease of unknown cause, which is characterized by recurrent oral (aphthous) ulcers, genital ulcers, uveitis and skin lesions. There maybe a variety of other manifestations including joint, central nervous system, vascular and intestinal lesions of variable severity (Lai 1995).

Patients with Behcet's disease usually have repeated exacerbations and remission of their clinical symptoms, and in these individuals treatment is essentially symptomatic. The choice of therapy depends on whether the clinical manifestations of the disease are local or systemic.

Local treatment with corticosteroids often controls oral and genital ulcers, and immunosuppressive therapy is reserved for severe cases of mucocutaneous involvement (Yazici 1991).

Immunosuppressive therapy is the mainstay of treatment for Behcet's disease. Successful treatment consists of anti-inflammatory agents that modify neutrophil activity. In the acute phase, prednisone, at doses of 40-60 mg/day, may be helpful, used alone or in combination with other immunosuppressive agents (Reich 1998).

Systemic corticosteroids continue to be used extensively, and may be administered as intravenous pulse therapy.

2.3. Oral Lichen Planus (OLP)

Lichen Planus (LP) is an unique inflammatory disorder that affects the skin, mucous membranes, nails and hair was first described and named by Erasmus Wilson in 1869 (Oztas 2003). The pathogenesis of LP is not entirely understood. It is a disorder of altered cell mediated immunity with exogenous antigens targeting the epidermis.

Various medical therapies are used for the treatment of Phototherapy has been used in the treatment of LP for many years. The therapeutic properties of corticosteroids were first demonstrated by Edward Kendall and Philip Hench in 1948 (Hench 1949).

Corticosteroids may be applied topically as ointments, pastes, lozenges or mouthwashes or through an inhaler with a special adapter.

The best treatment for OLP includes the use of high-potency topical corticosteroids (Setterfield 2000, Bruce 2007).

It has been reported that topical corticosteroids, which have fewer side effects, are equally or even more effective than systemic corticosteroids (Lodi 2005).

2.3.1. Topical corticosteroids

Topical corticosteroids are the main stay in treating mild to moderately symptomatic lesions. They are widely used in the treatment of OLP to reduce pain and inflammation. Options (presented in terms of decreasing potency) include 0. 05% clobetasol proprionate gel, 0. 1-0. 05% betamethasone valerate gel, 0. 05% fluocinonide gel, 0. 05% clobetasol ointment or cream and 0. 1% triamcinolone acetonide ointment (Levin 2002).

Triamcinolone acetonide is commonly used either in orabase or lozenge (Thongprasom 1992, Zegarelli 1969). A number of investigations have determined the efficacy of triamcinolone acetonide 0. 1% suspension in the treatment of OLP. This drug is available over the counter and is useful in the treatment of OLP (Rabiyi 2003).

An aqueous suspension of triamcinolone acetonide 0. 1% was used as an oral rinse in the treatment of 46 patients with symptomatic oral lichen planus (Vincent 1990). This method proved to be effective, resulting in "complete relief " in 27 patients. Although these results most likely refer to improvement in patients' symptoms, no specific information is provided regarding the clinical improvement with this therapy.

Betamethasone valerate, an even more potent anti-inflammatory agent, produced dramatic results in a number of controlled studies in patients with oral lichen planus. In a double-

blind study, Cawson treated 30 patients with symptomatic oral lichen planus with betamethasone (0.1 mg) pellets. In 8 patients, all lesions virtually disappeared within 1 month, and during the same period, 20 of 30 patients showed substantial improvement. Only two patients failed to respond to this therapy (Cawson 1968).

Similarly, Tyldesley and Harding showed betamethasone valerate aerosol fitted with a special intraoral adaptor was an excellent treatment in the majority of 23 patients tested in a double-blind study (Tyldesley 1977). Greenspan et al. confirmed the efficacy of both betamethasone valerate aerosol and pellets in a double-blind study, noting improvement in 17 of 19 patients (Greenspan 1978).

High-potency steroid mouthwashes such as disodium betamethasone phosphate or clobetasol propionate, can be used in widespread oral LP but these may cause a significative systemic absorption leading to a pituitary- adrenal axis suppression (Gonzalez-Moles 2002).

Fluocinolone is another steroid, which has been used for treatment of OLP. Compared with the placebo, this drug has been found to be more effective (Voute 1993).

Recently, fluticasone propionate spray has been used effectively in the short-term management of symptomatic OLP, but 10% of the patients did not tolerate such treatment for more than 3 weeks (Hegarty 2002). The more potent fluorinated steroids can be very effective and include fluocinonide 0. 05% (Silverman 1991; Lozada 1980) and fluocinolone acetonide 0. 1%. (Thongprasom 1992) Fluocinonide 0. 05% and fluocinolone acetonide 0. 1% have been found to be effective in the treatment of severe oral LP that has failed to respond to other medications (Thongprasom 1992; Voute 1993).

A study evaluated fluocinolone acetonide 0. 1% in three groups: solution (FAS), Orabase (FAO), and both. The best results achieved with FAO (complete remission of 77. 3% of patients). This study had a long-term follow-up, without having a control group (Thongprasom 2003).

A study confirmed the efficacy of topical fluocinolone acetonide gel 0. 025 %, along with the topical antimicrobial drug chlorhexidine, in treatment of erosive OLP (Thongprasom 2003).

Another study showed no difference between the fluticasone propionate (FP) spray and betamethasone sodium phosphate (BSP) mouth rinse. But FP was found to be more acceptable to patients than BSP, because of the convenience of the spray form (Hegarty 2002).

The application of fluocinonide ointment (0. 05%) compounded with orabase 6 times per day or clobetasol propionate ointment (0. 05%) with orabase 3 times per day can control erosive lichen planus effectively in most patients (Edwards 2002).

Fluocinolone acetonide 0. 1% in orabase has been shown to be more effective than a similar triamcinolone acetonide 0. 1% preparation with no serious side effects (Thongprasom 1992).

Clobetasol propionate in aqueous solution, ointment, or orabase has also been shown to be effective in OLP. Clobetasol can be more effective than fluocinonide in improving lesions and the long-term use of clobetasol (6 months) may help to control the disease, offering

substantial disease-free periods in 65% of the patients after 6 months of follow-up (Carbone1999).

Clobetasol propionate, a very potent corticosteroid in the Miller and Munro classification, was used in a 4% hydroxy ethylcellulose bioadhesive gel (Carbone1997). Clobetasol propionate 0. 05% ointment has been shown to heal OLP, but this study had a small sample group, without any control group or follow-up (Roed-Petersen 1992). Among the three preparations of clobetasol propionate 0. 05% (ointment, Orabase, and the adhesive denture paste) the best results have been achieved with clobetasol propionate in an adhesive denture paste (Lo Muzio 2001).

Although there are some reports of systemic absorption and adrenal suppression from super-potent topical steroids in the treatment of chronic skin disorders, adrenal suppression has not been found in long-term oral application of topical corticosteroids such as fluocinonide 0. 05%, fluocinolone acetonide 0. 1%, and clobetasol 0. 05% (Carbone1999).

Acute pseudomembranous candidiasis is the only common side effect from topical corticosteroid therapy (Thongprasom 1992). This can be prevented with antifungal (miconazole gel) alone or with chlorhexidine mouthwashes (Carbone1999).

2.3.2. Intralesional corticosteroids

Intralesional injection of corticosteroid for recalcitrant or extensive lesions involves the subcutaneous injection of 0. 2–0. 4 mL of a 10 mg/mL solution of triamcinolone acetonide by means of a 1. 0-mL 23 or 25 gauge tuberculin syringe (Edwards 2002).

Intralesional injections of hydrocortisone, dexamethasone, triamcinolone acetonide and methylprednisolone have been used in the treatment of OLP (Zegarelli 1980). However, the injections can be painful, are not invariably effective, and have a localized effect such as mucosal atrophy. Three to four or twice weekly treatments of intralesional triamcinolone acetonide in doses of 0. 5–1 ml of a 1-mg/ml suspension seem to be a practical supplement for the treatment of erosions (Edwards 2002).

Zegarelli combined the use of topical and weekly intralesional corticosteroids in seven patients. After 3 weeks, five patients were graded as having 100% clinical improvement. Furthermore, in most cases, a remission of several months was noted; recurrences were milder than the original disease state and were managed with topical agents alone (Zegarelli 1983). It is unclear why the response to topical corticosteroid therapy is so variable. Undoubtedly, the frequency of application of topical corticosteroids makes compliance difficult because optimal effects are not achieved unless they are applied between five and ten times daily (Zegarelli 1980).

2.3.3. Systemic corticosteroids

Systemic corticosteroids are reserved for recalcitrant erosive or erythematous LP where topical approaches have failed. Systemic prednisolone is the drug of choice, but should be

used at the lowest possible dosage for the shortest duration (40-80 mg for 5-7 days) (Eisen 2005).

Systemic prednisone can be used to control the ulcers and erythema in OLP. Systemic corticosteroids may be indicated in patients whose condition is unresponsive to topical steroids or in patients with mucocutaneous disease and in high doses (1. 5-2 mg/kg/daily), but adverse effects are possible even with short courses (Zegarelli 1980; Chainani-Wu 2001).

The oral dose of prednisone for a 70-kg adult ranges from 10–20 mg/day for moderately severe cases to as high as 35 mg/day (0. 5 mg/kg daily) for severe cases (Zegarelli 1983). Prednisone should be taken as a single morning dose to reduce the potential for insomnia and should be taken with food to avoid nausea and peptic ulceration. Significant response should be observed within one to 2 weeks.

When systemic corticosteroids are prescribed for periods of longer than 2 weeks, the dosage of steroid must be gradually tapered to avoid precipitating an adrenal crisis. Tapering can be accomplished by decreasing the daily dose of prednisone by 5 mg per week (Edwards 2002).

Some studies have compared the efficacy of corticosteroids with some other drugs. For example in a double-blind randomized controlled study, compared the efficacy of topical zinc sulfate in combination with 0. 05% fluocinolone ointment in the treatment of OLP after 2 weeks of treatment, was founded that topical zinc sulfate in combination with 0. 05% fluocinolone ointment reduced the severity erosive OLP better than 0. 05% fluocinolone separately (Mehdipour & Taghavi 2010).

2.4. Erythema Multiforme (EM)

Erythema Multiforme is a skin condition considered to be hypersensitivity reaction to infections or drugs. It consists of a polymorphous eruption of macules, papules, and characteristic 'target' lesions that are symmetrically distributed with a propensity for the distal extremities. There is minimal mucosal involvement. Herpes simplex virus (HSV) is the most commonly identified etiology of this hypersensitivity reaction, accounting for more than 50 percent of cases. Although EM was first clinically recognized in the early 19th century and referred to by a variety of names, it was not until 1860 that Ferdin and von Hebra termed the disease "Erythema Multiforme (Forman 2002).

