Welcome to the latest issue of Child Health Research Review.

Highlights include confirmation of the benefits of propranolol for the treatment of infant haemangiomas, a report of paediatric teledermatology in a Californian institution, and an interesting comparison of human breast milk and hydrocortisone 1% ointment for the treatment of nappy rash. We have also included a report of the impact of inhaled budesonide in childhood on adult height. This issue’s comments have been provided by Paediatric Dermatologist Diana Purvis and Paediatric Endocrinologist Dr Craig Jefferies, both of whom work at Starship Children’s Hospital.

We hope you find the selected studies interesting and useful in your clinical practice.

Kind regards,
Dr Chris Tofield
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Propranolol and infantile hemangiomas four years later

Authors: Marqueling A et al.

Summary: This systematic review examined the efficacy and tolerability of propranolol in the treatment of infantile haemangiomas. 41 studies (n=1264) published in 2008–2012 were identified from a search of MEDLINE and Cochrane databases. Overall, propranolol was started at a mean age of 6.6 months, at a mean dose of 2.1 mg/kg/day and continued for a mean 6.4 months. The response rate (defined as any improvement) ranged from 82–100%. Studies that evaluated the use of propranolol for infantile haemangiomas at specific sites (e.g. periorbital) had comparable response rates. Rebound growth occurred in 17% of infantile haemangiomas in studies that followed patients after treatment completion. 371 adverse events were reported in 1189 patients, the most common of which were changes in sleep (n=136) and acrocyanosis (n=61). Serious adverse events were reported in 1189 patients, the most common of which were changes in sleep (n=136) and acrocyanosis (n=61). Serious adverse events were rare.

Comment (DP): The discovery in 2008 that propranolol was effective for treatment of infantile haemangiomas has resulted in a paradigm shift in the way we manage these common birthmarks. Although the majority do not cause complication and do not require treatment, a significant minority do benefit. This paper reviews published experience to date, and supports my clinical experience of prescribing propranolol. Firstly, infants tolerate this medication well, with good clinical response evident in the majority, in terms of cessation of growth, healing of ulceration and flattening of the haemangioma. Secondly, the average age of commencing treatment was late, as much of the growth of haemangiomas occurs by 3 months of age. Ideally infants should be referred by the time of their 6-week check if they have a haemangioma that may require intervention. Intervention should be considered for infants with haemangiomas of the face and neck – especially if close to the eye/nose/mouth or affecting the airway; ulcerated haemangiomas; haemangiomas at risk of ulceration (e.g. flexural); segmental haemangiomas or haemangiomas at risk of causing permanent significant cosmetic defect.


Abstract
Time trends, ethnicity and risk factors for eczema in New Zealand children: ISAAC Phase Three

Authors: Clayton T et al.

Summary: This British study evaluated the benefits of a multifaceted educational support programme for increasing emollient use and reducing atopic eczema in children. The programme comprised an educational DVD for parents and carers, an online daily diary and a telephone helpline. 136 children and their parents provided baseline and 12-week follow-up data. At 12 weeks, average emollient use had increased by 87.6g from baseline (p=0.001), and this increase was immediate and persistent. The Patient Oriented Eczema Measure (POEM) score decreased by a mean 47% from baseline and the Patient Eczema Severity Time (PEST) decreased by 48%. Sleep disturbance was reduced by 1.27 nights per week (p<0.001) and parental feelings of control improved by 1.32 points (p=0.001). The programme was found to be cost neutral.

Comment (DP): Underuse of topical therapies is the most common cause of eczema treatment failure. Regular emollient use may be achieved through the use of emollients, and use topical steroids in children with eczema. These are available on the Paediatric Society website. Useful resources:

Reference: ISAAC Phase Three

Eczema videos
http://www.kidshealth.org.nz/eczema-care-3-easy-steps

Eczema care plan for families

Improved emollient use reduces atopic eczema symptoms and is cost neutral in infants: before-and-after evaluation of a multifaceted educational support programme

Authors: Mason J et al.

Summary: This British study evaluated the benefits of a multifaceted educational support programme for increasing emollient use and reducing atopic eczema in children. The programme comprised an educational DVD for parents and carers, an online daily diary and a telephone helpline. 136 children and their parents provided baseline and 12-week follow-up data. At 12 weeks, average emollient use had increased by 87.6g from baseline (p=0.001), and this increase was immediate and persistent. The Patient Oriented Eczema Measure (POEM) score decreased by a mean 47% from baseline and the Patient Eczema Severity Time (PEST) decreased by 48%. Sleep disturbance was reduced by 1.27 nights per week (p<0.001) and parental feelings of control improved by 1.32 points (p=0.001). The programme was found to be cost neutral.

