Medical Dermatology Update

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I have no relevant disclosures

Will discuss off-label use of medications
Selected topics in Dermatology in the world of:

1. Atopic eczema
2. Psoriasis
3. Hidradenitis Suppurativa
4. Non-surgical treatment of NMSC: eBx
5. Photomedicine
Atopic dermatitis review

- Most common skin disease in general population/humans
  - 7% adults and 15-25% children in US
  - Age of onset: 85% are diagnosed by the age of 5

- Strong genetic component (30%). Not all explained by FLG mutation.

- Need for new agents to control the disease is unmet.
  - Majority treatment options for moderate to severe disease are still off-label

- Complex interplay of epidermal skin barrier dysfunction, atopic march, immune pathways & environmental factors
  - Need multipronged approach
AD: Guidelines of care

- Latest AAD Guidelines of treatment from 2014: Pre-crisaborole, & dupilumab

- Updated Guidelines

FROM THE ACADEMY

Guidelines of care for the management of atopic dermatitis


Special Article

Atopic dermatitis yardstick: Practical recommendations for an evolving therapeutic landscape

Mark Boguniewicz, MD  ; Luz Fonacier, MD  ; Emma Guttman-Yassky, MD, PhD  ; Peck Y. Ong, MD  ; Jonathan Silverberg, MD, PhD, MPH  ; Judith Rosen Farrar, PhD  

# AD guidelines article

<table>
<thead>
<tr>
<th>Maintenance Treatment</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Basic Management</strong></td>
<td>1. Skin Care</td>
<td>Basic Management + Topical Anti-Inflammatory Medication</td>
<td>Referral to AD Specialist</td>
</tr>
<tr>
<td>1. Skin Care</td>
<td>• Moisturizer, liberal and frequent (choice per patient preference)</td>
<td>Apply on areas of previous or potential symptoms (aka flare)</td>
<td>Phototherapy</td>
</tr>
</tbody>
</table>
| • Warm baths or showers using non-soap cleansers, usually once daily and followed by moisturizer (even on clear areas) | Maintenance TCS | 1. Low potency 1x-2x daily (including face) | Dupilumab
| 2. Antiseptic Measures | • Medium potency 1x-2x weekly (except face) | 2. Maintenance TCI (pimecrolimus, tacrolimus) | Systemic Immunosuppressants |
| • Dilute bleach bath (or equivalent) ≤2x/week according to severity (especially with recurrent infections) | • 1x-2x daily | • Cyclosporine A<sup>1</sup> | • Methotrexate<sup>2</sup> |
| • Antibiotics, if needed | • 2x-3x weekly (not an indicated dosage) | • Mycophenolate mofetil<sup>3</sup> | • Azathioprine<sup>3</sup> |
| 3. Trigger Avoidance | OR Crisaborole 2%<sup>1</sup> | • Corticosteroids<sup>4</sup> | Consider acute tx for some patients to help gain control: |
| • Proven allergens and common irritants (e.g., soaps, wool, temperature extremes) | 2x daily | • Wet wrap therapy | • Oral anti-inflammatory therapy |
| • Consider comorbidities | | • Hospitalization | |
| **Acute Treatment** | Apply TCS to Inflamed Skin | Medium to high potency TCS 2x daily for 3-7 days beyond clearance | • Non-adherence |
| Low to medium potency TCS 2x daily for 3-7 days beyond clearance | [Consider TCI, crisaborole] | • Infection | • Misdiagnosis |
| If not resolved in 7 days, consider | | • Contact allergy to medications | • Referral |

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*Ann Aller Asthma Immunol 120(2018): 10-22*
Prevention of AD

- Effective skin emollients since birth may prevent exposure to AD triggers, bacteria, microbes
  - Emollients from birth can prevent AD?
    - 2 prospective RCT, showed 50% reduction in risk for eczema by 6-8 months of age.
    - BEEP trial (2017), 1395 patients, emollients for 12 months, followed over 5 years
  - Emollients increase the threshold to fire Th2 responses
  - Very cost effective and moisturizers have steroid sparing effect

References:
When to initiate systemics?

- Expert panel recommendation from International eczema council states ...

