What’s New in the Pediatric Literature
2017

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• I have no conflicts of interest to disclose
• I will be discussing the off-label use of some medications
Cost-effectiveness of Prophylactic Moisturization for Atopic Dermatitis

• Statistical calculation of the effect of moisturization on infantile atopic dermatitis
• Dollars/QALYs (quality-adjusted life-years)
• A number of assumptions regarding QALYs for mild, moderate, and severe AD and percentage improvement accrued by using moisturizers
• Assume that the moisturizers chosen work the same

Cost-effectiveness of Prophylactic Moisturization for Atopic Dermatitis

- QALY for treating high risk (first degree relative with AD) infants with daily moisturizer
  - Petrolatum- $353/QALY
  - Sunflower seed oil- $882/QALY
  - CeraVe- $2206/QALY
  - Aquaphor Baby Healing Ointment- $2737/QALY
  - Cetaphil- $2825/QALY
  - Aveeno- $3972/QALY
  - Vaniply Ointment- $8386/QALY
Probiotics and Atopic Dermatitis

- Randomized, double-blind controlled trial of lactobacillus rhamnosus (10 billion CFU) supplementation for the first six months of life in high risk infants
- Eczema at two years and asthma at five years slightly lower in the intervention group but not statistically significant
- High breast feeding incidence which may exceed probiotic effect, JAMA Dermatol article – probiotic mix matters

Cabana MD, et al. Early probiotic supplementation for eczema and asthma prevention: a randomized controlled trial. *Pediatrics* 2017;140:e20163000
Molluscum Contagiosum in Atopic Derm

- Seven-year-old with AD
- Three months of pruritic skin lesions
- Topical steroid use
- Discontinued steroids with marked inflammatory reaction and resolution of mollusca in four months

**CARD11 in Severe Atopic Dermatitis**

- *DOCK8, STAT3, PGM3* are known to be linked to severe atopic dermatitis, high IgE, and severe infections.
- We tend to see severe atopic dermatitis with very high IgE levels but without syndromic associations or infections beyond the skin.
- Gain of function *IL4RA*, loss of function *IFNGR1*, others.

CARD11 in Severe Atopic Dermatitis

- CARD11 encodes a membrane-associated guanylate kinase (MAGUK) family protein that partners with BL10 and MALT1 to form the CBM complex, a scaffold classically required for activation of IκB kinase and nuclear factor-κB in response to lymphocyte receptor ligation.

- Homozygous mutation results in severe combined immunodeficiency.

- Heterozygous gain of function mutation results in B cell lymphoproliferative disease known as BENTA.
CARD11 in Severe Atopic Dermatitis

- Four unrelated families described with severe AD, high IgE, eosinophilia, skin infections, pneumonia
- Four patients and four additional family members found to be heterozygous for CARD11 mutation
  - Hypomorphic- reduction but not complete loss of protein expression
  - Dominant-negative- the resultant protein is antagonistic to the wild type protein
- Important in T-cell signaling pathways NF-κB and mTORC1
CARD11 in Severe Atopic Dermatitis

- Critical as a facilitator of T cell antigen receptor (TCR)-induced upregulation of ASCT2, an essential glutamine transporter required for extracellular glutamine import during cellular activation.
- T-cells with CARD11 mutation treated with added glutamine, partially restoring mTORC1 signaling.
- The four probands had significant AD and respiratory symptoms but four relatives just had AD. Maybe more common in the general population.
Psoriasis with Anti-TNF Agents

- Paradoxical psoriasis develops in about 5% of adults with IBD or RA treated with anti-TNF agents.
- Retrospective study out of Mayo Clinic in pediatric aged children treated with anti-TNF agents for IBD.
- Fourteen new-onset cases identified 2003-2015.
- Two with family history of psoriasis, one with personal hx.

