What’s New in the Pediatric Literature
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Pacifier Cleaning Practices and Atopy

• Birth cohort of 184 Swedish infants
• Those who “cleaned” the pacifier by sucking on it versus washing pacifier
  – Less asthma (OR of 0.12)
  – Less eczema (OR of 0.36)
  – Fewer allergic symptoms (OR of 0.37)
• Significant differences in oral microbiota

Hand Versus Machine Dishwashing

• Questionnaire-based study of atopic symptoms in Swedish 7-8 year olds

• Hand dishwashing versus machine with less atopic disease
  – Atopic dermatitis 23% versus 38%
  – Asthma 1.7% versus 7.3%
  – Rhinoconjunctivitis 10.3% versus 12.9%

Thumb-sucking, Nail Biting

• Dunedin (New Zealand) Multidisciplinary Health and Development Study
  – 1037 participants born 1972-1973
  – Follow-up at 3, 5, 7, 9, 11, 13, 15, 18, 21, 26, 32, and 38 years of age
• Parents questioned about thumb-sucking and nail biting at 5, 7, 9, and 11 years

Thumb-sucking, Nail Biting

• Skin prick testing at 13 and 32 years
• Asthma and hay fever questioned
  – Positive prick tests 49% nonsuckers or biters, 38% if one habit, 31% if both suckers and biters
  – No difference in groups for asthma or hayfever
Peanut Allergy in Infants

- Jewish children in the UK with similar ancestry to those in Israel have 10 times the incidence of peanut allergy.
- Peanut-based foods introduced in Israel at about 7 months of age.
- Randomized study to see if early introduction of peanut could prevent allergy.

Peanut Allergy in Infants

- Infants 4-10 months of age with severe eczema, egg allergy, or both
- Two cohorts - with and without positive skin prick test to peanut
- Assigned to avoid or consume peanuts (after baseline oral challenge) - Bamba
- Assessment at 13, 30, 60 months
Peanut Allergy in Infants

• Cohort with negative prick test
  – Avoidance – 13.7% peanut allergy
  – No avoidance- 1.9%
• Cohort with positive prick test
  – Avoidance – 35.3% peanut allergy
  – No avoidance- 10.6%

No statistical difference in adverse events
Peanut Allergy in Infants
What comes next?

• The LEAP trial did not address the general population or those at low risk

• Only studied high risk infants
  – Egg allergy $\geq 6$ mm wheal on skin prick test or smaller wheal but allergic symptoms related to ingestion
  – Severe eczema
  – What about other foods?
Introduction of Allergenic Foods
Enquiring About Tolerance (EAT) Study

- Exclusively breast-fed infants from general population 3 months of age
- Randomized to receive 6 allergenic foods or standard guideline of exclusive breast feeding for 6 month
- Primary outcome- allergy to any 1 of 6 foods


Wong GWK. Preventing food allergy in infancy— early consumption or avoidance? *New Engl J Med* 2016:374:1783-4
Introduction of Allergenic Foods

• Three rounded teaspoons of smooth peanut butter, one small egg, two portions of cow’s milk yogurt, three teaspoons of sesame paste, 25 grams of white fish, two wheat-based cereal biscuits every week.

• Only 42.8% adherence to trial protocol.
Introduction of Allergenic Foods

• Intention to treat analysis
  – Primary outcome of any food allergy
    • 5.6% in early introduction group
    • 7.1% in standard introduction group
    • \( P = 0.17 \)
  – Peanut allergy 1.2% versus 2.5%, \( P = 0.11 \)
  – Egg allergy 3.7% versus 5.4%, \( P = 0.17 \)
Introduction of Allergenic Foods

• Per-protocol analysis
  – Primary outcome of any food allergy
    • 2.4% in early introduction group
    • 7.3% in standard introduction group
    • P = 0.01
  – Peanut allergy 0% versus 2.5%, P = 0.003
  – Egg allergy 1.4% versus 5.5%, P = 0.009
  – No cases of wheat allergy in either group
  – No significant adverse effects
• What populations should be introduced to peanut?
• Do we need some type of testing beforehand?
• Are we going to overwhelm Allergists with referrals?
• How do we introduce peanuts?
• Is there readily available information for parents?
Peanut Guidelines