  **Severity-based scoring systems alone cannot determine the need for systemic therapy: a holistic assessment is needed**

  - Exclude: infections, contact allergens, ctcl, steroid phobia/misconceptions
  - Failed: phototherapy (home or in office) or not practical phototherapy candidate, “Soak and smear” and other intensive topical regimens

- Which systemic to initiate? Is Dupilumab superior to all others?
  - Azathioprine: lymphoma, CNS (PML)
  - Methotrexate: hepatotoxic, cytopenia, teratogen, GI
  - Cyclosporine: HTN, Renal
  - Mycophenolate: GI, teratogen
  - Dupilumab: No labs — conjunctivitis, injection site reaction

JAAD 2017;77:623-33
Should I take my baby to the allergist?

- Under age 1 with **severe eczema**, NIAID Food allergy guidelines identifies this group HIGH RISK for peanut allergy (new data from 2015)

- **LEAP** study (**Learning Early About Peanut Allergy**)
  - >600 kids at high risk for peanut allergy (severe eczema +/- egg allergy), 4-11 months old, followed up to 5 years of age
  - Randomized, open label: PEANUT AVOIDANCE vs. PEANUT CONSUMPTION
  - Peanut CONSUMPTION led to 81% relative reduction in likelihood of peanut allergy
### Summary of Addendum Guidelines

<table>
<thead>
<tr>
<th>Addendum Guideline</th>
<th>Infant Criteria</th>
<th>Recommendations</th>
<th>Earliest Age of Peanut Introduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Severe eczema, egg allergy, or both</td>
<td>Strongly consider evaluation with peanut-specific IgE and/or skin prick test and, if necessary, an oral food challenge. Based on test results, introduce peanut-containing foods.</td>
<td>4 to 6 months</td>
</tr>
<tr>
<td>2</td>
<td>Mild to moderate eczema</td>
<td>Introduce peanut-containing foods.</td>
<td>Around 6 months</td>
</tr>
<tr>
<td>3</td>
<td>No eczema or any food allergy</td>
<td>Introduce peanut-containing foods.</td>
<td>Age-appropriate and in accordance with family preferences and cultural practices</td>
</tr>
</tbody>
</table>
NIAID updated algorithm

Recommended Approaches for Evaluation of Children With Severe Eczema and/or Egg Allergy Before Peanut Introduction

Severe eczema or egg allergy or both

Peanut slgE*

- < 0.35
  - Risk of reaction low (more than 90% will have (+) SPT to peanut).
  - Options:
    a) Introduce peanut at home
    b) Supervised feeding in the office (based on provider/parental preference)
- ≥ 0.35
  - Refer to specialist for consultation/SPT protocol

Peanut skin prick test (SPT)

- 0 – 2 mm
  - Risk of reaction low (95% will not have peanut allergy).
  - Options:
    a) Introduce peanut at home
    b) Supervised feeding in the office (based on provider/parental preference)
- 3 – 7 mm
  - Risk of reaction varies from moderate to high.
  - Options:
    a) Supervised feeding in the office
    b) Graded oral food challenge in a specialized facility
- ≥ 8 mm
  - Infant probably allergic to peanut.
  - Continue evaluation and management by a specialist.
Immunology in AD

- FLG mutation are only found in a minority of AD pts (15-46%)
- Immune responses in AD likely to be critical in driving barrier dysfunction
- Predominantly Type 2 immune response
  - **Th2** cells, mast cells, innate lymphoid cells → inhibit terminal differentiation of keratinocytes
    - inhibits expression of genes required for skin barrier function
    - Suppress production of lipids
  - Keratinocytes secrete TSLP, activates Th2 pathway: **IL4, IL13**.
  - Dendritic cells, mast cells get activated (via IL23) → Th17, **Th22** → IL22
  - Differences in immune response based by race, age, severity of AD
    - American/Europan AD (High Th2 > Th22, Th1 > Th17)
    - Asian (High Th2 > Th22, Th17 > Th1)
    - Pediatric AD (High Th2 > Th22, Th17, no Th1)

J Allergy Clin Immunol. 2015; 136(5):1254-64
AD as a systemic disease?

- Meta analysis of 16 studies
- Increased activated T cells $\rightarrow$ increased circulatory cytokines $\rightarrow$ cardiovascular associated markers
- But study showed no association between AD and CVD (DM2 and MI)
- Eczema is not an independent predictor of CVD when controlling for other factors
Difficult to tease apart increase in CVE risk factors from AD inflammation vs modifiable lifestyle factors
Study on 25 patients, 19 were treated with Cyclosporine for 12 weeks.
- Pre and post Cy treatments, Th2 & Th22 serum biomarkers were studied and compared.
- Non lesional skin biomarkers showed correlation with lesional skin biomarkers.
- Non lesional biomarkers showed stronger correlation with clinical improvement than lesional biomarkers.
- Non lesional skin already has abnormal cytokine profile!

