Paediatric Dermatology. What's New?

Stephanie Menzies

Atopic Dermatitis

Emollients in the newborn

- Randomised controlled trial in US & UK
  - 124 neonates high risk for AD
- Full body emollient at least daily versus no emollient x 6/12
- **Prophylactic emollients in high risk newborns reduced risk of AD by 50%** (at 6 months)

  p=0.017

Simpson et al. J All Clin Immunol 2014

Emollients in the Newborn

- 49 patients (AD, non-AD)
- Petrolateum under occlusion versus control and occlusion only:
  - **Increased barrier differentiation markers** (filagrin, loricrin)
  - **Upregulation of antimicrobial peptides** and innate immune genes (IL6, IL8)
  - **Increased thickness of stratum corneum**
  - **Decreased T cell infiltrates**

Czarnowicki et al. Petrolateum: Barrier repair and antimicrobial responses underlying this 'inter' moisturizer. J Allergy Clin Immunol 2016

The hygiene hypothesis

- Those that ‘cleaned’ the pacifier by sucking it versus washing the pacifier
  - **Less asthma, eczema, fewer allergic symptoms**

  Hesselmar et al. Pacifiier cleaning practices and the risk of allergy development. Pediatrics 2013; 131:e1829-37

- Hand versus machine dishwashing
  - **Less eczema, asthma, rhinoconjunctivitis**

  Hesselmar et al. Allergy in children in hand versus machine dishwashing. Pediatrics 2015;135:e590-7

The hygiene hypothesis

- Population-based birth cohort study of 1,037 participants (born between 1972-1973).
- **Thumb-suckers or nail-biters had a lower risk of atopic sensitisation** at 13 years and 32 years (OR 0.67, p=0.013; OR 0.61, p=0.001)
- Non thumb-suckers or nail biters had a higher incidence of positive prick tests

Lynch SJ et al. Thumb sucking, nail biting, and atopic sensitisation, asthma, and hay fever. Pediatrics 2016;138:e1-8

Dysbiosis in AD

- Atopic skin was dysbiotic
  - Staphylcococcus aureus colonisation
- **Coagulase negative bacteria on skin produce beneficial antimicrobial peptides**
  - Prevent growth of S. aureus
  - Common in normal population, rare on AD subjects
- Transplantation of antimicrobial colonies (coagulase negative staph) onto atopic skin decreased colonisation by S. aureus

Nakatsuji et al. Antimicrobials from human skin commensal bacteria protect against Staphylococcus aureus and are deficient in atopic dermatitis. Science Translational Medicine. Feb 2017

Peanut exposure – LEAP trial

- In infants high risk of allergy
  - Sustained consumption of peanuts in the first 11 months of life
  - 81% reduction in peanut allergy at 60 months of age
  - Compared to children who avoided peanuts

Du Toit et al. Randomised trial of peanut consumption in infants at risk for peanut allergy. N Engl J Med 2015;372:803-13

Peanut exposure - Extension of the LEAP trial

- ?Reversion to allergy after cessation of consumption
- Participants asked to avoid peanut for 12 months
- Oral peanut challenge at 72 months
- Beneficial effect of early exposure persisted even when a period of avoidance subsequently occurred
  - 74% lower prevalence of peanut allergy

Du Toit et al. Effect of avoidance of peanut allergy after early peanut consumption. NEJM 2016

Introduction of allergenic foods

- Exclusively breast-fed infants (at 3 months; n=1,303)
- Randomised to receive 6 allergenic foods or standard guideline of exclusive breast feeding for 6 months
  - Peanut butter, egg, cow's milk, sesame paste, white fish, wheat based cereal
- 42.8% adherence

Perkin MR et al. Randomised trial of introduction of allergenic foods in breast-fed infants. New Engl J Med 2016;374:1733-43

Introduction of allergenic foods

- Primary outcome of any food allergy
  - **2.4%** in early introduction group
  - **7.3%** in the 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

Peanut guidelines

- Literature review and consensus expert opinion
- **‘Should have introduction of age-appropriate peanut containing foods as early as 4-6 months’**

Togias et al. Addendum guidelines for the prevention of peanut allergy in the United States: report of the National Institute of Allergy and Infectious diseases-sponsored expert panel. J Allergy Clin Immunol 2017;139:29-44

Peanut guidelines

- No eczema or allergies
  - No evidence for restricting any food
- Mild to moderate eczema
  - No testing needed
  - Introduce peanuts at about 6 months at home
- Severe eczema/egg allergy
  - IgE to peanut < 0.35 kU/L (peanut trial at home)
  - IgE to peanut > 0.35 kU/L (refer for skin prick testing)