- Report of the multi-specialty consensus conference of the National Institute of Allergy and Infectious Diseases
- In recognition of the need to “operationalize” the findings of the LEAP trial

Peanut Guidelines

• Twenty-six stakeholder organizations in Coordinating Committee
  – Larry Eichenfield from the AAD

• Literature review (64 publications) and consensus expert opinion
Peanut Guidelines
Severe Eczema or Egg Allergy

• “Should have introduction of age-appropriate peanut containing foods as early as 4-6 months…Other solid foods should be introduced before peanut-containing foods to show that the infant is developmentally ready.”
Peanut Guidelines
Severe Eczema or Egg Allergy

• IgE to peanut tested first
  – < 0.35 introduce peanut at home or in the physician office if parents are uncomfortable
  – ≥ 0.35 refer to specialist for consultation and/or skin prick testing protocol

• Food allergen testing panel is not recommended due to poor positive predictive value
Peanut Guidelines
Severe Eczema or Egg Allergy

• How much peanut protein?
  – About 6-7 grams over 3 or more feedings per week
  – Can be done in the home
  – Some parents may be nervous and it is reasonable to do
    first feeding in the office
Peanut Guidelines
No Severe Eczema or Egg Allergy

• Adverse effect on breast feeding?
  – None noted in studies

• What if family member is peanut allergic?
  – Discuss the risks versus the benefits with your practitioner

• What if the infant is known to be allergic to peanuts?
  – Don’t give peanuts
Peanut Guidelines
No Severe Eczema or Egg Allergy

• Mild-to-moderate eczema
  – No testing is needed
  – Introduce peanut at about 6 months at home

• No eczema or allergies
  – No evidence for restricting any food
  – Early introduction of peanut is “anticipated to be safe and to contribute modestly to an overall reduction in the prevalence of peanut allergy”
Peanut Guidelines

• Patient handout given in the article
• Four recipes
  – Softened Bamba
  – Thinned smooth peanut butter in water
  – Thinned smooth peanut butter puree mixed with fruit or vegetable
  – Peanut flour or peanut butter powder mixed with fruit or vegetable
Atopic Comorbidities

- Population of children enrolled in Taiwan’s National Health Insurance Program 2000-2010
- Cohort of 287,262 patients with AD and matched 1:1 to those without
- **Autism** spectrum 0.5% versus 0.4%
- **ADHD** 3.7% versus 2.9%

Atopic Comorbidities

• Data from National Health Interview Survey (NHIS), National Survey of Children’s health (NSCH)
• Incidence of headaches higher in those with eczema (10.7%) versus those without (5.4%)
• Especially correlated with fatigue, excessive daytime sleepiness, insomnia, 0-3 nights of sufficient sleep

Melatonin for Atopic Sleep Disturbance

- Randomized, double-blind, placebo-controlled, crossover study of 38 children with atopic dermatitis
- Given 3 mg at bedtime for 4 weeks, 5-6 week washout, 4 weeks on opposite treatment
- Primary outcome was drop in SCORAD

Melatonin for Atopic Sleep Disturbance

- Decrease in SCORAD by 9.1 compared to placebo
- Sleep-onset latency decrease by 21.4 minutes more than placebo
- No correlation between decrease in sleep latency and decrease in SCORAD
- May have immunomodulatory or antioxidative properties
Finally, a Biologic Agent for AD
Dupilumab

• Three double-blinded, placebo-controlled, studies of dupilumab at various doses versus placebo in adults with mod-to-severe AD


Finally, a Biologic Agent for AD
Dupilumab

• Fully human monoclonal antibody that binds specifically to the alpha chain subunit of IL-4 and IL-13 receptors, inhibiting signaling of IL-4 and IL-13
• Both are Th2 inflammatory cytokines felt to be important drivers of atopic and allergic diseases
Finally, a Biologic Agent for AD
Dupilumab