Ungar et al. JID 2017;137(3):603-613
AD nonlesional skin cytokine profile is abnormal
Dupilumab – a year later...

- Fully humanized monoclonal antibody against IL4/ IL 13
- Dosing is 300 mg SC injections q 2 weeks, loading dose 600 mg at week 0.
- Results:
  - Week 16 - 39% were clear or very clear vs 12% placebo
  - 64% EASI 75 vs 23% placebo
  - Mean EASI improvement 77%
  - Results replicated in week 52

- Difficult to obtain for Medicare patients, relatively accessible for commercial patients
Comparing FDA approval and efficacy

- Azathioprine: **26-39%** reduction in severity scores
- Methotrexate: **42%**
- Cyclosporine: **53-95%** - FDA approval in Europe
- Mycophenolate: unknown
- Dupilumab: **77%** -- the only FDA approval in US

JAAD 2017;77:623-33
JAAD 2016; 75: 506-515
J All Clin Immunol 2014;133: 429-438
JAAD 2014; 71:327-349
Dupilumab AEs

- Side effects: conjunctivitis (15%), injection site reactions (14%)
- Scarring ectropion
- Worsening psoriasis

JAAD Case Reports 2018;4:708-10.
Dupilimumab AEs

- Systematic review of studies on inhibition of IL4/IL-13 between 2006-2016 found increase risk of helminthic infections but **no increased risk for malignancy, cardiovascular events**

- Fleming, Drucker, JAAD 2018 ;78(1): 62-9
- Meta analysis of RCT (8RCTs, n=2706, follow up 4-52 weeks) shows dupilumab reduces risk of skin infection, eczema herpeticum.
Down the pipeline

- Lebrikizumab: IL-13 blockade, without IL-4 blockade
  - Proves IL-13 blockade alone is useful in treating AD.
- Tralokinumab (IL-13)
- Nemolizumab (IL31)
- Fezakinumab (IL-22)
- Ustekinumab (IL12/23)
- JAK inhibitors

- NAE website link: > a dozen biologics, topicals, Phase II/III studies
- https://nationaleczema.org/research/eczema-treatment-research/
Psoriasis update

- Psoriasis as systemic disease
- Overwhelming choice of biologics
  - How to approach?
  - Safety data
- Special population
  - Pregnancy
  - Malignancies and side effects

Bolognia et al. Dermatology 2nd ed.
Psoriasis review

- Psoriasis is a chronic inflammatory disease, with systemic and cutaneous manifestations.
- Affects 1-3% of the population
- Disease has a polygenic genetic basis, predominantly Th1 and Th17 mediated.
- More recognition of quality of life changes + increasing cardiovascular risk
  - ~5 years of lifespan reduction
  - Relative risk for CV event is highest in younger and severe psoriasis patients vs older patients.
  - For pediatric patients... **each psoriasis year means 1 % increase in CV event risk**

Gelfand et al. JAMA 2006;296:1735-1741
J Am Acad Dermatol 2017;77:650-6
Figure. Adjusted Relative Risk of Myocardial Infarction in Patients With Psoriasis Based on Patient Age

Table 4. Univariable and Multivariable Cox Proportional Hazard Regression Models of the Risk of MI in Patients With Mild and Severe Psoriasis Compared With Control Patients

<table>
<thead>
<tr>
<th>Covariate</th>
<th>Model Hazard Ratio (95% CI)†</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Mild Psoriasis</td>
</tr>
<tr>
<td>Psoriasis (unadjusted)</td>
<td>1.11 (1.07-1.17)</td>
</tr>
<tr>
<td>Psoriasis</td>
<td>1.54 (1.24-1.91)‡</td>
</tr>
<tr>
<td>Age per year</td>
<td>1.077 (1.076-1.079)</td>
</tr>
<tr>
<td>Age × psoriasis (interaction term)</td>
<td>0.994 (0.991-0.997)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.61 (1.53-1.70)</td>
</tr>
<tr>
<td>History of MI</td>
<td>3.24 (3.07-3.41)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>3.08 (2.93-3.23)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.11 (1.07-1.16)</td>
</tr>
<tr>
<td>Male sex</td>
<td>2.12 (2.04-2.19)</td>
</tr>
<tr>
<td>Smoking</td>
<td>1.15 (1.10-1.20)</td>
</tr>
</tbody>
</table>

Adjusted relative risk is shown on a log scale.