Psoriasis with Anti-TNF Agents

- Twelve Crohn’s, two ulcerative colitis
- Quiescent IBD at time of outbreak in 93%
- Median age 15 years
- Median latency 14.5 months if naive to anti-TNF-α, 6 months if second exposure
- Plaque psoriasis 85%, palmoplantar pustulosis 15%
- Scalp 45%, umbilicus 31%, extremities 31%, face and postauricular region 21%
Psoriasis with Anti-TNF Agents

• Infliximab, adalimumab, certolizumab all involved
• Needed to stop initial anti-TNF-α therapy in 50%
• Continued on anti-TNF-α therapy in 71% after topical therapy
• Stop all anti-TNF-α therapy in 29%
Urticaria Pigmentosa

- Prospective study of children with UP from Children’s Hospital of Wisconsin, 2002-2007
- Three or more mastocytomas
- Telephone once per year, visit once every three years
- CBC, biochem, tryptase
- Children’s Dermatology Quality of Life Index

Urticaria Pigmentosa

- Cohort of 43 subjects
- Followed median of 8.1 years
- Twenty-six (60%) followed through completion of study
- Most had at least 8 years of follow-up
- Four elevated platelet level, only one with a barely elevated tryptase level
Urticaria Pigmentosa

- Symptoms: flushing (63%), pruritus (60%), abdominal cramping (30%), diarrhea (23%)
- Trigger of flare: illness (47%), food (21%),
- No reactions with ibuprofen (37), two with non-opioid cough medicine (2/35)
- No anaphylaxis after bee sting (22) or anesthesia (17)- “costly epinephrine autoinjectors may not be necessary…”
- QOL basically unaffected
Urticaria Pigmentosa

• Median age of resolution 10 years of age but…
• Only 8/26 with complete follow-up had resolution
• At age 12 years, 14/20 still had active lesions
• Good prognosis for resolution
  – Male
  – Younger at onset
  – Fewer affected areas, fewer and smaller lesions
  – Fewer symptoms
Incontinentia Pigmenti Inherited From a Father

- Incontinentia pigmenti is X-linked dominant, always inherited from affected mother to daughter or spontaneous mutation in daughter, lethal in males
- Males with IP are XXY or postzygotic mosaics
- Inhibitor of κ polypeptide gene enhancer in B cells, kinase γ (IKBKG)/nuclear factor κB, essential modulator (NEMO)

Incontinentia Pigmenti Inherited From a Father

• Case report of two families
  – Girl whose father had known, biopsy proven IP
  – Two sisters with IP, father with neonatal rash of linear, Blaschkoid vesicles on the trunk and extremities

• Both fathers with genetic analysis of blood, skin, urine, sperm
  – Father 1: in skin (20%), urine (8.3%), and sperm (16.7%) but not in blood
  – Father 2: only in sperm
Tinea Capitis in Infants

• Not common in children less than 2 years of age
• Generally assumed to be seborrhea or eczema, diff dx also neonatal lupus, LCH, syphilis
• Case series of four patients out of Johns Hopkins and review of the literature
• 18 day old, 14 day old, 12 month old, 16 month old

Tinea Capitis in Infants

• Organism heavily dependent on geography, not noticeably different than older children
• Griseofulvin (67%), itraconazole (19%), terbinafine (9%), fluconazole (4%) all with good success
• Hopkins standard- ultramicrosize griseofulvin 15-20 mg/kg/day for minimum 8 weeks, repeat culture at 8 weeks, treat 2 more weeks awaiting results, stop at 10 weeks if negative, 12 weeks if positive and another culture if possible
Laboratory Monitoring and Isotretinoin

• Laboratory abnormalities are rare and happen, if at all, early in therapy
• No need for CBC, UA, renal function
• Triglycerides, cholesterol, AST, ATL at baseline, one month, two months

Dietary Supplements, Isotretinoin, and Liver Toxicity

• Retrospective report of eight patients with elevated transaminase levels prior to or during isotretinoin therapy
• All were using protein supplements, creatine, or green tea
• Alcohol use, viral infection, very vigorous exercise causing muscle breakdown not present
• Improved with stopping supplements

Dietary Supplements, Isotretinoin, and Liver Toxicity

• Case 2- normal baseline, elevation AST 49 and ALT 55 after starting body building supplements
  – Instructed to stop supplements and continue isotretinoin
  – He stopped isotretinoin and continued supplements
  – Levels remained high

• Case 6- normal baseline, AST to 116 after starting protein shakes
  – Normalized off supplements
  – Up to 187 after admitting he had restarted them
Dietary Supplements, Isotretinoin, and Liver Toxicity

• Significance of elevations unknown
• No CPK’s were done and most all the supplements were taken for athletics and body building
• Best to stop supplements during isotretinoin therapy to avoid confusion and unnecessary cessation of therapy
• Are we making ourselves needlessly anxious by checking liver enzymes in the first place?
Depression in Adolescents

