ASM18 Annual Spring Meeting

Ontario Dental Association

Oral Health Strategy: Oral Manifestations of Drugs Taken by Patient with Immunological Disease

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Objectives

- Medication classes
  - Mechanism of action
  - Conditions treated
  - Oral complications
    - Short-term
    - Long-term
  - Interactions with commonly prescribed medications
- Impact on dental management- Cases

Disease-Modifying Antirheumatic Drugs (DMARDS)

- Suppress the body's overactive immune and/or inflammatory systems
- Work over weeks to months vs. NSAIDS and corticosteroids
- Often used in combination with NSAIDS and corticosteroids or other DMARDS

Disease-Modifying Antirheumatic Drugs (DMARDS)

DMARD	Mechanism of Action	Condition Treated
Methotrexate	Folic acid analogue: (-) purine and pyrimidine synthesis. Anti-inflammatory effects	Cancer, RA, Other rheumatic dis.- decrease inflammation and joint damage
Sulfasalazine	Anti-inflammatory and/or immunomodulatory	RA, ankylosing spondylitis, inflammatory bowel disease
Hydroxychloroquine	anti-malarial, exact mech of action for rheumatic disease is unknown	Arthritis management, RA, SLE, Sjogren's
Cyclosporine	Inhibit calcineurin: (-) inflammatory cytokines. Decrease proliferation of T cells	RA, immunosuppression in solid organ transplantation

DMARDS- Case 1

- Developed painful oral lesions approximately one month ago coinciding with RCT. Had skin lesions on leg develop at the same time.
- Diagnosed with “thrush” and was given both antibiotics and Nystatin with minor benefit.
- Current oral pain is an 8/10, described as "burning" in character and states it prevents her from eating comfortably.
- Diagnosed with cutaneous lichen planus by a Dermatologist and treated with topical Triamcinolone for this complaint.
- A previous biopsy of the oral lesions has not been completed. She had no other oral complaints.

DMARDS- Case 1

PMH:

- RA
- HTN
- Hypercholesterolemia
- Vitamin B12 deficiency
- Ischemic colitis
- Stomach ulcers
- Osteoporosis
- Degenerative joint disease
- History of breast cancer 1998 (surgery, RT and tamoxifen)
- Bilateral knee, right hip and right shoulder replacement.

DMARDS- Case 1

MEDICATIONS

- Dolobid-500 mg daily
- Opana ER (Oxymorphone Hydrochloride) ; 30 mg daily
- lisinopril 5 mg oral tablet: 5 mg, 1 tablet, ORAL BID
- furosemide 20 mg oral tablet: 20 mg, 1 tablet, ORAL, Daily
- **Methotrexate** 7.5 mg oral tablet Wednesdays
- **Prednisone** 5 mg oral tablet: 5 mg, 1 tablet, ORAL, qAM
- Myrbetriq 50 mg daily
- **Folic acid** 1 mg oral tablet: 2 mg, 2 tablet, ORAL, qHS , (total 2 mg),
- Cymbalta 60 mg oral delayed release capsule: 60 mg, 1 capsule, ORAL, qAM
- Simvastatin 40 mg daily
- ASA 81 mg oral enteric coated tablet: 81 mg, 1 tablet, ORAL, QODay
- **Actemra** (Tocilizumab) infusion-monthly
- **Prolia** 60 mg/mL subcutaneous solution, q 6 months

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DMARDS- Case 1

- Management
  - Physician decreased methotrexate dose to 2.5 mg/week
  - MBX rinse for oral pain

DMARDS- Case 1

- Pain lower right started 7 months later with swelling and pain – lower right.
  - Prolia for 2 years
  - Initially managed with clindamycin 300 mg QID for 1 week managed swelling of the jaw, but continued to return

DMARDS- Case 1

- Extracted by OMFS in our community
- Presented back to our office 11 months after extraction with MRONJ - 9x6 mm and 8x3 mm exposed bone.
  - Placed on pentoxifylline 400 mg bid, Vitamin E 400 mg bid, amoxicillin 500 mg q6h and chlorhexidine bid.
  - One month later- one area of bone removed- 5x8 mm
  - 2 months later- 2 smaller areas of bone removed- 5x3 and 8x3mm
  - 3 months later- complete resolution

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Drug-related

- Dilantin-50%
- Calcium channel blockers (Nifedipine most common)-25%
- Cyclosporine-25%
- Sodium Valproate less frequent
- Role of oral hygiene, CSA least responsive.