Gelfand et al. JAMA 2006;296:1735-1741
97 patients, randomized to photo, ada, or placebo

Marker of vascular inflammation: $^{18}$FDG PET/CT
- Proven to predict cardiovascular events
- Changes short term (months/weeks) in response to therapy

Adalimumab and phototherapy group had reduction in IL6, and CRP
Adalimumab-only group had reduction in TNF
No significant reduction of vascular inflammation in treatment arm by end of study >1 year

VIP-U study with ustekinumab presented at Annual AAD 2018 showed more promising results.
- Need to assess with IL-17 or apremilast?
Psoriasis and atherosclerosis

- Being on a biologic agent reduces the overall inflammation burden and reduces overall cardiovascular risk in psoriasis patients.
- MTX shows cardioprotective effect but in long run ends up risking end organ damage.
  - Cyclosporine causes hyperlipidemia, HTN, and increased radicals that can lead to myocardial damage.
- TNFa inhibitors shown to help reduce risk of MI by 50-75% in psoriasis patients.
  - 8845 patients in the Kaiser Permanente System, retrospective review.
  - TNFa group and oral/phototherapy group had decreased MI risk compared to topical treatment cohort.
    - Greater risk reduction in TNFa group but not statistically significant.
  - Lack of psoriasis response to TNFa inhibitors correlates to decreased reduction in MACE risk.

Treat to target campaign

Similar to goals for cholesterol, HgBA1c, BP, ACR20

Why not for psoriasis?
Free clinical resource

- Download for free at https://www.psoriasis.org/pocket-guide

- Easy teaching tool for patients, trainees, PAs and clinicians
  - Explains standard psoriasis care
  - when discussing more aggressive treatment options and behavioral changes with “suspicious patients”
  - Algorithms for special population patients

- **Undertreatment of psoriasis is common, dissatisfied patients are very common ( >50%)**
Oral molecules

Healthy patients with Psoriasis
- Adults
- Pediatric
- Pregnant

Complex patients with Psoriasis
- Cardiovascular risk
- Autoimmune patient
  - Lupus, MS, IBD
- Cancer or Immunosuppressed
  - HepB/C
  - Latent Tb

Healthy
- Apremilast
- acitretin
- Cyclosporine
- MTX

At risk
- Apremilast
- MTX
- acitretin
- Cyclosporine
Biologics available to us

- **Anti TNF**
  - Receptor: Etanercept
  - Antibody: Adalimumab, Infliximab, Certolizumab
- **Anti IL 12/23:** Ustekinumab
- **Anti IL-23:** Gusekumab, Tildrakizumab
- **Anti IL 17:** Secukinumab, Ixekizumab
- **Anti IL 17RA:** Brodalumab
- **Anti IL 4/13:** Dupilumab
- **IL1-RA:** Anakinra
- **Anti IL-1B:** Canakinumab
- **Anti IgE:** Omalizumab
- **Anti CD20:** Rituximab

Psoriasis, SJS/TEN, HS
Psoriasis, HS, ?AD
Psoriasis
Psoriasis
Psoriasis, AD
Eczema
FMF, cryopyrin mediated syn
Urticaria, AD
Pemphigus
Etanercept

- Adult and pediatric patients (>4yo for Ps)
- FDA approved for: Ps, PsA, AS, RA.
- NO GI efficacy for Crohns/UC, can worsen IBD
- Limited by slower onset and less efficacy compared to newer biologic classes
- Good long term data available

- TNF class effect: risk of lymphoma, drug induced lupus, worsening CHF, MS symptoms
Adalimumab

- FDA approval for: Psoriasis, PsA, AS, HS, RA/JIA, Crohns/UC, uveitis
  - Peds psoriasis data in Europe
- New less stinging solution vehicle (citrate free), no latex, 29G needle
- First-line approved biologic option on most insurance plans
- Dosing 80 mg SQ week 0, then 40 mg week 1, then 40 mg SQ q 2 weeks
  - Higher dosing in HS patients
- VIP Study: reduces inflammatory markers in skin and blood but NO reduction in vascular inflammation
Infliximab