Erythema multiforme (EM) was once thought to be the early presentation of a continuum of diseases related to Stevens-Johnson syndrome (SJS), with toxic epidermal necrolysis (TEN) believed to be a distinct entity. It is now generally accepted that a separation exists between EM and SJS. Currently, two different classifications exist: first, an erythema multiforme spectrum (minor and major) and second, an SJS and TEN spectrum (Lamoreux 2006; French 2008).

SJS and its more severe progression, TEN, are both rare mucocutaneous diseases that can be life-threatening and almost always caused by drugs (49). SJS was first described in 1922 by

two physicians, Stevens and Johnson, who described a skin eruption similar to EM that also included purulent conjunctivitis, stomatitis,, and fever (Forman 2002).

Management of erythema multiforme involves determining the etiology when possible. The first step is to treat the suspected infectious disease or to discontinue the causal drug.

2.4.1. Topical steroid therapy

Mild cases of Erythema Multiforme do not require treatment. Oral topical steroids may be used to provide symptom relief (Shin 2001).

Lozada-Nur and Zhong Huang reported that an adhesive paste (Orabase) form of clobetasol propionate, the most potent topical corticosteroidis a safe and efficacious alternative to systemic therapy in erosive oral lesions (Lozada-Nur F 1994).

Mouthwashes of clobetasol propionate in aqueous solution may offer an alternative topical approach to this patient population. The mouthwash solution provides ready access to all lesional areas, and there is excellent control over the contact time between drug and lesion (Jacobson 1986).

2.4.2. Systemic steroid therapy

The role of systemic corticosteroids in Erythema Multiforme Major (EMM) and SJS is controversial. There is no literature to date based on a large, prospective, randomized, or double-blind study evaluating use of systemic corticosteroids in EMM/SJS.

Moderate to severe oral Erythema Multiforme may be treated with a short course of systemic glucocorticosteroid in patients without significant contraindications to their use. Prednisone may be used in patients with many lesions at dosages of 40 to 80 mg per day for one to two weeks then tapered rapidly (Lamoreux 2006). There have been no controlled studies of prednisone's effectiveness, and its use in patients with herpes-associated Erythema Multiforme may lower the patient's resistance to HSV and promote recurrent HSV infection followed by recurrent Erythema Multiforme (Volcheck 2004).

The dosing and route of administration that provides the most benefit for EMM and SJS patients is in question. Early therapy with systemic prednisone (0. 5 to 1. 0mg/kg/day) or pulse methylprednisolone (1mg/kg/day for 3 days) has been shown to be effective (Scully 2008). One author suggests tapering the oral prednisolone over 7 to 10 days, while Patterson et al. suggests a high dose of corticosteroids for EMM patients followed by a four-week tapering course (Chrousos 2004). Still another suggests a bolus infusion for 3 to 7 days of coricosteroids, which showed no relapses after treatment was discontinued (Kakourou1997). Intravenous (IV) pulsed dose methylprednisolone (3 consecutive daily infusions of 20–30mg/kg to a maximum of 500 mg given over 2 to 3 hours) has also been reported, with the suggestion that this approach is superior to oral prednisone because the greatest benefit is seen when treatment is administered as early as possible in the progression of the cutaneous insult (Martinez 2000).

Kardaun and Jonkman recently proposed dexamethasone pulse therapy (1. 5mg/kg IV over 30 to 60 minutes on 3 consecutive days) to avoid long-term use of systemic corticosteroids (Kardaun 2007). The authors described the pleomorphic effects of dexamethasone on the immune system, including inhibition of epidermal apoptosis by several mechanisms. These mechanisms include suppression of various cytokines, such as TNF-alpha; inhibition of interferon-gamma-induced apoptosis; and inhibition of Fas-mediated keratinocyte apoptosis (Yeung 2005).

When treating TEN, it is generally agreed that after widespread sloughing occurs, any risk of infection outweighs the potential benefits of systemic corticosteroid therapy (Wolverton 2007).

Recurrent Erythema Multiforme often is secondary to HSV-1 and -2 reactivation, although the HSV may be clinically silent (Huff 1992).

2.5. Pemphigus

Pemphigus refers to a group of rare chronic mucocutaneous diseases characterized by painful lesions caused by intraepidermal antholytic structures in the skin and mucous membrane (Sirois 2000).

Oral mucosal lesions in Pemphigus are common (50%-70%) and predominantly appear as buccal erosions in the occlusal line, which is most exposed to trauma and also on the palate, gingival and tongue (Sirois 2000).

The exact nature of the disease remains unknown. Pemphigus is characterized by intra-epithelial bulla formation, due to autoantibodies directed against proteins of the desmosome-tonofilament complex between keratinocytes (Sirois 2000).

Pemphigus vulgaris (PV) has a high morbidity and mortality rate without treatment. Because of the rarity of the disease, there is not yet a standard treatment regimen (Cotell 2000).

The aim of treatment in pemphigus vulgaris is the same as in other autoimmune bullous diseases, which is to decrease blister formation, promote healing of blisters and erosions, and determine the minimal dose of medication necessary to control the disease process (Knudson 2010).

Until now, treatment consists mostly of the use of corticosteroid and immunosuppressive drugs. The use of corticosteroids in the 1950s had reduced mortality from 60% to 90% to about 30%. The current mortality was about 6. 2% (range 0 to 10%) and did not show further significant reduction (Bystryn 1996).

The treatment depends on the prognostic elements of the condition, such as the extent of the lesions and antibody levels. Treatment is administered in 2 phases: a loading phase, to control the disease, and a maintenance phase, which is further divided into consolidation and treatment tapering. The basic treatment for pemphigus consists of either local or systemic corticosteroid therapy (Fellner 2001).

2.5.1. Topical corticosteroids

Local corticosteroid therapy is used in cases where the PV is not extensive and lesions are limited to the oral cavity. Corticosteroids can be prescribed in the form of a paste, an ointment or a mouthwash administered as monotherapy or as adjunctive therapy with a systemic treatment (Fellner; Ruocco 2001).

In patients with no progressing oral lesions, moderate to high potency topical corticosteroids are recommended, applied 2-3 times a day, such as 0. 05% fluocinolone acetonide or 0. 05% clobetasol propionate (Hashimoto; Prajapati 2008).

Dumas et al. described 7 pemphigus patients, 3 of whom were treated with clobetasol propionate 0. 05% cream as monotherapy for their mild PV. PV was defined as "mild" if fewer than 10 new bullae appeared per week and if the circulating pemphigus antibody titer was 1:320. The cream was applied twice a day for at least 15 days, and then tapered. Lesions were controlled in only 1 of the 3 PV patients (Dumas 1999).

2.5.2. Systemic corticosteroid therapy

In patients with severe disease and spreading of the lesions to skin surfaces, systemic corticosteroids are the treatment of choice (Knudson 2010).

The dosing schedule of systemic corticosteroids in pemphigus is largely empirical (Ratnam 1990). Prednisolone was the first drug used to treat this disease and almost in all situations, is the first line of treatment (Camisa 1998).

The starting dose is high; a total oral dose of 100–200 mg Prednison is administered daily until subsidence of clinical signs. This dose can gradually be decreased to a maintenance level of 40 to 50 mg daily. Topical application of corticoids is effective if small, isolated areas of the oral mucosa are involved. The acute phase of pemphigus is associated with changes in gastric mucosa and this condition is further aggravated by ingestion of corticosteroids (Fassmann 2003).

Corticosteroids taken by mouth have many long-term harmful effects, including adrenal atrophy, abnormal sensitivity to infection, high blood pressure, hypertriglyceridemia, hyperglycemia, cortisone myopathy, erosive duodenitis and stress fracture, as in the case presented here. To minimize iatrogenic effects, Lever and Schaumburg recommended a treatment called the "high Lever scheme" with very high loading doses (100–175 mg taken twice daily for 5–10 weeks) , followed by the "low Lever scheme," which includes a rapid reduction in dosage over a few weeks, with a maintenance dose of 40 mg every 2 days accompanied by local adjuvant treatment (Lever 1984).

The British Association of Dermatologists recommends patients with mild disease to receive an initial prednisolone dose of 40-60 mg daily and in more severe cases, 60-100 mg daily. If there is no response within a week, the dose is increased by 50-100% until disease control. There is no unitized handling considering the tapering of corticosteroids. A 25% dose reduction may be performed biweekly with slower decrease after a dose of 20 mg/day has been reached (Harman 2003).

Two prospective controlled trials explored the effect of i. v. corticosteroid pulses in addition to oral prednisolone but did not observe statistical differences between treatment groups (Femiano 2002; Mentink 2006).

In one controlled trial, patients randomized to treatment with either low-dose oral prednisolone (45-60mg/day) or high-dose oral prednisolone (120-150mg/day) showed no significant difference in the time to achieve remission and in relapse rates at 5 years (Ratnam 1990).

A nonrandomized retrospective controlled trial of 71 pemphigus patients assigned participants to cohorts receiving prednisone 1 mg/kg/day or 2 mg/kg/day. No statistical difference was observed between cohorts in terms of response to treatment; however, there was a significantly higher frequency of adverse events, particularly infection, in the 2 mg/kg/day cohort. Despite the retrospective, nonrandomized nature of the study, the results indicate that higher doses of corticosteroid are no more effective than lower doses, and are associated with higher rates of complications. Overall, the limited evidence indicates that lower steroid dose regimens (=1 mg/kg/day) have equivalent efficacy in controlling disease as higher dose regimens, and may have decreased associated morbidity (Fernandes 2001).

Another nonrandomized, controlled trial of 20 PV patients studied participants receiving either a 125 mg/day tapering schedule of prednisone or a 50 mg/day tapering schedule of prednisone plus intravenous betamethasone 20 mg/day. In this study, the cohort receiving the pulse therapy was found to have faster clinical resolution of symptoms, with statistically significant difference (Femiano 2002).

Pulse corticosteroid usually seems to result only in short-term relief from the disease and most likely needs continued administration of oral corticosteroids (Funauchi 1997).

Werth has compared these two therapeutic protocols. It was only a retrospective study that included two heterogeneous groups of patients with completely different therapeutic regimens for each patient. It included nine patients who had received pulse therapy and six patients who had received conventional treatment. Some received only one course of pulse therapy, while others received two courses. This study showed the superiority of pulse therapy over conventional treatment (Werth 1996).

2.5.3. Intralesional corticosteroid therapy

Intralesional corticosteroid therapy accelerates the scarring process of a lesion or is used to treat persistent lesions. This treatment, which gives inconsistent results, involves sublesional injections given every 7 to 15 days; treatment is stopped after 3 injections if there is no improvement. Scarring is accompanied by cutaneous or mucosal atrophy the major drawback of this treatment (Fellner; Ruocco 2001). If the patient has extraoral lesions or if the oral damage is extensive, systemic corticosteroid therapy is initiated immediately. The initial dose depends on the chronicity of the lesions and the severity of the disease. A daily application of prednisone 0. 5–2 mg/kg is recommended (Fellner; Toth 2001). Depending on

the response, the dose is gradually decreased to the minimum therapeutic dose, taken once a day in the morning to minimize side effects.