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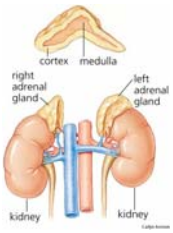
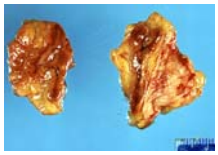
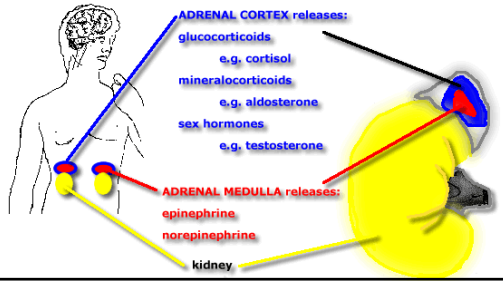
Corticosteroids

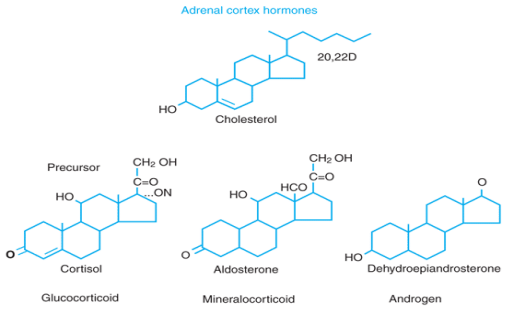
Adrenal Glands - Anatomy





Adrenal Glands



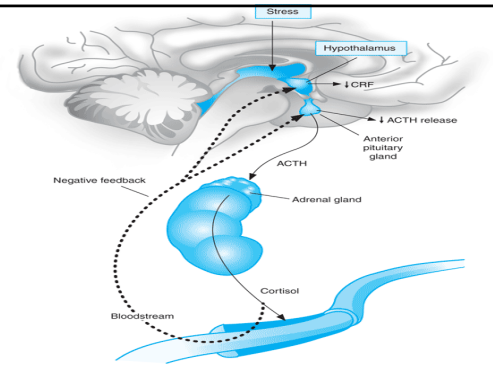


Secretion and regulation

Glucocorticoids - Cortisol
- 15~30mg/day, may up to 300mg under stress
- Regulated by ACTH (HPA axis)

Mineralcorticoids - Aldosterone
- 50~250μg/day
- Regulated by renin-angiotensin system
- ACTH

Androgen
- ACTH



Mineralocorticoids – Summary

Aldosterone

- Regulates the balance of water and electrolytes
- Acts primarily on the kidney tubules
- Active reabsorption of sodium, passive reabsorption of water
- Active secretion of potassium in the cortical collecting tubule
- Increase BP and blood volume

Physiology of Glucocorticoids

Metabolic effects

- Carbohydrate
  - Increase blood sugar
  - Increase gluconeogenesis in liver (and kidney)
  - Increase hepatic glycogenesis
  - Increase cellular resistance to insulin: decrease glucose uptake in tissues
- Lipid
  - Increase lipolysis
- Protein
  - Increase proteolysis

Immunologic effects

- Impairs cell-mediated immunity (T-lymphocyte dependent)
- Lymphotoxic
- Little effect on humoral immunity
  - no decrease in existing Ab levels
  - B-cell response to antigen not inhibited

Anti-inflammatory effects

- Hench (1949) – high dose cortisol in Cushingoid patients ameliorated RA symptoms
- Only in supraphysiological doses
- Decrease leukocyte migration, bradykinin
- Block histamine, interleukin-1 and 2, plasminogen activating factor (PAF)
- Decrease vascular permeability
- Decrease circulating eosinophil, basophil, and lymphocyte counts
- Increase ANC, platelet, WBC and RBC (dec. erythrophagocytosis)

Connective tissue effects

- Decrease collagen formation
- Impair granulation tissue formation and wound healing

Calcium and bone effects

- Decrease serum calcium
- Accelerate osteoporosis

Circulatory effects

- Increase response to catecholamines
- Increase cardiac output

Renal effects

- Increase renal blood flow and glomerular filtration rate
- Increase free water clearance
- Inhibit vasopressin