- Infusion center
- Rescue for severe psoriasis and HS, patients with coexisting UC/Crohn's
- Concern for autoantibody formation, use with MTX
- Dose 5-10 mg IV week 0, week 4, then q 8 weeks

- TNF class effect: risk of lymphoma, drug induced lupus, worsening CHF, MS symptoms
Certolizumab Pegol

- Safest in **pregnancy**
- FDA approved for PsA, PsO
- Dosing 400 mg SQ, week 0,2,4, then 200 mg q2-4 weeks
TNF inhibitors and malignancies

- **BASELINE** psoriasis risk of malignancy: **16-20%** increased risk, strongest with lymphoma

- 2 meta-analysis studies did NOT find an increased risk of an internal malignancy associated with TNF inhibitors

- TNF inhibitors also are associated with increased risk of NMSC, namely SCCs, and possibly melanoma (several conflicting reports)

- **PSOLAR**
  - NO increase in risk for new malignancies, infections, or other adverse events among TNF alpha inhibitors

Asgari MM et al. J AAD 2017;76(4):632-8

JID. 2006 126(10): 2194-2201.
Ustekinumab

- Pediatric approval for PsO ( >12 yo )
- Not as effective for joint symptom control
- Approved for Crohns but not UC ( needs IV dose)
- Very easy dosing regimen : 45 mg or 90 mg SQ week 0,4, then q 12 weeks
- No significant adverse events profile
- ONE case of RPLS ( Reversible posterior leukoencephalopathy syndrome) on ustekinumab
  - Also reported with patients on MTX,Cy, infliximab, etanercept in trials

Arch Dermatol. 2011; 147 (10):1197-1202
Guselkumab

- Only approved for PsO, no GI/arthritis indication
- Dosing regimen is simple, 100 mg SC week 0, 4, then q 8 weeks
- No significant adverse events

- PASI 100: almost 50%
- PASI 90: 70%
- PASI 75: 90%
Ixekizumab / Secukinumab

- Induction or exacerbation of crohns is a concern
- Incidence of IBD (Crohns+UC) in US population is 1.3%, vs <1% in IL-17 inhibitor trials

Brodalumab

- Also has one case of reported Crohns
Psoriasis & pregnancy

- Psoriasis incidence:
  - ~7.4 million people in US, with 200k new cases a year
  - Half of psoriasis patients are female, initial presentation often during childbearing age

- Normal pregnancy inflammatory stages
  - 1st trimester: Th1 proinflammatory period
  - 2nd trimester: Th2 anti-inflammatory period
  - 3rd trimester: Recurrence of Th1 inflammation (IFN and TNF dependent)
Placental transfer of TNF inhibitors

- There is an increase in adverse event rates in autoimmune pregnancies (even without biologic exposure)

- Organogenesis takes place prior to **week 13 EGA**

- Maternal IgG gets transferred to placenta via neonatal FC receptors, which becomes functional as early as week 13 EGA
  - 80% of maternal IgG transfer occurs during 3rd trimester.

- The most efficiently transferred IgG is IgG1, which includes:
  - Infliximab, adalimumab, golimumab and ustekinumab
  - Cord blood concentration is **4-fold** of maternal blood concentrations with infliximab, adalimumab
    - 4-7% with etanercept
  - Levels remain detected in newborn 1 year later (No live vaccines)

Biologic approach in pregnancy

- Try to stop biologics or systemic agents during pregnancy if clinically feasible. Notify peds and obgyn.
- DC any MTX!
- Transition to Certolizumab pegol > etanercept
- Trimester 1: ok to keep maintenance dosing
- Trimester 2-3: discuss dosing adjustments, risk to infant (no live vaccines in first 9 mo), risk of postpartum flare in mom
  - Last injection (based on half life) ref: G Martin AAD 2018 focus session
    - Ustekinumab, infliximab: week 30-32
    - Adalimumab: week 36-37
    - Golimumab: week 34-36
    - Certolizumab pegol: ok to continue
Hidradenitis Suppurativa

- Inflammatory skin disease with characteristic chronic suppurative lesions in apocrine gland bearing areas.
- Up to 4% of population affected (underdiagnosed).
  - 2:1 F:M, 2-3:1 Af Am: Cauca
- Incidence is rising (more detection).
- Mean delay in establishing diagnosis is SEVEN years.
- Average wait time is 7.2 years between onset of symptoms and diagnosis and 2.3 years between onset of symptoms and any physician visit.
- Only 1 in 5 patients use a dermatologist.