The lack of randomized controlled trials precludes any conclusions as to whether these protocols are superior to those using higher loading doses. An adjuvant drug is prescribed for most patients with severe PV, with the objectives of reducing the cortisone dose and ensuring stable remission. However, the use of adjuvant therapy remains controversial (Mutasim 2004).

2.6. Mucous Membrane Pemphigoid (MMP)

Mucous Membrane Pemphigoid (MMP) or Cicatricial pemphigoid is a rare autoimmune blistering disorder that affects the mucous membranes and skin. It was first described by Thost in 1911 (Thost 1911).

This disease is extremely difficult to treat despite the use of aggressive combination immunosuppressive regimens. Cicatricial pemphigoid with multiple mucosal site involvement has the worst prognosis due to its high resistance to medical therapy resulting in loss of function through scarring (Tht Yu 2007).

During the past 50 years, the mainstay of treatment for MMP has been systemic glucocorticoids. However, the high doses needed to obtain clinical response are generally poorly tolerated, especially in young patients, and are associated with many adverse effects (Borradori 2004).

2.6.1. Topical steroid therapy

Mild localized lesions usually respond to topical steroids, including triamcinolone, fluocinonide and clobetasol propionate. Patients with mild oral disease should be treated with topical and intralesional steroids.

Desquamative gingivitis can often be managed with topical steroids in soft dental splint that covers the gingiva, although the clinician using topical steroids over large areas of mucosa must closely monitor the patient for side effects such as candidiasis and effects of systemic absorption (Reich 1998).

Lozada -Nur and Zhong Huang treated patients with severe erosive disease, using clobetasol propionate mixed in an adhesive paste. They reported a complete response in 62. 5% of the series (15 patients), an excellent response in 29. 7% (7 patients), and a failed response in 8. 3% (2 patients). They concluded that their treatment was efficacious and safe (Lozada-Nur 1991).

In low risk patients with lesions confined to the oral mucosa and/or skin, topical corticosteroids are advised, such as 0. 1% triamcinolone acetonide, 0. 05% fluocinoloneacetonide, or 0. 05% clobetasol propionate in orabase, applied 3-4 times a day during 9-24 weeks. In patients with isolated erosions, intralesional corticosteroid injections (triamcinolone in 5-10 mg/ml solution) can be used. In subjects presenting gingival lesions in

the form of desquamative gingivitis, 0. 05% clobetasol propionate is recommended, with nystatin 100,000 IU to avoid candidiasis overinfection (Bagan 2005, Scully 2008). When MMP affects the palate, esophagus or nasal mucosa, beclomethasone dipropionate or budesonide (50-200 μg) can be prescribed (Bagan 2005).

2.6.2. Systemic steroid therapy

MMP can be rapidly progressive, and systemic steroids have been used as initial treatment for patients with extensive oral ulceration or as additional treatment on patients who did not respond to topical steroids. Systemic corticosteroids such as prednisolone at 1- 2 mg/kg/day are the first-line medications in CP because of their potent anti-inflammatory and immunosuppressive effects (Mondino 1981).

The serum autoantibody titers remain very high after the disappearance of clinical lesions. Therefore the benefit of steroids in benign mucous membrane pemphigoid might be due to anti-inflammatory actions, including lowered enzyme release, reduced cell migration and decreased leakage of humoral factors (Knudson 2010).

In high risk patients with multiple oral lesions, rapidly progressing spread of the disease to other mucosal membranes such as the eyes, genital, esophagus or nasopharyngeal zone, or recurrent lesions, the administration of prednisone 1-2 mg/kg/day, with gradual dose reduction, and immune suppressors such as cyclophosphamide (0. 5-2 mg/kg/day) , azathioprine 1-2 mg/ kg/day, or mycophenolate mofetil 2-2. 5 g/day has been described (Bagan 2005; Knudson 2010).

2.7. Bullous Pemphigoid (BP)

Bullous Pemphigoid (BP) is an autoimmune disease characterized by subepidermal blistering , which are often pruritic (Fitzpatrick 2008).

Bullous pemphigoid occurs most commonly in the elderly, with an onset between 65 and 75 years of age. Prognosis is influenced by age and general condition of the patient, not by extent of disease activity.

Treatment includes topical and systemic corticosteroids, steroid-sparing immunosuppressants, and tetracycline in combination with niacinamide (Joly 2005).

2.7.1. Topical steroid therapy

In a study of 10 patients with extensive and generalized BP, treatment with 0. 05% clobetasol propionate cream achieved complete healing in all patients within 17 days of treatment. Seven of the 10 patients remained in remission at the time of reporting (1–10 months) (Westerhof 1989).

Twenty patients with BP (involvement of less than 60% body surface) in a second study were treated with very potent topical corticosteroids: in seven patients BP was completely suppressed and the same number obtained remission with an 11-month follow-up. There

were mild side-effects of cutaneous infection and skin atrophy. The use of topical corticosteroids has also been reported in a large number of case reports and smaller series of fewer than five patients (Zimmermann 1999).

Potent topical corticosteroids should be considered in patients with limited or moderate disease (Mutasim 2004).

In a large randomized controlled trial, initial disease control and 1-year survival were significantly better when treating extensive BP with clobetasol propionate cream 40 mg daily compared with oral prednisolone 1mg/kg/day while in moderate BP (< 10 blisters/day) outcomes using clobetasol cream and prednisolone 0. 5mg/kg were similar (Joly 2002).

Recently, lower doses of topical clobetasol propionate (10-30g daily) were shown to have similar short-term efficacy but reduced side-effects compared to the high dose topical regimen (40g daily clobetasol propionate) (Joly 2009).

2.7.2. Systemic steroid therapy

High-doses of systemic corticosteroids are the standard for initial treatment of BP to gain control over the eruptions, and prolonged high-doses are often used in severe cases. Adverse side effects from systemic corticosteroids seem to be the main cause of mortality in BP (Mamelak 2007).

Recommended initial doses of prednisolone are 20 mg/day or 0. 3 mg/kg/day in localised or mild disease, 40 mg/day or 0. 6 mg/kg/day in moderate disease, and 50-70 mg or 0. 75-1 mg/kg/day in severe disease (Wojnarowska 2002).

In patients with limited disease, clobetasol propionate cream alone is used; in patients with moderate disease, clobetasol propionate cream is combined with dapsone (1. 0-1. 5mg/kg/day) and in severe cases, oral prednisolone (0. 5mg/kg/day) is added. Instead of dapsone, doxycycline (200mg/day) may be given (Kasperkiewicz 2009).

2.7.3. Intralesional corticosteroid therapy

Intralesional triamcinolone acetonide 3-10 mg per ml can be administered to resistant lesions. Experience in injecting correctly is necessary to maximise efficacy and minimise atrophy. Where pemphigoid does not respond to steroids, or large maintenance doses are required, other 'steroid-sparing' agents can be used. However, the evidence for effectiveness of these drugs is limited and many have worrying side effect profiles. They should therefore be used cautiously by those with experience in their actions (Reich 1998).

2.8. Systemic Lupus Erythematosus

Lupus Erythematosus may run in one of the two well recognized forms. Systemic (acute) or Discoid (chronic). Both of them may have oral manifestations. Discoid Lupus Erythematosus (DLE) is a chronic skin condition of sores with inflammation and scarring

favoring the face, ears and scalp. It probably occurs in genetically predisposed individuals (Khare 2011).

Systemic Lupus Erythematosus (SLE) is a chronic disease characterized by protean manifestations, often with a waxing and waning course. In the past, a diagnosis of SLE often implied a decreased life span caused by internal organ system involvement or the toxic effects of therapy, but recent improvements in care have dramatically enhanced the survival of SLE patients. Nonetheless, increased mortality remains a major concern and current treatments for SLE remain inadequate (Ippolito 2008).

Oral ulcerations of systemic lupus erythematosus are transient, occurring with acute lupus flares. Symptomatic lesions can be treated with high potency topical corticoids or intralesional steroid injections. Systemically low dose prednisone 10-20 mg /day or an alternate day dose of 20-40 mg may be needed (Pedersen 1984; Reich 1998).

Reducing corticosteroid use is an important goal in treatment of patients with SLE if it occurs in the context of a treatment that effectively controls disease activity. Therefore, for a medical product to be labeled as reducing corticosteroid usage, it should also demonstrate another clinical benefit, such as reduction in disease activity as the primary endpoint.

The evaluation of efficacy should be based on the proportion of patients in treatment and control groups that achieve a reduction in steroid dose to less than or equal to 10 mg per day of prednisone or equivalent, with quiescent disease and no flares for at least 3 consecutive months during a 1-year clinical trial. For a result to be clinically meaningful, the patient population should be on moderate to high doses of steroids at baseline. Trials should also assess the occurrence of clinically significant steroid toxicities (Ad Hoc Working Group on Steroid-Sparing Criteria in Lupus 2004).

In the localized variety of Discoid Lupus the lesions tend to be confined to the head and neck and in the generalized variety they occur both above and below the neck. The disease may occur at any age; with higher incidence between 20 to 40 years of age. It has a prolonged course and can have a considerable effect on quality of life. Potent topical steroids and antimalarials are the mainstay of treatment (Khare 2011).

Topical steroids are the mainstay of treatment of DLE. Patients usually start with a potent topical steroid (e. g., betamethasone or clobetasol) applied twice a day, then switch to a lower-potency steroid as soon as possible. The minimal use of steroids reduces the recognized side effects like atrophy, telengiaectasiae, striae, and purpura.

Intralesional injection of corticosteroids (typically, this author uses triamcinolone acetonide 3 mg/mL) is useful as adjunctive therapy for individual lesions. Potential for atrophy relates to the amount of corticosteroid injected in any area; therefore, dilute concentrations are preferred. In addition, the treating physician must take care to limit the total dose of the injections at any given office/clinic visit to avoid systemic toxicity from the steroids; eg, if a patient is given 10 mL of triamcinolone 3 mg/mL, this means that the patient has received a total of 30 mg, and toxicity is the same as if it had been delivered orally or by intramuscular injection (Panjwani 2009).

Oral steroids may be required for the control of systemic lupus but are not generally beneficial in DLE. For patients with progressive or disseminated disease or in those with localized disease that does not respond to topical measures, the addition of systemic agents should be considered.

3. Facial pain

3.1. Bell's palsy

Idiopathic facial palsy, also called Bell's palsy, is an acute disorder of the facial nerve, which may begin with symptoms of pain in the mastoid region and produce full or partial paralys is of movement of one side of the face (Valença 2001).

Facial nerve paralysis may be congenital or neoplastic or may result from infection, trauma, toxic exposures, or iatrogenic causes. Increasing evidence suggests that the main cause of Bell's palsy is reactivation of latent herpes simplex virus type 1 in the cranial nerve ganglia. How the virus damages the facial nerve is uncertain (Gilden 2004).