Atopic comorbidities

- Children enrolled in Taiwan's National Insurance Program 2000-2010 (longitudinal cohort)
- 387,262 patients with eczema and matched controls (1:1)
- **Autism spectrum 0.5%** vs **0.4%**
- **ADHD 3.7%** vs **2.9%**

Liao T et al. Comorbidities of atopic disorders with autism spectrum disorders and attention/deficit/hyperactivity disorders. J Pediatr 2016;171:248-55

Atopic comorbidities

- Large population based study (US; >400,000)
- **Incidence of headaches higher in patients with eczema**
  - **10.7%** vs **5.4%**
  - OR 1.52 (CI 1.45-1.59)
- Correlated with fatigue, excessive daytime sleepiness, insomnia, 0-3 nights of sufficient sleep

Silverbery et al. Association between childhood eczema and headaches: an analysis of 19 US population based studies. J Allergy Clin Immunol 2016:137:492-9

Melatonin supplementation

- Randomised, double-blind, placebo-controlled, crossover study of 38 children with atopic dermatitis
- Melatonin 3mg at bedtime for 4 weeks, 2 week washout, 4 weeks of placebo
- Primary outcome:
  - **Decrease in SCORAD by 9.1 in melatonin group** (vs placebo) $p<0.001$

Chang Y et al. Melatonin supplementation for children with atopic dermatitis and sleep disturbance a randomised clinical trial. JAMA Pediatrics 2016;170:35-42

Biologics in Paediatrics

Biologics in Paediatrics

- 69 pediatric patients completed 264 weeks of therapy for psoriasis (etanercept)
  - PASI-75 60-70%
  - PASI-90 30-40%
- Adverse events (89%):
  - Upper respiratory tract infection 38%
  - Nasopharyngitis 26%
  - Headache 21.5%
  - Cellulitis in 1 case
  - **No opportunistic infections or malignancy**

Paller AS et al. Long-term safety and efficacy of etanercept in children and adolescents with plaque psoriasis. J Am Acad Dermatol. 2016; 74:280-7

Biologics in Paediatrics

- 127 patients with arthritis (etanercept)
- **No malignancy, active TB, demyelinating disorders or death**
- Adverse events:
  - Headache, pyrexia, diarrhea, URTI, pharyngitis, bronchitis, gastroenteritis

Constantin T et al. Two-year efficacy and safety of etanercept and safety of etanercept in pediatric patients with extended oligoarthritis, enthesitis-related arthritis, or psoriatic arthritis. J Rheumatol 2016;43:816-24

Infantile hemangioma

Pathogenesis

Castren et al. Inheritance patterns of infantile hemangiomas. Pediatrics 2016

- 185 patients
- Questionnaire and review of hospital records
- **1/3 had +ve family history**
- Segregation patterns match with:
  - Autosomal dominant inheritance with incomplete penetrance
  - Maternal transmission

Nasal infantile hemangioma

Kryatova et al. Retrospective study of nasal infantile hemangioma. Pediatr Dermatol 2016

- Retrospective study of 89 patients
- **Complications in 39%** of patients
  - Segmental and indeterminate IH > focal IH (p=0.01)
  - Ulceration occurred more frequently in mixed > deep or superficial (p=0.01)
- 80% had treatment, 19% had surgery
- Complete involution by kindergarten in 70%
  - **78% had residual skin changes**
  - Mixed and superficial > deep p=0.04

Infantile hemangioma - Treatment

Léaute-Labreze et al. Safety of oral propranolol for treatment of infantile hemangioma: A systematic review. Pediatric 2016.

- 5862 propranolol-treated patients
- Up to 3mg/kg per day x 6-36 months
- Most serious AEs – AV block, bradycardia, hypotension, bronchospasm, hypoglycemic-related seizures
- Well tolerated if appropriate pre-treatment screening is done
- **ECHO/ECG is not considered necessary in all**

Is routine ECG necessary?

Yarbrough et al. Is routine electocardiography necessary before initiation of propranolol for treatment of infantile hemangiomas. Pediatr Dermatol 2016 Nov

- 162 patients
  - **43% abnormal ECGs**
  - 17% cardiology review
- No patients were excluded from treatment
- No patients experienced any adverse effect

Indications for ECG

- Physical examination:
  - Bradycardia
  - Cardiac arrhythmia
- Family history of congenital heart defects/cardiac arrhythmias
- Maternal history of connective tissue disease
- Large segmental IH that require cardiac evaluation for PHACE syndrome

When to stop propranolol?