- Patient Advocacy Group:
  - http://hopeforhs.org/what-is-hs
New insights into the diagnosis of hidradenitis suppurativa: Clinical presentations and phenotypes

Hessel H. van der Zee, MD,a and Gregor B. E. Jemec, MDb
Rotterdam, The Netherlands, and Roskilde, Denmark

(J Am Acad Dermatol 2015;73:S23-6.)

- Family history
- Recurrent folliculitis or open comedones in typical lesions (more than 2 recurrences over 6 months)
- Typical lesions in atypical locations
- Hx or presence of pilonidal sinus
- Absence of microbes on cultures
HURLEY Staging

- Stage I: singular abcess formation without scarring/sinus tracts (68%)
- Stage II: recurrent abcesses with tract formation, widely separated lesions (28%)
- Stage III: diffuse involvement and sinus and tract formations (fistulas) across the entire area (4%)
  - Does not take into consideration erythema and purulence

- Other scoring systems:
  - Sartorius score
  - PGA
  - HSSI (HS Severity Index)
  - HiSCR (Hidradenitis Suppurativa Clinical Response Score)
Comorbidities

- Metabolic syndrome
  - Obesity / increased BMI
  - Hyperlipidemia (high triglycerides, low LDL)
  - Insulin resistance
  - HTN
- Smoking
- Polycystic ovarian syndrome
- Depression
- Substance abuse
Hs associated diagnoses

- Acne, Pyoderma gang, Spondyloarthtopathies, Thyroid disease
- Lymphoma
- PCOS
- Crohns
- Trisomy 21
- OSA
- KID
Autoimmune diseases and HS

- Inflammatory bowel disease: 9x more likely to develop HS
  - In HS subset of pts: 3x more likely to develop Crohns
- Spondyloarthropathies and arthritis : HLAB27 negative
- Pyoderma Gangrenosum
- Follicular occlusion tetrad
- Acne vulgaris
- PASH, PAPASH, PsAPASH
- NMSC
  - Consider biopsy to rule out NMSC
  - 4.6 x Increased risk in gluteal or perineal HS with chronic symptoms

Garg et al, JAMA dermatol Aug 2018)
Pathophysiology

- Genetics: gamma secretase mutations
  - Loss of function mutations
  - Notch signaling defective in follicular pathway
  - Hair follicle development, cyst formation is affected
  - Proinflammatory cytokines

- Microbiome
  - Coagulase negative staph in sinuses and tracts
  - Anaerobe bacteria
  - Role of biofilm

- Hormonal
HS treatment options

**First line**
- Topical antimicrobials: BPO, Clindamycin, Dapsone, Metronidazole, Gentamicin, ILK
- Oral: Rifampin + clindamycin (tapering off of effects beyond 10 Days), Doxycycline, Dapsone
  - Rifampin interacts with diabetes meds and OCPs (P450 inducer)
  - Minocycline has much fewer reported case series and more potential AE/SE
  - 64% bacterial isolates are tetracycline resistant

**Second line**
- Oral: Rifampin + Levaquin, Metronidazole, Ertapenem
- Spironolactone, OCPs, finasteride (androgenic symptoms)
- Retinoids (Soriatane 25 mg daily, no isotretinoin for HS)

**Third line**
- Adalimumab, infliximab (5-10 mg/kg)
- Ustekinumab (report q 8 weeks may be needed)
- Surgical deroofing, wide excision, CO2 laser, BTX, NdYag laser
Bacterial biofilm in HS

- Breaking biofilm with:
  - Resorcinol, IV ertapenem
  - Hibiclens does not break apart coag neg staph biofilm
  - Compound at local pharmacy
    - Mixture of xylitol, several topical antifungal, antibacterial and steroid topicals (email me if interested)

- Good strategy to bridge to surgery while on IV antibiotics or while on biologics
Triamcinolone 10mg/cc

- Improvement in redness, suppuration, edema by Day 7 (p<0.0001)
- Notable improvement in pain since Day 1

Riis PT et al, JAAD, 2016
Two Phase 3 Trials of Adalimumab for Hidradenitis Suppurativa