Treatment of Bell palsy should be conservative and guided by the severity and probable prognosis in each particular case. Studies have shown the benefit of high-dose corticosteroids for acute Bell palsy (Sullivan 2007; Engström 2008).

Taverner in 1954 was the first to design a controlled treatment trial of steroids but unfortunately the number of patients was too small to permit a signifcant statistical evaluation (Taverner 1954).

Attempts to treat Bell's palsy with steroids changed in the 1970s. After the initial publication of Adour et al. several series of treatments with prednisone for Bell'spalsy were designed, but almost all of them were of unsatisfactory quality (Adour 1972). Nevertheless, the majority of authors claimed that they had shown steroids to be benefcial to a statistically signifcant degree.

Two recent systematic reviews concluded that Bell's palsy could be effectively treated with corticosteroids in the first seven days, providing up to a further 17% of patients with a good outcome in addition to the 80% that spontaneously improve (Ramsey 2000; Grogan 2001).

Other studies have shown the benefits of treatment with steroids; in one, patients with severe facial palsy showed a significant improvement after treatment within 24 hours (Shafshak 1994; Williamson 1996).

Immunocompetent patients without specific contraindications are prescribed prednisone at 1 mg/kg/d (maximum 80 mg) for the first week, which is tapered over the second week. Around a fifth of patients will progress from partial palsy, so these patients should also be treated (Ramsey 2000).

However the Sullivan study with 496 participants compared different combinations of prednisolone, acyclovir and placebo. They found significant benefit from prednisolone but not acyclovir (Sullivan 2007).

Hato assessed the efficacy of valacyclovir with 296 participants divided into two groups (valacyclovir with prednisolone,and placebowith prednisolone) and found significant benefit from valacyclovir (Hato 2007).

3.2. Ramsay Hunt syndrome

Ramsay Hunt syndrome (RHS) is caused by the reactivation of a previous Varicella zoster virus (VZV) infection. RHS is a potentially serious viral infection that accounts for approximately 12% of all facial nerve palsies (Robillard 1986; Uri 2003).

VZV is also the cause of "shingles," which frequently presents with a classic painful dermatomal distribution of vesicles and crusted skin ulcerations. In addition to the alarming facial palsy, RHS may also be characterized by severe otalgia, sensorineural hearing loss, vertigo, painful skin vesicles and aguesia in the ipsilateral anterior tongue (Hiroshige 2002).

The treatment of Ramsay Hunt syndrome is not entirely agreed upon. Definitive treatment consists of antiviral therapy and sometimes includes steroids. Adjunctive steroid therapy can be helpful in the management of the facial paralysis of RHS (Kinishi 2001).

However, many authors caution against implementing steroid therapy, especially with periocular lesions, as they fear dissemination of the VZV infection (Van de Steene 2004; Hyvernat; Hill 2005).

The largest retrospective treatment study showed a statistically significant improvement in patients treated with acyclovir and prednisone within 3 days of onset. Complete recovery occurred in 75% of patients treated within the first 3 days, but in only 30% of those treated after 7 days. This suggests that prompt diagnosis and management improves outcome in Ramsay Hunt syndrome. Importantly, no statistically significant outcome differences were noted between patients treated with intravenous or oral acyclovir (Murakami 1997).

A large prospective study demonstrated that combination therapy with acyclovir and steroids led to better recovery of facial nerve function than steroids alone (Kinishi 2001). These findings were confirmed by responses to nerve excitability testing. Although there are no evidence-based dosing recommendations, published trials typically administered acyclovir at 800 mg by mouth 5 times/day for 7-10 days and prednisone at 1 mg/kg/day by mouth for 5 days followed by a taper (Murakami 1997).

RHS may present with a spectrum of clinical variations, including facial swellings that appear to be of odontogenic origin. As a result, dentists may be challenged to make the correct diagnosis of RHS versus an odontogenic infection in a timely manner. Appropriate supportive and prompt antiviral therapy combined with close follow-up is associated with significantly better functional recovery and outcomes (Kinishi 2001).

3.3. Postherpetic Neuralgia (PHN)

Postherpetic Neuralgia (PHN) continues to be a significant clinical problem, with an average of 25% of patients developing persistent neuropathic pain after acute herpes zoster (HZ) (Pavan-Langston; Schmader 2008).

This condition signals damage to the affected nerve. Patients may continue experiencing pain and discomfort even after blisters have already cleared. Usually, patients may feel a sharp or deep pain along the area were blisters first appeared. It is believed that repetitive painful stimuli that reach the central nervous system might lead to central sensitization of the nociceptive system, the most important mechanism underlying long-lasting chronic pain. Interventions that decrease the repetitive painful stimuli and inflammation during the acute phase of HZ may attenuate central sensitization and substantially reduce the incidence of chronic pain (Kelly 2001; Johnson 2002).

Treatment includes corticosteroids, which are used to treat pain, swelling and effectively reduces the risk of recurrence of post-herpetic neuralgia. Steroids were found to accelerate the resolution of acute neuritis and provide a clear improvement in quality-of-life measures in comparison to those patients treated with antivirals alone. The use of oral steroids had no effect on the development or duration of postherpetic neuralgia (Dworkin 2007).

Historically, epidural, intrathecal, and sympathetic nerve blocks have all been used in the treatment of pain caused by HZ and PHN. It was accepted by some investigators that nerve blocks do not provide lasting relief in established PHN, but injection of corticosteroids has been suggested to be of some benefit.

Prednisolone, a corticosteroid, is the most common drug administered in heavy doses to herpes patients. Moderate doses of prednisone 40 mg daily for 10 days, which is gradually tailed off over the following 3 weeks is an effective and safe regime which reduces the occurrence of postherpetic neuralgia.

The use of steroids in conjunction with an antiviral for uncomplicated herpes zoster is controversial. Steroids were found to accelerate the resolution of acute neuritis and provide a clear improvement in quality-of-life measures in comparison to those patients treated with antivirals alone. The use of oral steroids had no effect on the development or duration of postherpetic neuralgia. The optimal duration of steroid therapy is not known. If prescribed, it seems reasonable for steroids to be used concurrently with antiviral therapy. The duration of steroid use should not extend beyond the period of antiviral therapy. Steroids should not be given alone (without antiviral therapy) , owing to concern about the promotion of viral replication (Van Wijck 2006).

Intrathecal administration of corticosteroids has also been attempted. A trial involving a series of 4 intrathecal injections of methylprednisolone and lidocaine in patients with established postherpetic neuralgia demonstrated a significant and persistent reduction in pain among corticosteroid-treated patients when compared with untreated patients or those treated with intrathecal lidocaine alone. Kotani et al. published remarkable results after the intrathecal injection of methylprednisolone in patients with intractable PHN for at least 1 yr, which showed a 50% decrease in interleukin-8 concentrations, and this decrease correlated with the duration of neuralgia and with the extent of global pain relief (Kotani 2000).

The use of oral or epidural corticosteroids in conjunction with antiviral therapy has been found to be beneficial in treating moderate-to-severe acute zoster, but to have no effect on the development or duration of postherpetic neuralgia (Wood1994; Whitley 1996).

3.4. Temporomandibular joint disorders

Temporomandibular joint (TMJ) disorders are the main cause of chronic facial pain and a major cause of disability (Horten 1953).

Several decades ago, Toller suggested that intra-articular corticosteroid injections were only useful in adult patients with TMJ disorders; a single intra-articular injection resulted in resolution of TMJ pain and other symptoms in 62% of adult patients, compared to only 17% of pediatric patients (Toller 1977).

Intra-articular injection of steroids into the temporomandibular joint (TMJ) space is not a recent subject. Horten in 1953, was the first who reported this procedure which was based on the work of Hollander et al. in which they described the effect of intra-articular injection of hydrocortisone in various joint disorders. Since then, a number of papers have reported varying degrees of success (Wood1994; Hollander 1951).

A variety of methods are currently used for intra-articular corticosteroid injection to the TMJ, each with the goal of minimizing the potential for tissue damage. Intra-articular corticosteroid formulations are often diluted with a local anesthetic prior to injection into the TMJ (Kopp 1981; Alstergren 1996).

Numerous corticosteroid formulations are available for intra-articular injection, ranging from solutions of more soluble agents to suspensions of triamcinolone hexacetonide and other relatively insoluble steroids. Although the efficacy of various corticosteroids is presumed to differ, studies of this topic have been limited (Wise 2005; Gerwin 2006; Lavelle 2007).

Triamcinolone acetonide which has been used for intra-articular injection is very slowly absorbed from the injection sites. The dose ranges between 2 to 40 mg, depending upon the size of the joint injected (Hollander 1951; Silbermann1978). In cases of TMJ, the dose is usually 10 mg (Gray 1994). Triamcinolone acetonide is a safe drug, although anaphylactic shock following injection of triamcinolone acetonide has been reported. A repeat injection is occasionally used but the third injection should be used with caution as the expectation of further improvement decreases with successive injections (Larsson 1989).

In recent studies of juvenile idiopathic arthritis, intra-articular corticosteroid (triamcinolone) injections improved or even completely eliminated TMJ pain in 77-88% of children for several months (Arabshahi 2005; Cahill 2007; Ringold 2008).

In a controlled study of adults with TMJ arthritis, a single intra-articular injection of corticosteroid (methylprednisolone) diluted with lidocaine significantly reduced joint pain and other symptoms for 4-6 weeks. The pharmacologic effect of intra-articular methylprednisolone lasts 3-4 weeks, so these findings were consistent with the expected timeline of corticosteroid effect. No adverse events were reported (Alstergren 1996).

However, the efficacy may vary depending on the specific cause of TMJ degeneration.

3.5. Temporal arteritis (TA)

Temporal arteritis (TA) , also known as cranial arteritis or Giant Cell Arteritis (GCA) , was first clinically recognized in 1890 when Hutchinson described an 80-year-old man whose painful inflamed temporal arteries precluded his wearing a hat (Hutchinson 1890). In 1932, Horton et al. correlated the histopathologic features with the clinical features and applied the name arteritis temporalis. Other names include arteritis cranialis, Horton disease, granulomatous arteritis, and arteritis of the aged (Horton 1932).

There is universal agreement that glucocorticosteroids are the mainstay of treatment for GCA and should be initiated immediately and aggressively, with the goal of suppressing inflammation and preventing visual loss and ischemic stroke (Hayreh 2003; Rahman; Pipitone 2005).

Oral prednisone is first-line acute therapy for GCA. Although no consensus exists for initial dose of prednisone, the vast majority of patients respond to a dose of 1 mg/kg/d, or between 40 and 60 mg/d (Salvarani 2002; Weyand 2003). The dose of prednisone is lowered after 2–4 weeks, and slowly tapered over 9–12 months (Chan 2001).

Higher doses of 80 to 100 mg/d are suggested for patients with visual or neurological symptoms of GCA. IV pulse methylprednisolone has been proposed as an induction therapy, particularly in cases where vision is at risk (Rahman; Rahman 2005).