• Information from the National Surveys on Drug Use and Health 2005 and 2014
• Adolescents aged 12-17 years
• 176,245 with 98.9% response rate
• Computer-assisted interviews
• Lifetime and 12-month major depressive episodes

Depression in Adolescents

- 8.7% with major depressive episode in 2005, 11.3% in 2014
- Worse in older adolescents, nonstudents, unemployed, households with single or no parent, substance abuse disorders, females
- Females went from 13.1% (2005) to 17.3% (2014) or 1 in 6
Isotretinoin Use and Risk of Depression

• Meta-analysis of 31 studies that met inclusion criteria
• Mean depression scores significantly decreased from baseline
• Reassuring but not proof that there is no association in some teenagers

Isotretinoin Use and Risk of Depression

• Take a typical group of 100 teenagers with severe enough acne to warrant isotretinoin therapy
  – 40 of them stay at their baseline orneriness
  – 40 of them stay at their baseline pleasantness
  – 16 of them come out of their shell and are happy
  – 4 become depressed during therapy
Isotretinoin and Olfactory Function

- There is evidence that retinoic acids play a role in the recovery of olfactory function following injury in mice.
- Forty five patients with acne treated with isotretinoin studied at baseline and third month of therapy using Sniffin’ Sticks Test.
- Score increased from 8.7 to 9.5 (P< 0.001)
- Hyposmia 40% to 24%, normosmia 60% to 75%

Titanium Dioxide and Yellow Nail Syndrome

- Yellow Nail Syndrome = yellow/dystrophic nails, lymphedema, respiratory symptoms, usually 40-60 year-old
- Article in 2011 linked YNS to titanium in dental or joint implants, titanium detected in the nails
- Case report of 9-year-old girl with yellow nails, chronic cough, lobar pneumonia, bronchiectasis

Hsu TY, et al. Titanium dioxide in toothpaste causing yellow nail syndrome. *Pediatrics* 2017;139:e20160546
Titanium Dioxide and Yellow Nail Syndrome

• Yellow nails noticed for a year
• No lymphedema
• Nails sent for energy dispersive radiograph fluorescence, elevated titanium level found
• No implants, but she did have a habit of swallowing a significant amount of toothpaste
• Nails grew out normally in 3 months after stopping swallowing, respiratory symptoms improved.
Drug Facts (continued)

directed by a dentist
- do not swallow
- to minimize swallowing use a pea-sized amount in children under 6
- supervise children’s brushing until good habits are established
- children under 2 yrs.: ask a dentist

Inactive ingredients sorbitol, water, hydrated silica, sodium lauryl sulfate, trisodium phosphate, flavor, sodium phosphate, cellulose gum, carbomer, sodium saccharin, titanium dioxide, blue 1

Questions? 1-800-492-7378
Piranha Bites: What Antibiotic Prophylaxis?

- Case report of 22-month old boy who stuck his hand in a fish tank, grandparents were fish-sitting a piranha
- Completely removed distal phalanx of fourth finger
- Fish gutted, finger tip and boy brought to ED
- Irrigated and stump sown over without trying to re-attach the tip

Piranha Bites: What Antibiotic Prophylaxis?

- What antibiotic would have been a good choice for prophylaxis?
  - Study out of Uruguay 2000: Cultured buccal mucosa of 6 piranhas and grew *Enterobacter aerogenes*, *Bacillus* species, *Streptococcus* species, and *Micrococcus* species
  - What about the tank water? – Article in *Appl Microbiol* in 1974- 23 genera of bacteria, mostly gram negatives, *Citrobacter* species and *Pseudomonas* species the most common
  - 2012 study using rRNA from pet store tanks found 30 phyla of bacteria with most common human pathogens being *Plesiomonas shigelloides*, *Legionella pneumophila*, *Vibrio cholerae*, *Coxiella Burnetii*, *Vibrio vulnificus*, *Aeromonas* species
Piranha Bites: What Antibiotic Prophylaxis?

- What antibiotic would have been a good choice for prophylaxis?
  - Irrigation and good wound care
  - Culture
  - Prophylaxis with ciprofloxacin or other fluoroquinolone for uncomplicated case
  - Complicated infections should be treated with broad spectrum antibiotics (third generation cephalosporin, vancomycin) awaiting culture, involve ID