- abx, higher BMI patients
  More severe pts

+ abx, lower BMI patients
  Less severe pts

Kimball et al., NEJM, 2016
Clinical trials and biologics in HS

- Ustekinumab - anti IL12/23 (Janssen)
- Anakinra – IL1(a,b) receptor antagonist
- MABp1 - anti IL1a (Xbiotech)
- INCB054707 – JAK inhibitor (Incyte)
- Secukinumab - anti IL17a (Novartis)
- Bimekizumab – anti IL17a,f (UCB Biopharma)
  - Vs ustekinumab
  - Vs adalimumab
Outside the box

- Zinc gluconate 90 mg daily
- Cholcicine with antibiotics
- Metformin
Pitfalls

- Anemia, sepsis
- No dapsone + mtx
- SCC ... rule out with biopsy prior to biologic start
- Perianal, urethral strictures
- SCC + chronic HS + high risk HPV = aggressive course and potentially fatal
- Culture for bacterial infection and think of anti TNF antibodies if failing biologics
Electronic Brachytherapy

- Radiation technology using miniaturized x-ray source, to deliver low energy, high dose, radiation therapy.
- NMSC can be treated over several sessions, few days a week, and sessions lasting minutes.
- Safer side effect profile to treatment staff
- Co-management with rad onc and derm
- Use in NMSC in 2009, other usage in cervical and breast CA
- ~ < 1% failure rate (recurrence)

Clinical trials inclusion criteria:

- Age ≥ 60 years old
  - Clinical stage T1N0M0 (by AJCC 2010 criteria), T1<2cm
    - Basal cell carcinoma with morpheaform, sclerosing, mixed, infiltrative or micronodular features must be ≤1 cm

Exclusion:

- BCC/SCC that was previously treated (i.e., recurrent BCC/SCC)
- BCC/SCC in region adjacent to or overlapping with region of prior radiotherapy
- BCC/SCC on irregular surface (i.e., target area not flat)
- BCC/SCC adjacent to or overlapping with burn or scar
- BCC/SCC in area prone to trauma (including, but not limited to the skin overlying the tibia, dorsum of hands and elbow)
- BCC/SCC in area with compromised lymphatic drainage or vascular supply

ClinicalTrials.gov Identifier: NCT02131805

Inclusion Criteria:

1. Previously completed treatment for non-melanoma skin cancer using Xoft eBx Electronic Brachytherapy System or Mohs surgery;
2. Provides informed Consent;
3. Greater than 40 years of age;
4. Pathological diagnosis confirmed to be squamous cell or basal cell carcinoma prior to treatment;
5. Cancer Staging included in this study:
   - Stage 0: Tis, N0, M0
   - Stage 1: T1, N0, M0
   - Stage 2: T2, N0, M0 and ≤ 4cm in diameter

Exclusion Criteria:

1. Target area is adjacent to a burn scar
2. Any prior definitive surgical resection of the cancer, prior to Radiation Treatment
3. Known perineural invasion
4. Actinic Keratosis
5. Known spread to regional lymph nodes
6. Known metastatic disease
Inclusion Criteria:

- Patient has signed the informed consent form
- Pathological diagnosis confirmed of squamous cell or basal cell carcinoma
- Histopathological Grade: G1 (well differentiated), G2 (moderately differentiated), or Gx (Not assessed in report)
- Clinical Staging Tis, T1, or T2 (Must be ≤ 4 cm in diameter)
- One lesion is treated, or more than 1 lesion is treated with a minimum of a 5 mm gap between the edges of the lesion margins.

Exclusion Criteria:

- T2 > 4 cm and T3 and T4
- American Joint Committee Staging for NMSC Stages III and IV
- Histopathologic Grade 3 (poorly differentiated) or higher grade
- Target area is adjacent to a burn scar
- Target area is on the lip
- Patient < 50 years of age
- Any prior definitive surgical resection of the cancer
- Perineural invasion
- Lesion depth > 5mm on clinical assessment or as assessed by ultrasound or CT.
- Patient is pregnant (pregnancy test required if standard of care).
- Target area is prone to trauma.
- Target area with compromised lymphatic or vascular drainage.
- Participation in another investigational device or drug study concurrently.
- Patient has undergone prior radiation therapy to this specific anatomic location.
- Patient is receiving pharmacologic agent(s) at or around the time of the Radiation therapy that is/are known to produce skin reactions that will influence cosmesis grading during study.
- Patient is receiving chemotherapeutic agent(s) Six (6) weeks before or six (6) weeks after radiation therapy.
- Life expectancy less than five (5) years.
Criteria