4. Medical emergencies in dental practice

4.1. Adrenal crisis prophylaxis

Patients with a history compatible with adrenal suppression and presenting with features of adrenal crisis should be treated urgently.

Acute adrenal crisis, with insufficiency of mineralocorticoids and glucocorticoids, is a medical emergency. The patient presents with abdominal pain, weakness, hypotension, dehydration, nausea and vomiting. Laboratory findings may include decreased sodium (hyponatraemia), elevated potassium (hyperkalaemia) , decreased blood glucose (hypoglycemia), acidosis and uraemia. Few patients have all these findings, with hypotension and nausea being most common.

Patients with secondary Addison's most typical presentation is of hypotension, and hyponatraemia without volume depletion. Additional symptoms may include fatigue, weakness, arthralgia, nausea, and orthostatic dizziness associated with hypotension.

Patients taking exogenous glucocorticoids. Exogenous glucocorticoids can cause adrenal gland suppression and resultant atrophy. With atrophy of the adrenal glands there is a decreased glucocorticoid response to stress, and this may precipitate an adrenal crisis (Edwards 1995).

4.1.1. Management

i. Intravenous fluids, in the form of 5% dextrose in normal saline, should be given to address the volume depletion that is often present.

ii. Primary adrenal insufficiency: start on 20–25 mg hydrocortisone per 24 h

iii. Secondary adrenal insufficiency: 15–20 mg hydrocortisone per 24 h; if borderline fail in cosyntropin test consider 10 mg or stress dose cover only

iv. Hydrocortisone should be given intravenously initially. If improvement has occurred within 24 hours, which is common, the hydrocortisone dose can be decreased. This can be changed to an oral formulation whenever the patient is stable. The dose can be decreased by one third to one half the dose daily until a maintenance dose of 20 mg in the morning and 10 mg in the afternoon or at night is attained. Some patients may need only a dose of 20 mg/day total (i.e., 20 mg every morning, or 15 mg in the morning and 5 mg in the afternoon or at night).

v. A search for the condition that precipitated the crisis, such as infection, should be undertaken. Treatment of the underlying cause should be instituted.

vi. Patients will not need mineralocorticoid replacement, because the renin-angiotensin-aldosterone axis is intact (Arlt 2009).

4.2. Anaphylaxis shock

Anaphylaxis is the quintessential disease of emergency medicine. The term anaphylaxis literally meaning "against protection" was introduced by Richet and Portier in 1902 (Brown 1995).

It is a potentially fatal illness with rapid onset that can affect young, healthy people. It must be diagnosed clinically, and is potentially curable if treated immediately (Golden 2007).

A systematic review of the literature has failed to demonstrate the effectiveness of any of these medications in the treatment of anaphylaxis (Ewan 2010).

Steroids are unlikely to be helpful in the treatment of acute anaphylaxis. They have a delayed onset of 4 to 6 hours. Steroids are thought to play a role in preventing rebound anaphylaxis; however, this has never been proven (Review Anaphylaxis in the emergency department 2008).

As with the antihistamines, despite their many theoretical benefits on mediator release and tissue responsiveness, there are no placebo-controlled trials to confirm the effectiveness of steroids in anaphylaxis.

Most clinicians however give prednisone 1 mg/kg up to 50 mg orally or hydrocortisone 1. 5-3 mg/kg IV particularly in patients with airway involvement and bronchospasm, based empirically on their important role in asthma (Soar 2008).

It is unclear if steroids prevent a biphasic reaction with recrudescence of symptoms following recovery, as supporting data are unconvincing (Lieberman 2005).

Steroids are of course fundamental to the management of recurrent idiopathic anaphylaxis (Ring 2002; Greenberger 2007).

5. Emergency drugs in general dental practice

5.1. Intracanal corticosteroid in root canal therapy

The application of antiinflammatory agents on exposed pulp tissue in an attempt to prevent or minimize inflammatory reaction and to favor healing has been investigated for a long time. Corticosteroid can be used as a dressing agent for deep cavities and exposed pulp tissue in order to control the inflammatory pulp response and reduce postoperative pain. The therapeutic effect of a corticosteroid agent seems to depend upon its potency, concentration and ability to diffuse into connective tissue (Holland 1991; Gordon Marshall 2002).

The results of studies that employ corticosteroids as a cavity liner support that these medications are effective in reducing or preventing postoperative thermal sensitivity. Researchers have shown that application of corticosteroid/ antibiotic association for short period of time was effective to control inflammation in the pulp tissue without determining changes in the healing process (Santini 1983).

Triamcinolone acetonide is a potent corticosteroid that could be used effectively to eliminate or at least reduce the severe inflammation that might occur secondary to endodontic treatment (Negm 2001).

5.2. Perioperative corticosteroid use in dentoalveolar surgery

Several authors have examined the effects of corticosteroids for prevention of pain and edema associated with oral surgery. Dental surgeons are often advised to use corticosteroids during and after third molar removal and other dentoalveolar surgery to reduce postsurgical edema. The most commonly used forms of corticosteroids in dentoalveolar surgery include dexamethasone (oral), dexamethasone sodium phosphate and dexamethasone acetate, and methylprednisolone acetate and methyl prednisolone sodium succinate. Dexamethasone has a longer duration of action than methlyprednisolone and is considered more potent (Alexander 2000).

Methylprednisolone has been used in a number of studies. Methylprednisolone is usually administered via the intramuscular or intravenous route though the possibility of topical (intraalveolar) application has been described, with a reduction in morbidity and possible side effects. This drug is five times more potent than cortisol, with scant associated saline retention and an intermediate duration of action (12-36 hours) (Micó-Llorens 2006; Leone 2007; Vegas-Bustamante 2008).

Based on the literature review, interim recommendations for the use of corticosteroids are proposed, including dosages and regimens that appear rational for oral, intramuscular, or intravenous corticosteroid administration before and after extractions and other dentoalveolar surgery. These largely empiric recommendations might require adjustment when evidence-based data become available in future studies

6. Adverse effects of steroids

Corticosteroids are chemical compounds of hormonal nature derived from cholesterol. Their biological power and actions depend on their chemical structure. Due to the remarkable anti-inflammatory and immunoregulatory effects of the corticosteroids, they have been employed as first step in the management of different diseases, and sometimes they are the only possible drug to use in daily medical practice. Despite their clinical efficacy, they can induce multiple severe adverse effects.

Adverse effects of corticosteroids may be due to local effects on the skin or mucosa at the site of or to systemic effects following absorption of the oral drugs. Systemic side effects are rarer than local side effects.

6.1. Systemic adverse effects

Systemic side effects occur because the steroids contained in the corticosteroid become absorbed into the blood stream and begin to affect other parts of the body, such as the adrenal gland (a gland that produces many of the body's natural steroids).

Systemic side effects can include (Lozada-Nur 1991; Bircher 1996):

- Hypothalamic-Pituitaryadrenal Axis and Secondary Adrenal
- Insufficiency
- Weight gain
- Osteoporosis
- Diabetes
- High Blood Pressure (hypertension)
- Psychological Effects
- Indigestion or Heartburn
- Cushing's Syndrome
- Moon Face
- Bone Damage
- Decreased Growth in Children
- Skin can become thin, easily bruised and slow to heal
- Avascular Necrosis (a painful bone condition)
- Glaucoma

6.2. Local adverse effects

While topical steroids have tremendous benefit in reducing inflammation, they also have significant side effects. Most of these side effects are seen with long-term use, but some may be noticed within days of starting therapy. The risk of side effects from topical corticosteroids is related to drug potency, duration of therapy, frequency of application and anatomical area. Local side effects can include (Key2003; Baid 2006):

- Tachyphylaxis
- Burning Mouth
- Hypogeusia

- Oral Hairy Leukoplakia
- Hypersensitive Reactions to the Drug
- Topical Steroid Allergy
- Skin Atrophy
- Striae - Stretch Marks
- Acne form/Rosacea like eruptions
- Candidosis
- Delayed Healing
- Fine Hair Growth

6.2.1. Special Considerations

Because corticosteroids cause the adrenal glands to slow or stop the production of cortisol, they cannot be discontinued abruptly. It takes some time for the adrenal glands to begin producing cortisol again. Gradually tapering the dose of corticosteroids allows the body to begin producing its own supply of cortisol again.

- Undertake weight bearing exercise (such as brisk walking)
- Stop smoking
- Avoid excess alcohol intake
- Contraindications for acute HSV Infection
- Creams are less effective in the mouth than ointments, and the ointment form is preferred.

7. Guidelines on the management of dental patients on corticosteroid therapy in community dental clinics

General dental procedures for patients receiving long-term steroid medication do not warrant supplementation with additional glucocorticoids.

The aims of these guidelines are to assist and support Dentists and Dental therapists when providing dental treatment to patients who are currently receiving, or who have received Corticosteroid therapy in the past twelve months.

7.1. For routine conservative dentistry or minor oral surgery (to include one simple extraction) under local anaesthesia

Although Opinions Conflict On Whether Any Significant Suppression Of Adrenal Function Occurs In Patients Taking Low Doses Of Steroids (Under 7. 5 Mg Prednisolone) Available Evidence Suggests That Supplementation Is Unnecessary For Local Anaesthetic Procedures.

7.2. For minor surgery under general anesthesia for patients undergoing general anesthesia for minor surgery

100 Mg Hydrocortisone Intramuscularly Should Be Administered And The Usual Glucocorticoid Medications Maintained.

7.3. For major surgery

100 Mg Hydrocortisone Delivered As A Bolus Pre-Operatively Followed By 50 Mg 8-Hourly For 48 Hours Is Adequate.

7.4. American Society of Anaesthesiologists (ASA) Physical Classification Status

1. A normal healthy patient
2. A patient with mild systemic disease
3. A patient with severe systemic disease
4. A moribund patient who is not expected to survive without surgery
5. A declared brain-dead patient whose organs are being removed for donor purposes.

Patients with ASA score 1 and 2 who are currently on or who have been on corticosteroids in the last year.

Patients with ASA score 3 and 4 who are currently on or who have been on corticosteroids in the last year.

Any patient that does not fit the above criteria or if the clinician is in any doubt then the patient should not be treated in the primary care setting and should be referred (Gibson 2004).

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8. References

Ad Hoc Working Group on Steroid-Sparing Criteria in Lupus. (2004). Criteria for Steroid-Sparing Ability of Interventions in Systemic Lupus Erythematosus: Report of a Consensus Meeting, Arthritis & Rheum, 50:3427

Adour KK, Wingerd J, Bell DN, Manhing JJ, Hurley JP. (1972). Prednisone treatment for idiopathic facial paralysis (Bell's palsy). N Engl J Med. 287: 1268–72.

Alexander RE, Throndson RR (2000). A review Of Perioperative Corticosteroid use In Dentoalveolar Surgery, Oral Surg Oral Med Oral Path . 90:406-15

Alstergren P, Appelgren A, Appelgren B, Kopp S, Lundeberg T, Theodorsson E. (1996). The effect on joint fluid concentration of neuropeptide Y by intra-articular injection of glucocorticoid in temporomandibular joint arthritis. Acta Odontol Scand. 54:1–7.