Shah et al. Rebound growth after propranolol cessation. Pediatrics 2016

- Multicentre retrospective study (997 patients)
- Incidence of rebound growth 25%
- Mean age 17.1 months
- **The odds of rebound among those who discontinued therapy at <9 months** was 2.4 compared with those who discontinued therapy between 12-15 months of life (OR 2.4; p=0.004)

When to stop propranolol?

- Increased risk of rebound with:
  - Mixed/deep
  - Head and neck
  - Segmental
  - Female
  - Treatment stopped <9 months of age

- **Taper after >9 months**

Topical Timolol

Puttgen et al. Topical timolol maleate treatment of infantile hemangiomas. Pediatrics 2016.

- Multicentre, retrospective cohort study (731 patients)
- **Best response:**
  - **Superficial infantile hemangioma <1mm thick**, regardless of size
- Other predictors of response:
  - Younger patients
  - Duration of Rx
- Side effect: ulceration, apnoea, bradycardia, local irritation

Systemic absorption of timolol

Weibel et al. Topical timolol for infantile hemangioma: Evidence. Pediatr Dermatol 2016

- 40 infants – small proliferating haemangiomas
  - Timolol gel 0.5% BD
  - Urinary excretion and serum levels
- **High systemic absorption** (83% urine, 100% serum)
- 6 ulcerated – all had urinary presence

PHACE syndrome

Garzon et al. PHACE syndrome: Consensus derived diagnosis and care recommendations. Journal of Pediatrics 2016.

- **New age related comorbidities**
  - Headache
  - Hearing loss
  - Dysphagia
  - Feeding disorders
  - Endocrinology abnormalities (hypothyroidism, growth hormone deficiency)
  - Tooth enamel hypoplasia (intraoral hemangioma)
- Guidelines for screening and health surveillance

Alopecia Areata

Alopecia Areata

- **High rates of anxiety and major depressive disorders**
- HRQoL similar to AD and psoriasis
- SALT – severity of alopecia score tool

JAK Inhibitors

King et al. Tofacitinib for the treatment of severe alopecia areata and variants: A study of 90 patients. JAAD 2017 Jan

- Retrospective study, 90 patients
- Tofacitinib (JAK 1/3) 5mg BD x 3 months
- Change in SALT at 3 months:
  - **1/3 of patients achieved >50%**
  - **1/3 5-50% improvement**
  - 1/3 did not respond

JAK Inhibitors for AA

- No regrowth:
  - Increased up to 10mg BD
  - Add pulsed prednisolone
- Side effects:
  - URTI 28%
  - Headache, acne
- **Most likely to fail treatment**
  - **Alopecia totalis or universalis >/= 11 years**
- Disease relapse in 12% on discontinuing tofacitinib

JAK Inhibitors in Adolescents

Brett King et al. Tofactinib for the treatment of alopecia in adolescents. *J Am Acad Dermatol. 2017 Jan;76(1):29-32*

- 12-17 years old
  - 9 responders
  - 4 non-responders
  - Mean percent change in SALT was 60% at 6.5 months
- Limitations:
  - Small sample size, retrospective, lack of control

Topical JAK Inhibitor

- Topical JAK Inhibitor
  - Compounded ruxolitinib 0.6% cream BD x 12 weeks
  - 1 case report – 10% scalp regrowth and total eyebrow regrowth
  - Effective in mouse models

Alternative uses

- Severe AA associated nail dystrophy also responded to treatment
- No effect on male pattern baldness

- Vitiligo
  - Case report – tofacitinib 5mg OD in 1 case

Atopic dermatitis

- **Systemic**
  - 6 patients, refractory AD
  - Tofacitinib 5mg BD x 6 months
  - SCORAD and pruritus scores reduced

  Levy et al. Treatment of recalcitrant atopic dermatitis with the oral Janus kinase inhibitor tofacitinib citrate. JAAD 2015

- **Topical**
  - Tofacitinib 2% ointment
  - 4 week randomised, double blind placebo controlled trial
  - 69 patients
  - Efficacy for mild to moderate AD

  Bissonnette et al. Topical tofacitinib for atopic dermatitis: a phase IIa randomised trial. Br J Dermatol. 2016 Nov; 175(5):902-911

Thank you for your attention