Central nervous system effects

- Increase mood lability
- Cause euphoria
- Produce psychosis
- Decreased libido

Eye effects

- May induce posterior subcapsular cataracts
- Glaucoma

Cushing Syndrome

1) – too much pituitary gland function
   ACTH ↑
   - Pituitary tumor (Cushing disease)
   - Ectopic ACTH syndrome

2) – too much adrenal function
   ACTH ↓
   - Primary adrenal tumor
   - Adrenocortical carcinoma

3) – Iatrogenic ACTH ↓
   - Long term steroid use

Cushing Syndrome

Central obesity
Moon face
Buffalo hump
Proximal muscle weakness
Psychological disturbance
Stretch mark, skin thinning
Pigmentation

Systemic steroid treatment – incomplete list

Respiratory disease, Crohn's disease, psoriasis, croup, immunosuppression, chickenpox, rheumatoid arthritis, temporal arteritis, Bell's palsy, transplantation, hypopituitarism, hypoadrenalism, systemic lupus erythematosus, polyarteritis nodosa, dermatomyositis and polymyositis, polymyalgia rheumatica, Wegener's granulomatosis, sarcoidosis, eczema, pemphigus, ulcerative colitis, hemolytic anemia, idiopathic thrombocytopenic purpura, acute leukemia, cerebral edema, etc.

Comparative steroid potencies

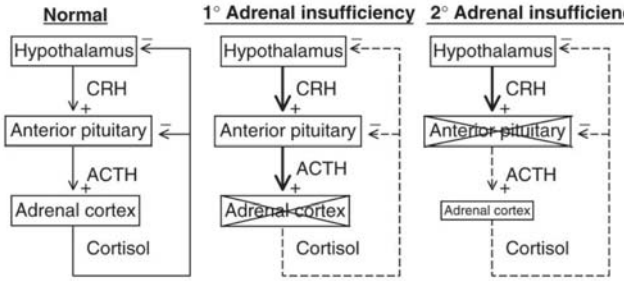
Name	Glucocorticoid potency	Mineralocorticoid potency	Duration of action ($t_{1/2}$ in hours)
Hydrocortisone (cortisol)	1	1	8
Cortisone acetate	0.8	0.8	oral 8, intramuscular 18+
Prednisone	3.5-5	0.8	16-36
Prednisolone	4	0.8	16-36
Methylprednisolone	5-7.5	0.5	18-40
Dexamethasone	25-80	0	36-54
Betamethasone	25-30	0	36-54
Triamcinolone	5	0	12-36
Beclometasone	8 puffs 4 times a day=14 mg oral prednisone once a day	-	-
Fludrocortisone acetate	15	200	-
Deoxycorticosterone acetate (DOCA)	0	20	-
Aldosterone	0.3	200-1000	-

Adrenal Insufficiency

The physiological definition of adrenal insufficiency is the inadequate secretion of cortisol from the adrenal gland regardless of the cause

Chronic adrenal insufficiency (Addison's disease)
- Primary
- Secondary

Acute adrenal insufficiency
- Adrenal crisis (Addisonian crisis)



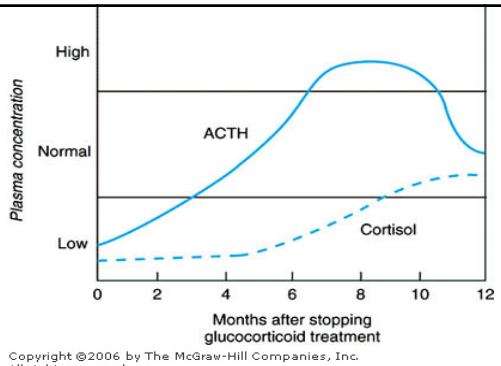
Causes of Adrenal Insufficiency

Primary Adrenal Insufficiency

- Autoimmune
- Infection (e.g., tuberculosis, fungal infections, and HIV)
- Tumors metastatic to the adrenal glands
- Infiltration (e.g., hemochromatosis)
- Adrenal hemorrhage
- Congenital adrenal hypoplasia (e.g., DAX1 and SF1 mutations)
- ACTH resistance syndromes (e.g., mutation in the ACTH receptor [MC2R])
- Surgical (e.g., bilateral adrenalectomy for adrenal cancer)