Arabshahi B, Dewitt EM, Cahill AM, Kaye RD, Baskin KM, Towbin RB, Cron RQ. (2005). Utility of corticosteroid injection for temporomandibular arthritis in children with juvenile idiopathic arthritis. Arthritis Rheum. 52:3563–3569.

Arlt W. (2009). The Approach to the Adult with Newly Diagnosed Adrenal Insufficiency J Clin Endocrinol Metab. 94 (4) :1059–1067

Bagan J, Lo Muzio L, Scully C. (2005). Mucosal disease series. Number III. Mucous membrane pemphigoid. Oral Dis. 11:197-218.

Baid SK, Nieman LK. (2006). Therapeutic doses of glucocorticoids: implications for oral medicine. Oral Dis. 12:436-42.

Bircher AJ, Pelloni F, Langauer Messmer S, Müller D. (1996). Delayed hypersensitivity reactions to corticosteroids applied to mucous membranes. Br J Dermatol. 35:310-3.

Borradori L, Bernard P. (2004). Vesiculobullous diseases: pemphoid group. eds. *Dermatology.* Philadelphia, PA: Mosby/Elsevier; 463-- 470

Brown AFT. (1995). Anaphylactic shock: Mechanisms and treatment. J Acc Emerg Med. 12:89-100.

Bruce A , Rogers RS III. (2007). New and old therapeutics for oral ulcerations. Arch Dermatol. 143: 519–23

Bystryn JC. Steinmann NM. (1996). The adjuvant therapy of pemphigus. Arch Dermatol. 132:203-12.

Cahill AM, Baskin KM, Kaye RD, Arabshahi B, Cron RQ, Dewitt EM et al. (2007). CT-guided percutaneous steroid injection for management of inflammatory arthropathy of the temporomandibular joint in children. AJR Am J Roentgenol. 188:182–186

Camisa C, Warner M. (1998). Treatment of pemphigus. Dermatol Nurs . 10 (2) :115-31.

Carbone M, Carrozzo M, Conrotto D, Garzino Demo P, Broccoletti R, Gandolfo S . (1997). Topical treatment of atrophic-erosive oral lichen planus with clobetasol in bioadhesive gel as well as chlorhexidine and miconazole in oral gel. Minerva stomatologica. 46 (7-8):423-8.

Carbone M, Conrotto D, Carrozzo M, Broccoletti R, Gandolfo S, Scully C. (1999). Topical corticosteroids in association with miconazole and chlorhexidine in the long-term managementof atrophic-erosive oral lichen planus: a placebo-controlledand comparative study between clobetasol and fluocinonide. Oral Dis . 5:44-9.

Cawson RA. (1968). Treatment of Oral Lichen Planus with Betamethasone. Br. Med. J. 2:86-89.

Chainani-Wu N, Silverman S Jr, Lozada-Nur F, Mayer P, Watson JJ. (2001). Oral lichen planus: patient profile, disease progression and treatment responses. J Am Dent Assoc. 132:901-9.

Chan CC, Paine M, O'Day J. (2001). "Steroid management in giant cell arteritis". Br J Ophthalmol 85 (9) :1061–4.

Chrousos GP. (2004). Adrenocorticosteroids and adrenocortical antagonists. In: Katzung BG, ed. Basic & Clinical Pharmacology. 9th ed. New York, NY: Lange Medical Books/McGraw-Hill. 641–660.

Cotell S, Robinson ND, Chan LS. (2000). Autoimmune blistering skin diseases . Am J Emerg Med . 18:288-99.

Dumas V, Roujeau JC, Wolkenstein P, Revuz J, Cosnes A. (1999). The treatment of mild pemphigus vulgaris and pemphigus foliaceus with a topical corticosteroid. Br J Dermatol. 140 (6) :1127-9.

Dworkin RH, Johnson RW, Breuer J, Gnann JW, Levin MJ, Backonja M, et al. (2007). Recommendations for the management of herpes zoster. Clin Infect Dis. 44 Suppl 1:S1-26.

Edwards CR, Baird JD, Frier B M, Shepherd J, Toft AD. (1995). Endocrine and metabolic diseases, including diabetes mellitus. In Edwards C R, Bouchier I A, Haslett C, Chilvers E R (eds) Davidson's principles and practice of medicine. 17th ed. pp 706-719. Edinburgh: ChurchillLivingstone

Edwards PC, Kelsch R. (2002). Oral Lichen Planus: Clinical Presentation and Management. J. C. D. 68:494-9.

Eisen D, Carrozzo M, Bagan Sebastian JV, Thongprasom K. (2005). Oral lichen planus: Clinical features and management. Oral Dis. 11:338-49.

Engström M, Berg T, Stjernquist-Desatnik A, Axelsson S, Pitkäranta A, Hultcrantz M et al. (2008). Prednisolone and valaciclovir in Bell's palsy: a randomised, double-blind, placebo-controlled, multicentre trial. Lancet Neurol. 7 (11) :993-1000.

Ewan PW, DuguéP, Mirakian R, Dixon TA, Harper JN, Nasser SM. (2010). BSACI guidelines for the investigation of suspected anaphylaxis during general anaesthesia. Clin Exp Allergy. 40 (1) :15.

Fassmann A, Dvo. akova N, Izakoviaova Holla L, Vanuk J, Wotke J. (2003). Manifestation of Pemphigus Vulgaris in the orofacial region. Case report. Scripta Medica (brno). 76:55–62.

Fellner MJ, Sapadin AN. (2001). Current therapy of pemphigus vulgaris. Mt Sinai J Med . 68 (4-5) :268–78.

Femiano F, Gombos F, Scully C. (2002). Pemphigus vulgaris with oral involvement: Evaluation of two different systemic corticosteroid therapeutic protocols. J EurAcadDermatolVenereol . 16 (4) :353-6.

Fernandes NC, Perez M. (2001). Treatment of pemphigus vulgaris and pemphigus foliaceus: experience with 71 patients over a 20 year period. Revista do Instituto de Medicina Tropical de Sao Paulo . 43 (1) , 33-36.

Field EA, Allan RB. (2003). Review article: oral ulceration – aetiopathogenesis, clinical diagnosisand management in the gastrointestinal clinic. Blackwell Publishing Ltd, Aliment

Fitzpatrick TB, Freedberg IM, Eisen AZ, Wolff K, Austen KF,Goldsmith LA, et al. (2008). Fitzpatrick's dermatology in general medicine (7th ed.). New York: McGraw-Hill.

Forman R, Koren G, Shear NH. (2002). Erythema mutliforme, Stevens-Johnson syndrome and toxic epidermal necrolysis in children: a review of 10 years' experience. Drug Saf. 25 (13) :965–972.

French L, Prins C. (2008). Erythema multiforme, Stevens-Johnson syndrome and toxic epidermal necrolysis. In: Bolognia JL, Jorizzo JL, Rapini RP, eds. Dermatology. 2nd ed. Philadelphia PA: Elsevier. 287–300.

Funauchi M, Ikoma S, Imada A, Kanamaru A. (1997). Combination of immune adsorption therapy and high dose methyl prednisolone in patients with lupus nephritis; possible indications in patients with early stage. J Clin Lab Immunol. 49: 47 – 57.

Gerwin N, Hops C, Lucke A. (2006). Intraarticular drug delivery in osteoarthritis. Advanced Drug Delivery Reviews. 58:226–242.

Gibson N, Ferguson JW. (2004). Steroid cover for dental patients on long-term steroid medication: proposed clinical guidelines based upon a critical review of the literature British Dental Journal . 197 (11) : 681–685

Gilden DH. (2004). Clinical Practice. Bell's palsy. The New England Journal of Medicine. 351 (13) :1323–31.

Golden DB. (2007). What is anaphylaxis? Curr Opin Allergy Clin Immunol. 7 (4) :331–6

Greenberger PA. (2007). Idiopathic anaphylaxis. Immunol Allergy Clin N Am 27:273-93.

Gonzalez-Moles MA, Morales P, Rodriguez-Archilla A, Isabel IR, Gonzalez-Moles S. (2002). Treatment of severe chronic oral erosive lesions with clobetasol propionate in aqueous solution. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 93:264-70.

Gordon Marshall J. (2002). Consideration of steroids for endodontic pain Endodontic Topics . 3, 41–51

Gray RJM, Davies SJ, Quayle AA. (1994). A clinical approach to temporomandibular disorders: Treatment planning, general guidelines and case histories. Br Dent J. 171: 171-178.

Greenspan JS, Yeoman CM, Harding SM. (1978). Oral Lichen Planus: A Double-Blind Comparison of Treatment with Betamethasone Valerate Aerosol and Pellets. Br. Dent. J. 144:83-84.

Grogan PM, Gronseth GS. (2001). Practice parameter: steroids, acyclovir, and surgery for Bell's palsy (an evidence-based review) : report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology. 56: 830-6.

Grover VK, Babu R, Bedi SPS. (2007). Steroid Therapy – Current Indications in Practice. Indian Journal of Anaesthesia. 51 (5) : 389-393

Harman KE, Albert S, Black MM. (2003). Guidelines for the managementof pemphigus vulgaris. Br J Dermatol. 149 (5) : 926-37.

Hashimoto T. (2008). Treatment strategies for pemphigus vulgaris in Japan. Expert OpinPharmacother. 9:1519-30.

Hato N, Yamada H, Kohno H, Matsumoto S, Honda N, Gyo K et al. (2007). Valacyclovir and prednisolone treatment for Bell s palsy: A multicenter, randomized, placebo-controlled study. Otology andNeurotology. 28:408–13.

Hayreh SS, Zimmerman B. (2003). Management of giant cell arteritis. Our 27-year clinical study: new light on old controversies. Ophthalmologica. 217:239–259

Hegarty AM, Hodgson TA, Lewsey JD, Porter SR. (2002). Fluticasone propionate spray and betamethasone sodium phosphate mouthrinse: a randomized crossover study for the treatment of symptomatic oral lichen planus. J AmAcad Dermatol. 47: 271 – 279.

Hench PS, Kendall EC, Slocumb CH, Polley HF. (1949). The effect of a hormone of the a drenal cortex (17-hydroxy-11-dehydrocorticosterone:compound E) and of pituitary adrenocorticotropic hormone on rheumatic arthritis. Proc Staff Meet Mayo Clin. 24:181

Hill G, Chauvenet AR, Lovato J, McLean TW. (2005). Recent steroid therapy increases severity of varicella infections in children with acute lymphoblastic leukemia. Pediatrics . 116 (4) :523–9.

Hiroshige K, Ikeda M, Hondo R. (2002). Detection of varicella zoster virus DNA in tear fluid and saliva of patients with Ramsay Hunt syndrome. Otol Neurotol. 23 (4) :602–7.