Inclusion Criteria:
- Men or women ≥18 years old.
- Estimated life expectancy of ≥5 years
- Histopathologic diagnosis of early and primary Basal Cell Carcinoma (BCC)
- Clinical stage of BCC: T1 or T2 (by AJCC 2010 criteria, see Table 1)
- Histological subtypes: Superficial BCC or nodular BCC
- Maximum diameter of lesion: 20 mm
- Maximum depth of invasion: 4 mm.
- Ability to provide informed consent
- Punch biopsy of primary tumor to depth of reticular dermis

Exclusion Criteria:
- Men or women <18 years old.
- Estimated life expectancy <5 years.
- BCC that was previously treated (i.e., recurrent BCC)
- BCC in region adjacent to or overlapping with region of prior radiotherapy
- BCC on irregular surface (i.e., target area not flat)
- BCC adjacent to or overlapping with burn or scar
- BCC in area prone to trauma
- BCC in area with compromised lymphatic drainage or vascular supply
- Inflammatory process in target area
- Pregnancy or lactation
- Collagen vascular disease (lupus, scleroderma, rheumatoid arthritis)
- Diabetes that is poorly controlled (Hg A1c >7%)
Case reports

Initial KA of the lower extremity treated with radiation

Multiple biopsy proven KAs, three weeks after treatment with radiation. Each lesion was injected with 0.2 cc of fluorouracil 50mg/ml

8/18 Eruptive SCC

Pearls for eBx

- Know that the clinical trials so far are still looking at 5 year out data
- Advise patients that clearance rate in real life most likely will not be as optimal as achieved with stringent inclusion/exclusion criteria in clinical trials
- eBx can be done to avoid surgical trauma, but educate patients who are suboptimal candidates according to clinical trial standards that they may be at risk for recurrence or other side effects.
  - younger than 50 yo
  - Lesion size inching towards the 4 cm size
  - Recurrent NMSCs
  - Any lesions on the legs / prone to trauma areas
  - Any “field AK” affected areas
Photomedicine updates

- PDT code updates:
  - CPT 96567 vs 96573, 96574 (Physician must be involved in application of photosensitizer as well as initiate the light)
  - J7308 vs J7305

- Next generation sunblocks
  - Photolyase sunscreens (marine plant derived) better at reducing p53 expression (apoptosis), and Ki67 expression (proliferation)
  - Suppression of AK development after PDT

Understanding the Role of Photolyases: Photoprotection and Beyond

Neal Bhatia MD, Brian Berman MD PhD, Roger I. Ceilley MD, and Leon H. Kirkik MD
30 mins of SPF before going out?

Time required for a standard sunscreen to become effective following application: a UV photography study.

de Gálvez MV¹, Aguilera J¹, Buendía EA¹, Sánchez-Roldán C¹, Herrera-Ceballos E¹,².

- Study out of Spain
- Looked at in vitro spectral analysis with in vivo absorption measurement with UV photography on patients
- Standard in house formulation of sunscreen, SPF 16
- Results:
  - UV blockade was almost instant upon sunscreen application
  - UV blockade peaked and stabilized after 10 mins of application
Polypodium leucotomos

- Tropical fern from Central and South America
- Extract exhibits photoprotective effect against nBUVB

**Fig 1.** Ultraviolet B response. Pre-
Polypodium leucotomos extract (PLE) minimal erythema dose (MED) site 1 (left) and post- Ple MED site 2 (right); set of representative clinical photographs demonstrating an increase in MED for a subject from 100 mJ/cm² pre-PLE to 150 mJ/cm² post-PLE administration.
Polypodium leucotomos

- Marketed OTC, in drugstores, online
- Daily dosing OTC is 240 - 480 mg
- Antioxidant effect as polyphenol
- Once daily prior to sun exposure would benefit as photoprotection
- In clinical setting for adjunct treatment with PMLE, Vitiligo and melasma patients may need to titrate up to 960 mg dosing or higher?
  - Useful to increase tolerance to phototherapy in fair skin patients
  - No pediatric dosing (yet)
  - OTC Oral formulation is not crushable
- More data to be expected
Thank you 😊

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