Secondary Adrenal Insufficiency

- Discontinuation of chronic pharmacological glucocorticoid therapy (adrenal atrophy)
- Hypopituitarism (inadequate ACTH secretion)
- After removal of an ACTH-secreting tumor or cortisol-secreting adrenal tumor (suppression of the hypothalamus and normal corticotrophs)
- Pituitary apoplexy
- Postpartum pituitary apoplexy (Sheehan's syndrome)
- Granulomatous disease (e.g., sarcoid)
- Tumors invading the pituitary fossa
- Isolated ACTH deficiency (e.g., POMC processing defect)



Addison's Disease

signs and symptoms

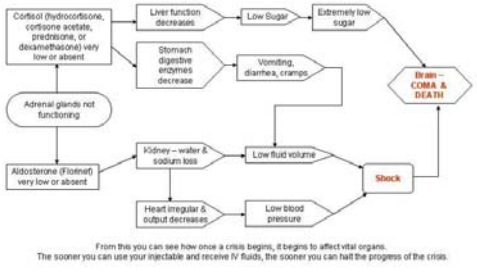
- Chronic fatigue
- Muscle weakness
- Weight loss, loss of appetite
- Nausea, diarrhea, vomiting
- Hypotension
- Hyperpigmentation
- Depression
- Hypoglycemia
- Increase eosinophils
- Dehydration
- Tachycardia
- Diaphoresis
- Hyponatremia
- Hyperkalemia

Frequency of Symptoms and Signs in Addison's disease (%)	
Weakness	99
Pigmentation of skin	98
Weight loss	97
Anorexia, nausea, and vomiting	90
Hypotension (<110/70)	87
Pigmentation of mucous membranes	82
Abdominal pain	34
Salt craving	22
Diarrhea	20
Constipation	19
Syncope	16
Vitiligo	9

Adrenal Crisis - Causes

- May occur in the course of treatment of chronic insufficiency or as its presenting manifestation
- Primary adrenal insufficiency >> secondary
- Stress (eg, trauma, surgery, infection, or prolonged fasting)
- Sudden withdrawal of high dose adrenocortical hormone
- Bilateral adrenalectomy or removal of a functioning adrenal tumor that had suppressed the other adrenal
- Injury to both adrenals (trauma, hemorrhage, infection, anticoagulant, thrombosis or metastatic carcinoma
- Pituitary necrosis, or when thyroid hormone replacement is given to a patient with adrenal insufficiency

Addison Crisis Pathway



Adrenal Crisis
key features for diagnosis

- Weakness, abdominal pain, fever, confusion, nausea, vomiting, and diarrhea.
- Low blood pressure, dehydration; skin pigmentation may be increased.
- Serum potassium high, sodium low, BUN high.
- Cosyntropin (ACTH1–24) unable to stimulate a normal increase in serum cortisol

Adrenal Crisis – Management

- IV line
- 100 mg hydrocortisone
  - Stat then q6-8h
- Fluid and electrolyte replacement
- Correction of hypoglycemia

Risk of adrenal crisis in dental patients

Results of a systematic search of the literature

Mohd W. Khalaf, BDS; Ruba Khader, BDS; Gregory Cobetto, DMD; Juan Fernando Yepes, DDS, MD, MPH, DrPH; Dennis G. Karounos, MD; Craig S. Miller, DMD, MS

JADA 2013;144(2):152-160.

Criteria for diagnosis of adrenal crisis.*

FEATURE INVOLVED	MAJOR CRITERIA	MINOR CRITERIA
Gastrointestinal	Abdominal pain, nausea, vomiting	Loss of appetite, weight loss, craving of salty food
Constitutional	Hyperthermia (fever) or hypothermia (loss of consciousness, toxic appearance)	Pale, fatigue, dizziness, unusual sweating, slow sluggish movement, confusion, headache
Cardiovascular	Hypotension, features of shock (such as loss of consciousness)	Rapid heart rate/pulse
Laboratory Test Abnormality	Hyponatremia, hyperkalemia, metabolic acidosis, low cortisol levels, low stimulation test results	Concurrent serum hypoglycemia
Other	None	Hyperpigmentation of skin or mucosa

* Each case was categorized according to the number and type (major or minor) of criteria met. The categories were as follows: consistent with adrenal crisis—two or more major criteria from separate categories that include at least one laboratory test abnormality; suggestive of adrenal crisis—at least one major criterion plus one or more minor criteria; unlikely adrenal crisis—no major criteria plus one or more minor criteria.

