Paediatric Dermatology. What’s New?

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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)

• Petrolatum 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**

The hygiene hypothesis

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

- Hand versus machine dishwashing
  - Less eczema, asthma, rhinoconjunctivitis
    
The hygiene hypothesis


- **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
  • Staphylococcus 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

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

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

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’

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%

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

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
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- 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

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


- 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

- 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


- 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?


- 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

- 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

- 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


- 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

- **New age related comorbidities**
  - Headache
  - Hearing loss
  - Dysphagia
  - Feeding disorders
  - Endocrinology abnormalities (hypothyroidism, growth hormone deficiency)
  - Tooth enamel hypoplasia (intraoral hemangiomma)

- 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
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 $\geq 11$ years

- Disease relapse in 12% on discontinuing tofacitinib
JAK Inhibitors in Adolescents


- 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

Thank you for your attention