Hollander JL, Brown EM, Jessar RA, Brown CY. (1951). Hydrocortisone and Cortisone injected into arthritic joints: Comparative effect of and use of hydrocortisone as a local antiarthritic agent. JAMA. 147: 1629-1236.

Holland R, Okabe JA, Souza V, Saliba O. (1991). Diffusion of corticosteroid antibiotic solutions through human dentine. Rev Odontol UNESP. 20: 17-23.

Horten CP. (1953). The Treatment of Arthritic Temporomandibular Joints by Intra-articular Injection of Hydrocortisone. Oral Surg. 6: 826-829.

Horton B, Magath T, Brown G. (1932). An undescribed form of arteritis of the temporal vessels. Proc Staff Mtg MayoClin. 7:700-701.

Huff JC. (1992). Erythema multiforme and latent herpes simplex infection. Semin Dermatol. 11:207–10.

Hutchinson J. (1890). Diseases of the arteries. On a peculiar form of thrombotic arteritis of the aged which is sometimes productive of gangrene. ArchSurg. 1:323-9.

Hyvernat H, Roger PM, Pereira C, Saint-Paul MC, Vandenbos F, Bernardin G. (2005). Fatal varicella hepatitis in an asthmatic adult after short-term corticosteroid treatment. Eur J Intern Med. 16 (5) :361–2.

Ippolito A , Petri M. (2008). An Update on Mortality in Systemic Lupus Erythematosus, Clin Exp Rheumatol, 26 (5 Suppl 51) :S72-9.

Jacobson C, Cornell R, Savin R. (1986). A comparison of clobetasol propionate 0. 05% ointment and optimized betamethasone dipropionate 0. 05% ointment in the treatment of psoriasis. Cutis. 37:213-20.

Johnson RW. (2002). Consequences and management of pain in herpes zoster. J Infect Dis. 186 (suppl 1) :S83–S90

Joly P, Roujeau JC, Benichou J, Picard C, Dreno B, Delaporte E, et al. (2002). A comparison of oral and topical corticosteroids in patients with bullous pemphigoid. N Engl J Med. 346 (5) : 321-7.

Joly P, Benichou J, Lok C, Hellot MF, Saiag P, Tancrede-Bohin E et al. (2005). Prediction of survival for patients with bullous pemphigoid. Arch Dermatol. 141: 691-698.

Joly P, Roujeau JC, Benichou J, Delaporte E, D'Incan M, Dreno B et al. (2009). A comparison of two regimens of topical corticosteroids in the treatment of patients with bullous pemphigoid: A multicenter randomized study. J Invest Dermatol. 129 (7) : 1681-7.

Kakourou T, Klontza D, Soteropoulou F, Kattamis C. (1997). Corticosteroid treatment of erythema multiforme major (Stevens-Johnson syndrome) in children. Eur J Pediatr. 156:90–93.

Kardaun S, Jonkman M. (2007). Dexamethasone Pulse Therapy for Stevens-Johnson syndrome/toxic epidermal necrolysis. Acta Derm Venereol. 87:144–148.

Kasperkiewicz M, Enno Schmidt E. (2009). Current Treatment of Autoimmune Blistering Diseases. Current Drug Discovery Technologies, , 6, 270-280

Kelly DJ, Ahmad M, Brull SJ. (2001). Preemptive analgesia I: physiological pathways and pharmacological modalities. Can J Anaesth.:1000–10

Khare V. (2011). Discoid Lupus Erythematosus - A Case Report JIDA, Vol. 5, No. 1

Key SJ, Hodder SC, Davies R, Thomas DW, Thompson S. (2003). Perioperative corticosteroid supplementation and dento-alveolar surgery. Dent Update. 30:316-20.

Kinishi M, Amatsu M, Mohri M, Saito M, Hasegawa T, Hasegawa S. (2001). Acyclovir improves recovery rate of facial nerve palsy in Ramsay Hunt syndrome. Auris Nasus Larynx. 28 (3) :223–6. 9

Knudson RM, Kalaaji AN, Bruce AJ. . (2010). The management of mucous membrane pemphigoid and pemphigus. Dermatol Ther. 23:268-80.

Kopp S, Wenneberg B.(1981). Effects of occlusal treatment and intra-articular injections on temporomandibular pain and dysfunction. ActaOdontol Scand. 39:87–96.

Kotani N, Kushikata T, Hashimoto H, Kimura F, Muraoka M, Yodono M. et al. (2000).Intrathecal methyl prednisolone for intractable postherpetic neuralgia. N Engl J Med.; 343 (21):1514-9.

Lai DR, Chen HR. (1995). Clinical Evaluation of Different Treatment Methods for Oral Submucous Fibrosis. A 10-year experience with 150 cases, JOPM. 24, 402-614.

Lamoreux MR, Sternbach MR, Hsu WT. (2006). Erythema multiforme. Am Fam Physician. 74:1883–1888.

Larsson L. (1989). Anaphylactic shock after administration of triamcinolone acetonide in a 35 year old female. Scand J Rheamtol. 18: 441-444.

Lavelle W, Lavelle ED, Lavelle L. (2007). Intra-articular injections. Med Clin North Am. 91:241–250.

Leone M, Richard O, Antonini F, Rousseau S, Chabaane W, Guyot L, et al. (2007). Comparison of methylprednisolone and ketoprofen after multiple third molar extraction: a randomized controlled study. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 103:e7-9.

Lever WF, Schaumburg-Lever G. (1984). Treatment of pemphigus vulgaris. Results obtained in 84 patients between 1961 and 1982. Arch Dermato. 120 (1) :44–7.

Levin C, Maibach HI. (2002) :Topical corticosteroid-induced adrenocortical insufficiency: clinical implications. Am J Clin Dermatol. 3:141–7.

Lieberman P. (2005). Biphasic anaphylactic reactions. Ann Allergy Asthma Immunol . 95:217-26.

Lodi G, Scully C, Carrozzo M, Griffiths M, Sugerman PB, Thongprasom K. (2005). Current controversies in oral lichen planus: report of an international consensus meeting – Part 1. Viral infections and aetiopathogenesis. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 100: 40-51.

Lo Muzio L, della Valle A, Mignogna MD, Pannone G, Bucci P, Bucci E, et al. (2001). The treatment of oral aphthous ulceration or erosive lichen planus with topical clobetasol propionate in three preparations: a clinical and pilot study on 54 patients. J OralPathol Med . 30:611-7.

Lozada –Nur F, Silverman S Jr. (1980). Topically applied fluocinonide in an adhesive base in the treatment of oral vesiculoerosive diseases. Arch Dermatol . 116:898-901.

Lozada-Nur F, Huang MZ, Zhou GA. (1991). Open preliminary clinical trial of clobetasol propionate ointment in adhesive paste for treatment of chronic oral vesiculoerosive diseases. Oral Surg Oral Med Oral Pathol . 71:283-7.

Lozada-Nur F, Miranda C, Maliksi R. (1994). Double-blind clinical trial of 0. 05% clobetasol propionate ointment in orobase and 0. 05% fluocinonide ointment in orobase in the treatment of patients with oral vesiculoerosive diseases. Oral Surg Oral Med Oral Pathol. 77: 598–604.

MacPhee IT, Sircus W, Farmer ED, Harkness RA, Cowley GC. (1968). Use of steroids in treatment of aphthous ulceration. Br Med J. 2:147-9.

Mamelak AJ, Eid MP, Cohen BA, Anhalt GJ. (2007). Rimximab therapy in severe juvenile pemphigus vulgaffs. Cutis. 80 (4) , 335–340.

Martinez AE, Atherton DJ. (2000). High-dose systemic corticosteroids can arrest recurrences of severe mucocutaneous erythema multiforme. Pediatr Dermatol. 17 (2) :87–90.

Mehdipour M, Taghavi Zenouz A, Bahramian A, Yazdani J, Poura- libaba F,Sadr K. (2010). Comparison of the Effect of Mouthwashes with and without Zinc and Fluocinolone on the Healing Process of Erosive Oral Lichen Planus. JODDD. 4 (1) :25-28

Mentink LF, Mackenzie MW, Tóth GG, Laseur M, Lambert FP, Veeger NJ, et al. (2006). Randomized controlled trial of adjuvant oral dexamethasone pulse therapy in pemphigus vulgaris: PEMPULS trial. Arch Dermatol. 142 (5) :570-6.

Merchant HW, Gangarosa LP, Glassman AB, Sobel RE. (1978). Betamethasone-17-benzoate in the treatment of recurrent aphthous ulcers. Oral Surg. 45:870-5.

Micó-Llorens JM, Satorres-Nieto M, Gargallo-Albiol J, Arnabat-Domínguez J, Berini-Aytés L, Gay-Escoda C. (2006). Efficacy of methylprednisolone in controlling complications after impacted lower third molar surgical extraction. Eur J Clin Pharmacol. 62:693-8.

Mondino BJ, Brown SI. (1981). Ocular cicatricial pemphigoid. Ophthalmology. 88:95-100.

Murakami S, Hato N, Horiuchi J, Honda N, Gyo K, Yanagihara N. (1997). Treatment of Ramsay Hunt syndrome with acyclovir-prednisone: significance of early diagnosis and treatment. Ann Neurol. 41:353-7.

Mutasim DF, Cincinatti. (2004). Management of Autoimmune Bullous Disease: Pharmacology and Therapeutics, J. Am. Acad. Dermatol. 51:859-77.

Natah SS, Konttinen YT. (2004). Recurrent Aphthous Ulcers Today: a review of the growing knowledge, IJOMS. 33:221-34.

Negm M M. (2001). Intracanal use of a Corticosteroid – antibiotic compound for the management of post treatment endodontic pain. Triplo. 92:435-9.

Oztas P, Onder M, Ilter N, Oztas MO. (2003). Childhood lichen planus with nail involvement: a case. Turkish J Pediatrics. 45:251-253.

Panjwani S. (2009). Early Diagnosis and Treatment of Discoid Lupus Erythematosus. J Am Board Fam Med. . 22 (2) :206-213.

Pavan-Langston D. (2008). Herpes zoster antivirals and pain management. Ophthalmology. 115:S13–S20

Pedersen A, Klausen B. (1984). Glucocorticosteroids and Oral Medicine, Oral Pathology & Medicine J. 13:1-15

Pimlott SJ, Walker DM. (1983). A controlled clinical trial of the efficacy of topically applied fluocinonide in the treatment of recurrent aphthous ulceration. Br Dent J. 154:174-7

Pipitone N, Boiardi L, Salvarini C. (2005). Are steroids alone sufficient for the treatment of giant cell arteritis? Best Pract Res Clin Rheumatol. 19:277–292

Prajapati V, Mydlarski PR. (2008). Advances in pemphigus therapy. Skin Therapy Lett. 13:4-7.

Rabiyi M, Sahebjamee M. (2003). Effect of aqueous triamcinolone actonide 0. 2% suspension in treatment oforal lichen planus. Journal Medical Faculty GuilanUniversity of Medical Sciences. 12: 6 – 14.