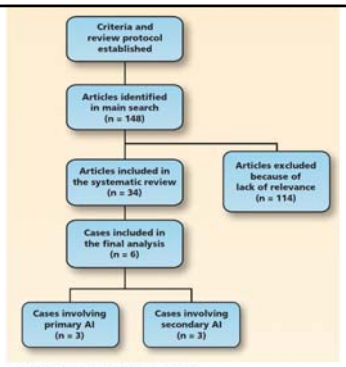


Figure 1. Search strategy. AI: Adrenal insufficiency.

Case reports of adrenal crisis in dental settings.

DENTAL CASES	AGE (YEARS), SEX	PREDISPOSING CONDITION	DENTAL CARE-RELATED FACTORS	MAJOR CRITERIA	MINOR CRITERIA	EVIDENCE SUPPORTING ADRENAL CRISIS	PROPHYLACTIC STEROID COVERAGE/ SURVIVED
Parnell, 1964[16]	57, male	Secondary AI,* fractured mandible, delayed wound healing, prednisolone therapy for five years	Extraction resulting in jaw fracture requiring immobilization, fracture site debridement, general anesthesia (halothane and thiopentone)	**GI†:** Vomiting **CV‡:** Low BP§ **Lab¶:** None	**Const#:** Patient collapsed **CV:** Rapid pulse	Suggestive	Yes/Yes
Broutsas and Seldin,[17] 1972	53, female	Primary AI, disseminated cancer	Periodontal disease, extractions (n = 11), general anesthesia (IV** methohexital)	**GI:** Diarrhea, vomiting **Const:** Hypothermia **CV:** Low BP **Lab:** None	**Const:** Profuse sweating **CV:** Rapid pulse	Suggestive	Yes/Yes
Cawson and James,[18] 1973	49, male	Secondary AI, prednisolone therapy for four years	Oral health status unknown, 15 extractions and significant bleeding, general anesthesia (IV methohexitone)	**CV:** Low BP, features of shock **Lab:** None	**Const:** Pale, sweating **CV:** Rapid pulse	Suggestive	Advised to double steroid dose morning of procedure/Yes

Case reports of adrenal crisis in dental settings.

DENTAL CASES	AGE (YEARS), SEX	PREDISPOSING CONDITION	DENTAL CARE-RELATED FACTORS	MAJOR CRITERIA	MINOR CRITERIA	EVIDENCE SUPPORTING ADRENAL CRISIS	PROPHYLACTIC STEROID COVERAGE/ SURVIVED
Schottler and Colleagues,[19] 1984	43, male	Secondary AI, acromegaly, irradiated pituitary gland, hydrocortisone therapy for an estimated 12 years	Periodontal abscess and endodontic abscess, oral pain likely, two extractions	**Const:** Fever **CV:** Low BP, features of shock **Lab:** None	**Const:** Dizziness, profuse sweating, chills, headache, malaise **CV:** Rapid pulse	Suggestive	Yes/Yes
Anne and Colleagues,[20] 1999	62, male	Undiagnosed primary AI, unknown bilateral adrenal calcification, history of tuberculosis with pleurisy and periostitis	Recurrent painful gingival carcinoma, admitted for lower maxillectomy and radical neck dissection; adrenal crisis occurred after gallium scan, during bleeding-time procedure as part of admission work-up (before dental procedure performed)	**Const:** Loss of consciousness **CV:** Low BP, features of shock **Lab:** Hyponatremia, low stimulation test results	**Lab:** Concurrent hypoglycemia **Other:** Hyperpigmentation on the hands and legs	Consistent	No/Yes
Milenkovic and Colleagues,[21] 2010	6, male	Undiagnosed primary AI	Spreading painful odontogenic infection	**GI:** Nausea **Const:** Fever, toxic appearance **CV:** Low BP **Lab:** Hyponatremia, metabolic acidosis, low cortisol, low stimulation test results	**GI:** Underweight, decreased appetite, craving salty food **Const:** Fatigue, confusion **CV:** Rapid pulse **Other:** Skin hyperpigmentation	Consistent	No/Yes