• SOLO 1 (671 patients) and SOLO 2 (708 patients) in NEJM
• Primary endpoint clear or almost clear
  – 36%, 38% 300 mg every other week
  – 36%, 37% 300 mg every week
  – 8%, 10% placebo P < 0.001
• At least 75% reduction in EASI score significantly better in both treatment groups
Finally, a Biologic Agent for AD
Dupilumab

• Lancet study with 379 patients
• EASI-75 used as the primary endpoint
  – 74% 300 mg once per week
  – 68% 300 mg once every other week
  – 65% 200 mg once every other week
  – 64% 300 mg once every fourth week
  – 45% 100 mg once every fourth week
  – 18% placebo
Finally, a Biologic Agent for AD
Dupilumab

• Adverse events
  – Injection site reactions
  – Conjunctivitis
  – Nasopharyngitis common but matches placebo
  – Previous studies have mentioned increase in HSV infections of the skin
  – No medication-related serious adverse events
• 69 pediatric patients completed 264 weeks of therapy for psoriasis
  – PASI-75 (60-70%) and PASI-90 (30-40%) maintained over the length of therapy
  – URI (38%), nasopharyngitis (26%), headache (21.5%), only one treatment-related serious adverse event with cellulitis, no opportunistic infections or malignancy

Biologics in Pediatrics

• 127 patients with arthritis
• No malignancies, active TB, demyelinating disorders, or death
• Most commonly headache, pyrexia, diarrhea, URI, pharyngitis, bronchitis, URI, gastroenteritis

Thyroid Dysfunction and Tetracycline Antibiotics

- Black minocycline-induced pigment has been found in thyroid glands at autopsy
- Autoimmune, minocycline-induced thyroid dysfunction reported twice in pediatric patients
- Study out of Wisconsin Hospital and Clinics
- Review of < 18 yo, abn TSH, tetracycline abx

Thyroid Dysfunction and Tetracycline Antibiotics

• Twenty-one patients
  – 14 autoimmune thyroid disease
  – 1 congenital thyroid disease
  – 1 thyroid cancer
  – 1 sick euthyroid syndrome
  – 1 on confounding valproate therapy
  – 3 on acne tetracycline-class medication therapy,
    hyperthyroidism, negative antithyroid antibodies, low uptake
    on radioiodine uptake scan
Thyroid Dysfunction and Tetracycline Antibiotics

• Two of the three had resolution after stopping doxycycline (1) and minocycline (1) and another had persistent dysfunction (minocycline)

• “appears to be a non-autoimmune chemical thyroiditis resulting in cytotoxic damage sufficient to cause marked release of thyroid hormone and, in some cases, subsequent persistent hypothyroidism.”
Thyroid Dysfunction and Tetracycline Antibiotics

• Twenty-one patients
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  – 1 on confounding valproate therapy
  – 3 on acne tetracycline-class medication therapy, hyperthyroidism, negative antithyroid antibodies, low uptake on radioiodine uptake scan
Thyroid Dysfunction and Tetracycline Antibiotics

• Minocycline-induced drug hypersensitivity syndrome followed by multiple autoimmune sequelae- Arch Dermatol 2010;145:63-66

• The difficulty in interpreting this type of study is that we are given the numerator of the fraction without knowing the denominator

• Not sufficient evidence to warrant routine thyroid screening
Antibiotics in Acne Do Not Cause Weight Gain

• Antibiotics lead to weight gain in farm animals.
• Retrospective cohort study of 1012 adolescents did not find a weight-promoting effect of antibiotics.