Rahman W, Rahman FZ. (2005). Major review – giant cell (temporal) arteritis: an overview and update. Surv Ophthalmol. 50:415–428

Ramsey MJ, Der Simonian R, Holtel MR, BurgessLPA. (2000). Corticosteroid treatment for idiopathic facialnerve paralysis: a meta-analysis. Laryngoscope. 110: 335–41.

Ratnam KV, Phay KL, Tan CK. (1990). Pemphigus therapy with oral prednisolone regimens: A 5-year study. Int J Dermatol. 29 (5) :363-7.

Rees TD, Binnie WH. (1996). Recurrent aphthous stomatitis. Dermatol Clin. 14:243-56.

Reich RF, Kerpel SM. (1998). Differential Diagnosis and Treatment of Ulcerative, Erosive and Vesiculobullous Lesions of Oral Mucosa, Oral and Maxillofacial Surgery Clinics of North America. 10: 95-129.

ReviewAnaphylaxis in the emergency department. (2008). a paediatric perspective. Curr Opin Allergy Clin Immunol. 8 (4) :321-9.

Ring J, Darsow U. (2002). Idiopathic anaphylaxis. Curr Allergy Asthma Reports . 2:40-5.

Robillard RB, Hilsinger RL Jr, Adour KK. (1986). Ramsay Hunt facial paralysis: clinical analyses of 185 patients. Otolaryngol Head Neck Surg. 1:292–7.

Ringold S, Torgerson TR, Egbert MA, Wallace CA. (2008). Intraarticular corticosteroid injections of the temporomandibular joint in juvenile idiopathic arthritis. J Rheumatol. 35:1157–1164.

Roed-Petersen B, Roed-Petersen J. (1992). Occlusive treatment of atrophic and erosive oral lichen planus with clobetasol propionate 0. 05% ointment (Dermovat) [Danish]. Tandlaegernes Tidsskr. 1:4- 7.

Ruocco E, Aurilia A, Ruocco V. (2001). Precautions and suggestions for pemphigus patients. Dermatology. 203 (3) :201–7.

Salvarani C, Cantini F, Bolardi L, Hunder GG. (2002). Polymyalgia rheumatica and giant-cell arteritis. N Engl J Med. 347:261–271

Santini A. (1983). Assessment of the pulpotomy technique in human first permanent mandibular molars. Br Dent J. 155: 151-4.

Setterfield JF, Black MM , Challacombe SJ. (2000). The management of oral lichen planus. Clin Exp Dermatol. 25: 176–82.

Schmader KE, Dworkin RH. (2008). Natural history and treatment of herpes zoster. J Pain. 9:S3–S9

Scully C, Bagan J. (2008). Oral mucosal diseases: erythema multiforme. Br J Oral Maxillofac Surg. 46:90–95.

Scully C, Lo Muzio L. (2008). Oral mucosal diseases: mucous membrane pemphigoid. Br J Oral Maxillofac Surg. 46:358-66.

Shin HT, Chang MW. (2001). Drug eruptions in children. Curr Probl Pediatr. 31:207–34.

Shafshak TS, Essa AY, Bakey FA. (1994). The possible contributing factors for the success of steroid therapy in Bell's palsy: a clinical and electrophysiological study. J Laryngol Otol. 108: 940-3.

Ship JA. (1996). Recurrent aphthous stomatitis. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 81:141-7.

Silbermann M, Moredohvich D, Toister Z, Azaria N. (1978). Mechanisms involved in mandibular condylopathy secondary to intra-articular injections of glucocorticoids. J Oral Surg. 36: 112-117.

Silverman S Jr, Gorsky M, Lozada-Nur F, Giannotti K. (1991). A prospective study of findings and management in 214 patients with oral lichen planus. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 72:665-70

Sirois D, Leigh JE, Sollecito TP. (2000). Oral pemphigus vulgaris preceding cutaneous lesions: recognition and diagnosis. J Am Dent Assoc. 131, 1156-1160.

Soar J, Pumphrey R, Cant A. (2008). Emergency treatment of anaphylactic reactions. Guidelines for health care providers. Resuscitation . 77:157-69

Sullivan FM, Swan IR, Donnan PT, Morrison JM, Smith BH, McKinstry B, et al. (2007). Early treatment with prednisolone or acyclovir in Bell's palsy. N Engl J Med. 357 (16) :1598-607.

Taverner D. (1954). Cortisone treatment of Bell's palsy. Lancet. ii:1052–4.

Thompson AC, Nolan A, Lamey J. (1989). Minor aphthous oral ulceration: a double-blind cross-over study of beclomethasone dipropionate aerosol spray. Scott Med J. 34:531

Thongprasom K, Luangjarmekorn L, Sererat T, Taweesap W. (1992). Relative efficacy of fluocinolone acetonide compared with triamcinolone acetonide in treatment of oral lichen planus.

Thongprasom K, Luengvisut P, Wongwatanakij A, Boonjatturus C. (2003). Clinical evaluation in treatment of oral lichen planus with topical fluocinolone acetonide: a 2-year follow-up. J Oral Pathol Med. 32: 315 – 322.

Thost A. (1911). Der chronische schleimhaut-pemphigus der oberen luftwege. Arch Laryng Rhinol. 25:459-78.

Toller PA. (1977). Use and misuse of intra-articular corticosteroids in treatment of temporomandibular joint pain. Proc Roy Soc Med. 70:461–463.

Toth GG, Jonkman MF. (2001). Therapy of pemphigus . Clin Dermatol. 19 (6) :761–7

Tht Yu J, Chong L, Kc Lee L. (2007). Pemphigoid, benign mucous membrane Hong Kong Med J. 13:157-60

Tyldesley WR, Harding SM. (1977). Betamethasone Valerate Aerosol in the Treatment of Oral Lichen Planus. Br. J. Dermatol. 96:659-662.

Uri N, Greenberg E, Kitzes-Cohen R, Doweck I. (2003). Acyclovir in the treatment of Ramsay Hunt syndrome. Otolaryngol Head Neck Surg. 129 (4) :379–81.

Valença MM, Valença LP, Lima MC. (2001). Idiopathic facial paralysis (Bell's palsy) : a study of 180 patients . Arquivos de Neuro-Psiquiatria. 59:733–9.

Van de Steene V, Kuhweide R, Vlaminck S, Casselman J. (2004). Varicella zoster virus: beyond facial paralysis. Acta Otorhinolaryngol Belg. 58 (1) :61–6

Van Wijck AJ, Opstelten W, Moons KG, van Essen GA, Stolker RJ, Kalkman CJ, et al. (2006). The PINE study of epidural steroids and local anaesthetics to prevent postherpetic neuralgia: a randomised controlled trial. Lancet; 367 (9506) :219-24.

Vegas-Bustamante E, Micó-Llorens J, Gargallo-Albiol J, Satorres-Nieto M, Berini-Aytés L, Gay-Escoda C. (2008). Efficacy of methylprednisolone injected into the masseter muscle following the surgical extraction of impacted lower third molars. Int J Oral Maxillofac Surg. 37:260-3.

Vincent SD, Lilly GE. (1992). Clinical, historic, and therapeutic features of aphthous stomatitis. Literature review and open clinical trial employing steroids. Oral Surg Oral Med Oral Pathol. 74:79-86.

Vincent SD, Fotos PG, Baker KA, Williams TP. (1990). Oral Lichen Planus: The Clinical, Historical, and Therapeutic Features of 100 Cases. Oral Surg. Oral Med. Oral Pathol. 70:165-171 .

Volcheck GW. (2004). Clinical evaluation and management of drug hypersensitivity. Immunol Allergy Clin North Am. 24:357–71.

Voute AB, Schulten EA, Langendijk PN, Kostense PJ, van der Waal I. (1993). Fluocinolone in an adhesive base for treatment of oral lichen planus. A double-blind, placebo controlled clinical study. Oral Surg Oral Med Oral Pathol. 75: 181 – 185.

Werth VP. (1996). Treatment of pemphigus vulgaris with brief , high-dose intravenous glucocorticoids. Arch Dermatol. 132:1435 – 1439

Westerhof W. (1989). Treatment of bullous pemphigoid with topical clobetasol propionate. J Am Acad Dermatol. 20: 458–61.

Weyand CM, Goronzy JJ. (2003). Medium- and large-vessel vasculitis. N Engl J Med. 349:160–169

Whitley RJ, Weiss H, Gnann JW Jr, Tyring S, Mertz GJ, Pappas PG et al. (1996). Acyclovir with and without prednisone for the treatment of herpes zoster. A randomized, placebo-controlled trial. The National Institute of Allergy and Infectious Diseases Collaborative Antiviral Study Group. Ann Intern Med. 125 (5) :376-83.

Williamson IG, Whelan TR. (1996). The clinical problem of Bell's palsy: is treatment with steroids effective? Br J Gen Pract. 46: 743-7.

Wise C. (2005). In: Kelley's Textbook of Rheumatology. Seventh. Harris ED Jr, Budd RC, Genovese MC, Firestein GS, Sargent JS, Sledge CB, editors. Elsevier Saunders; Philadelphia:pp. 695–696.

Wojnarowska F, Kirtschig G, Highet AS, Venning VA, Khumalo NP. (2002). Summary of Recommendations for Management of Bullous Pemphigoid. Br J Dermatol. 147: 214-221

Wolverton SE. (2007). Systemic corticosteroids. In: Wolverton SE, ed. Comprehensive Dermatologic Drug Therapy. 2nd ed. Philadelphia, PA: Saunders Elsevier. 127–161.

Woo SB, Sonis ST. (1996). Recurrent aphthous ulcers: a review of diagnosis and treatment. J Am Dent Assoc. 127:1202-13.

Wood MJ, Johnson RW, McKendrick MW, Taylor J, Mandal BK, Crooks J. (1994). A randomized trial of acyclovir for 7 days or 21 days with and without prednisolone for treatment of acute herpes zoster. N Engl J Med. 330 (13) :896-900.

Yazici H, Barnes CG. (1991). Practical treatment recommendations for pharmacotherapy of Behc¸et's syndrome. Drugs. 42:796–804.

Yeung AK, Goldman RD. (2005). Use of steroids for erythema multiforme in children. Can Fam Physician. 51 (11) :1481–1483.

Zegarelli EV, Kutscher AH, Mehrhof A. (1969). Long-lasting lozenges with triamcinolone acetonide. Treatment of erosive lichen planus of oral mucosa. N Y State J Med . 69:2463-4

Zegarelli DJ. (1980). Topical and intralesional steroid therapy of oral lichen planus. N Y State Dent J. 46:432, 434-432, 436.

Zegarelli DJ. (1983). Multimodality steroid therapy of erosive and ulcerative oral lichen planus. J Oral Med . 38:127-30.

Zimmermann R, Faure M, Claudy A. (1999). Prospective study of treatment of bullous pemphigoid by a class I topical corticosteroid. Ann Dermatol Venereol. 126: 13–16.