Key Points

- All cases- adrenal crisis recognized within 5 hours of dental procedure with fluids and corticosteroids administered.
- Acute interruption of steroids was not a factor, but chronic use (>4 years) of steroid was a factor
- Infection and poor health was a factor
- General anesthetic (barbiturate)
- Clinical features of adrenal crisis (weakness, hypotension, tachycardia, confusion) can overlap other conditions (e.g. hypoglycemia)
- Rare event (5 cases in orthopedic joint surgery literature)

TABLE 3-9. STEROID SUPPLEMENTATION GUIDELINES

- Patient has a previous history of regular steroid use that was discontinued recently or in the past or is currently using topical or inhalation steroids: NO SUPPLEMENTATION IS REQUIRED FOR ROUTINE DENTAL PROCEDURES.
- Patient is currently taking steroids and routine dental procedures are planned: NO SUPPLEMENTATION IS REQUIRED FOR ROUTINE DENTAL PROCEDURES.
- Patient is currently taking steroids and minor extractions or minor surgery (< 1 h) is being performed: Ensure that patient takes 25 mg of hydrocortisone equivalent prior to procedure AND ensure effective local anesthesia and adequate postoperative pain control. MONITOR BLOOD PRESSURE THROUGHOUT PROCEDURE.

Complicated or Stressful Procedure Managed with Local Anesthesia or Procedures Requiring General Anesthesia

- Patient is currently taking steroids (or has low adrenal reserve) and major surgery (lasting more than 1 h) or significant blood loss is anticipated: THE GLUCOCORTICOID TARGET IS ABOUT 50 TO 100 MG/D OF HYDROCORTISONE EQUIVALENT FOR THE DAY OF SURGERY AND AT LEAST 1 POSTOPERATIVE DAY. ENSURE EFFECTIVE LOCAL ANESTHESIA AND ADEQUATE POSTOPERATIVE PAIN CONTROL. MONITOR BLOOD PRESSURE THROUGHOUT PROCEDURE AND POSTOPERATIVE PERIOD.

- AAOM Guide- Medically Complex Dental Patients (3rd ed)- Rhodus, Miller

Salem (1994) – Cortisol equivalents

- reviewed multiple studies and found 75-150mg/24hr cortisol secretion after major surgery
- cortisol level rarely exceed 200mg/24hr (50mg prednisone)

Steroid Cover

- Would you cover for low dose steroid?
- Would you cover for high dose steroid?
- Would you cover during recovery?
- Would you cover all procedures?
- How much would you increase?

Case 1

- Should patient receive additional prednisone prior to/after extraction of #32?

Case 1

MEDICATIONS

- Dolobid-500 mg daily
- Opana ER (Oxymorphone Hydrochloride) ; 30 mg daily
- lisinopril 5 mg oral tablet: 5 mg, 1 tablet, ORAL BID
- furosemide 20 mg oral tablet: 20 mg, 1 tablet, ORAL, Daily
- **Methotrexate** 7.5 mg oral tablet Wednesdays
- **Prednisone** 5 mg oral tablet: 5 mg, 1 tablet, ORAL, qAM
- Myrbetriq 50 mg daily
- **Folic acid** 1 mg oral tablet: 2 mg, 2 tablet, ORAL, qHS , (total 2 mg),
- Cymbalta 60 mg oral delayed release capsule: 60 mg, 1 capsule, ORAL, qAM
- Simvastatin 40 mg daily
- ASA 81 mg oral enteric coated tablet: 81 mg, 1 tablet, ORAL, QODay
- **Actemra** (Tocilizumab) infusion-monthly
- **Prolia** 60 mg/mL subcutaneous solution, q 6 months

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Topical Steroids

- Ultrapotent
  - Clobetasol 0.05%
  - Halobetasol 0.05%
- Potent
  - Dexamethasone 0.5 mg/5 mL
  - Fluocinonide 0.05%
- Intermediate: Triamcinolone acetonide (Kenalog) 0.1%
- Low: Hydrocortisone 1%
- Gel, Ointment, Cream, Compounded

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Topical Steroids

- "for external use only"
- High cost
- Atrophy of mucosa
- Fungal side effects
- Systemic steroids effects

Adverse events from topical steroids (Clobetasol)

AEs occurred throughout the 14 clinical trials;

- candidiasis (13/350)
- burning sensation following application of ointment (6/350)
- mild cases of moon face (5/350)
- taste alterations (4/350)
- dyspepsia (3/350)
- skin rashes (2/350)
- female facial hair growth (2/350)
- GI distress (2/350)
- parotid swelling (1/350)

HPA axis suppression from topical steroids

- Physiologic - having a temporary lower than normal cortisol levels.
- Pathologic - consistently lower than normal cortisol levels.