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

Shinkai K, McMichael A, Linos E. Test monitoring—a call to decrease testing in an era of high-value, cost-conscious care. JAMA Dermatology 2016;152:17-9
Inflammatory Bowel Disease and Isotretinoin

• Huge cohort out of British Columbia studied retrospectively over 12 years
  – 46,922 treated with isotretinoin
  – 184,824 treated with topical acne medication
  – 1,526,946 untreated


Inflammatory Bowel Disease and Isotretinoin

• No difference among the three groups in development of IBD
  – Isotretinoin OR 1.14 (.92-1.41)
  – Topical acne medication OR 1.11 (.99-1.24)

• Subanalysis by age
  – 12-19 yo isotretinoin OR 1.39 (1.03-1.87)
  – 12-19 yo topical meds OR 1.15 (0.98-1.36)
  – Neither seen in 20-29 yo
Inflammatory Bowel Disease and Isotretinoin

• Subanalysis by IBD type
  – Isotretinoin no increase in UC or Crohns
  – Topical meds OR 1.19 (1-1.42) for UC but not Crohns

• More fuel for the argument that an association with inflammatory bowel disease stems from acne itself rather than the medications used to treat it
Isotretinoin and Inflammatory Bowel Disease

- Meta-analysis, pooled data of 6 studies
- Retrospective cohort studies (2) and case-control studies (4)
- Nearly 10 million patients
- No association found, development of IBD 0.32% in exposed, 0.32% unexposed

IBD and Other Inflammatory Skin Conditions

• Inflammatory bowel disease is significantly associated with rosacea, psoriasis, and atopic dermatitis
• Acne was not studied

IBD and Hidradenitis Suppurativa

- The prevalence of IBD in hidradenitis suppurativa patients is 4-8 times higher than the prevalence in the general northern European population.

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
- No commensurate increase in use of mental health providers
Topical Dapsone and Methemoglobinemia

• A 19-month-old presented with blue skin, lips, and nails
• Rubbed her brother’s acne medicine (5% dapsone gel over her arms the night before
• Methemoglobin level as high as 20.6%

Antibiotics for Abscesses

• Placebo-controlled, double-blind assessment of 7 days of trimethoprim-sulfa antibiotic (2 double strength tablets bid) versus no antibiotic after abscess drainage

• 1247 participants randomized

Antibiotics for Abscesses

• Clinical cure at 7 and 14 days,
  – 80.5% treatment group, more GI side effects
  – 73.6% placebo $P = 0.005$

• Secondary metrics
  – Rates of subsequent drainage 3.4% vs 8.6%
  – Skin infection at new sites 3.1% vs 10.3%
  – Infection in household members 1.7% vs 4.1%
Antibiotics for Abscesses

• Pediatric patients aged 3 months to 17 years
• Presented to ED with uncomplicated abscess that required surgical drainage
• Randomized to 3 or 10 days of TMP-sulfa
• Evaluated 10-14 days after drainage and followed for 6 months

Antibiotics for Abscesses

- *Staph aureus* in 87%, 64% of these MRSA
- All *Staph aureus* susceptible to TMP-sulfa
- Diarrhea, nausea, rash, emesis, and abd pain in 17.5%
- Thirteen treatment failures, no difference in the two groups
- Those with MRSA more likely to be failures with 3 day (9) vs 10 day (2) P = 0.03
Antibiotics for Abscesses

• Recurrent infection at 1 month more likely in 3 days (21) vs 10 days (9) $P = 0.02$

• Six times greater risk of recurrent infection if MRSA treated for just 3 days

• Treat everyone with 10 days to be sure or culture and extend a 3 day treatment to 10 days if MRSA?
Staph Aureus Susceptibility

- 41,745 Staph aureus isolates for 39,207 pediatric patients in US Military Health System
- Oxacillin susceptibility 59.4% in 2005, 53.6% in 2007, 68.4% in 2014
- Slightly more resistance to Clinda, cipro
- Mostly the same for TMP-sulfa, TCN, rifampin

Work-Life Balance

- Survey of 840 mid-career pediatricians
- Biggest effects on burnout, work-life balance, career satisfaction, life satisfaction
  - Excellent or very good self-reported health
  - Personal support from physician colleagues
  - Adequate resources for patient care

Mind-Body Therapies in Children

- Review prepared for the Section on Integrative Medicine from the AAP
- Overall, safe and positive benefits seen with biofeedback, clinical hypnosis, guided imagery, meditation, and yoga