Physiologic HPA suppression

- Three out of the 14 studies (n=111) assessed cortisol levels
  - 53 out of 111 treated with clobetasol experienced a decrease in cortisol.
  - All of these 53 patients with lower cortisol levels were part of 1 clinical study
  - Cortisol levels in 51/53 of these patients returned back to normal as soon as the frequency of treatment was reduced from 3 treatments per day to 1 treatment per day. (Gonzalez-Moles, M, 2010)

Pathologic HPA suppression

- 2/53 consistently experienced lower than normal cortisol levels, even after discontinuation of therapy.
- Patients used for at least 6 months.
- Used a mouthwash technique may also play a role in reduced cortisol levels (vs. gels and ointments)

Topical Steroids and Fungal Infection: Study Objectives

- **Primary**
  Determine the incidence of oral candidiasis in patients treated with topical steroids for oral lichen planus (OLP)
- **Secondary**
  Determine if different antifungal therapies are more effective than others in preventing the development of clinical fungal infections

Marable DR, Bowers, Stout T, Stewart CM, Berg KM, Sankar VS, DeRossi SS, Thoppay JR, Brennan MT. Oral candidiasis following steroid therapy for oral lichen planus. Oral Dis. 2016 Mar;22(2):140-7.

Methods

Multicenter, retrospective chart review of a well-characterized group of Lichen Planus patients

- Carolinas Medical Center (CMC)
- University of Florida College of Dentistry (UF)
- University of Texas Health Science Center at San Antonio (UTHSCSA)
- Georgia Regents University College of Dental Medicine (GRU)

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Methods

Inclusion Criteria

- Patients diagnosed with clinical oral lichen planus.
- Patients at CMC, UF, UTHSCSA, and GRU
- Patients treated for lichen planus with topical steroids for at least 2 weeks AND a follow-up visit within 5 weeks of the initiation of daily topical steroids.

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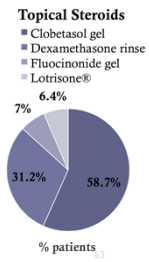
Results

Topical steroids were used in 303 (96.2%) patients.

Systemic steroids were used in 12 (3.8%).



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Results

- Objective improvement
  - Clobetasol
    - 91.1% with clobetasol
    - 81.5% without clobetasol (p=0.02)
  - Use of any preventive antifungal
    - 90.6% with antifungal
    - 80.5% without antifungal (p=0.02)
- Subjective improvement
  - Clotrimazole
    - 94.3% with clotrimazole
    - 85.4% without clotrimazole (p=0.04)

Results

- **Oral fungal infections at follow-up**
  - **Total**: 43 (13.7%) patients
  - No significant difference between sites (p=0.36).
    - CMC - 24/155 (15.5%)
    - UF - 11/67 (16.4%)
    - UTHSCSA - 6/59 (10.2%)
    - GRU - 2/34 (5.9%)

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Results

- **Fungal infections at follow-up, by steroid treatment**
  - **Clobetasol** - 32/183 (17.5%), (p=0.02)
  - **Dexamethasone** - 11/98 (11.2%), (p=0.39)
  - **Fluocinonide** - 1/22 (4.6%), (p=0.33)
  - **Lotrisone®** - 4/20 (20%), (p=0.50)
- Preventive antimycotic agents were used in 203 patients and no antimycotic in 111, with fungal infections occurring in 29 (14.3%) and 14 (12.6%), respectively.

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Frequency of Oral Fungal Infection Based on a Low vs. Normal Stimulated Salivary Flow

	Oral Fungal Infection	No Oral Fungal Infection	P Value
Low Stimulated Salivary Flow (≤ 0.7 mL/min) (n=23)	9 (37%)	14 (63%)	0.004
Normal Stimulated Salivary Flow (> 0.7 mL/min) (n=24)	1 (4%)	23 (96%)	

Conclusions

- The incidence of oral fungal infections in OLP patients following steroid therapy was higher than anticipated (13.7%).
- Clobetasol had a significantly higher incidence of fungal infection compared to all other steroid therapies.
- Low saliva is a major risk factor for a fungal infection

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