Comment (DP): Underuse of topical therapies is the most common cause of eczema treatment failure. Regular generous use of emollients (about 250g per fortnight) is recommended and has been shown to both reduce eczema severity and need for topical steroids. Emollients are an important part of the ‘care package’ for eczema, which also includes avoiding soap, topical steroids and addressing infection if present. Many parents report wanting more time spent explaining the nature of eczema and how to use prescribed treatments. Specialised nurse-led education has been shown to increase use of emollients, decrease eczema severity and improve parent satisfaction. However, not all families can access eczema nurse care. This study shows that provision of an educational DVD and a written handbook on emollient use significantly reduced eczema severity, reduced the number of nights of broken sleep and increased parental sense of control. The Paediatric Society Eczema Clinical Network has recently produced online videos with the aim of supporting education of families throughout New Zealand. These explain how to bath, apply emollients, and use topical steroids in children with eczema. These are available on the Paediatric Society website.


Useful resources:

Eczema videos
http://www.kidshealth.org.nz/eczema-care-3-easy-steps

Eczema care plan for families

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NZ GLL13.09.001 TAPS P34300 Prepared September 2013.
Pediatric teledermatology consultations: relationship between provided data and diagnosis

Authors: Phil J et al.

Summary: This retrospective cohort study reviewed the adequacy of data and photographs sent by referring providers to a paediatric teledermatology clinic in California, and examined the relationship between the provided data and subsequent diagnosis. A diagnosis was made in approximately two-thirds of cases. Prior treatment was the only historical data associated with receiving a diagnosis (odds ratio 2.01, p<0.05). Appropriate image distance from the target was associated with receiving a diagnosis for rashes and growths (odds ratios 2.69 and 4.16, respectively; both p<0.04). A lack of diagnosis was significantly associated with a recommendation for referral for biopsy or for in-person consultation. In conclusion, paediatric teledermatologists are able to make a diagnosis most of the time, regardless of the information provided or image quality.

Comment (DP): Telemedicine is being used with increased frequency to improve care for patients who may have barriers to access due to geography, limited numbers of specialists or difficulties attending appointments. This study looks at the use of paediatric teledermatology by a Californian institution. Images were reported to be of adequate quality in over three-quarters of cases (a greater frequency than my personal experience). This group was able to achieve a definite diagnosis in 64% of referrals, probable in 23% and a differential diagnosis in 13%. Other studies have shown concordance of teledermatology diagnosis with face-to-face diagnosis at rates ranging between 40% and 100%. I am frequently asked to assess photographs of skin problems by colleagues, patients and friends. In many cases it is not possible to reach a diagnosis. Occasionally I’m shown classical presentations making diagnosis more straightforward. However there is more to medical care than reaching a diagnosis and the other aspects of management and communication are even more challenging at a distance. Although there may be a role for teledermatology, face-to-face consultation will remain the gold standard of care for the foreseeable future.

Abstract

Comparison of the effect of human milk and topical hydrocortisone 1% on diaper dermatitis

Authors: Farahani L et al.

Summary: Diaper dermatitis affects 7–35% of infants and is one of the most common skin problems in infants and children. This study compared the efficacy of human breast milk and hydrocortisone 1% ointment in the treatment of acute diaper dermatitis. 141 infants with diaper rash were randomised 1:1 to have their diaper rash treated with either hydrocortisone 1% ointment or human breast milk for 7 days. The rash improved from baseline in both treatment groups on days 3 and 7; there were no significant between-group differences. In conclusion, human breast milk was as effective as hydrocortisone 1% ointment in the treatment of diaper dermatitis.

Comment (DP): Nappy rash (diaper dermatitis) is common and for the most part responds well to use of barrier creams alone. Topical antifungals may be needed if there is secondary candidal infection. Topical steroids are rarely required, and certainly would not be first-line therapy. This study compared human breast milk with topical 1% hydrocortisone for mild-moderate nappy rash and found the two treatments to be of similar efficacy. However it is interesting to note that the patient is right, they have upregulated their brown fat, and this persists for some time, even when the thyroid function is normalised.

Abstract

A lifetime of hypercalcaemia and hypercalcuiuria, finally explained

Authors: Jacobs T et al.

Summary: This case report described a patient with hypercalcaemia, hypercalcuiuria, and recurrent nephrolithiasis who was studied for over 30 years. The patient was treated with a low-calcium diet, low vitamin D intake, prednisone and ketoconazole. Dual isoalte absorptiometry showed that the patient’s calcium absorption was elevated (37.4%). Two different laboratories recorded very low serum levels of 24,25-dihydroxyvitamin D (0.62 and 0.18 ng/ml (normal 3.49 ng/ml). Genetic analysis of CYP24A1 revealed homozygous mutation E143del. Serum calcium and renal function improved after treatment with ketoconazole but not with prednisone. In conclusion, chronic hypercalcaemia, hypercalcuiuria, and/or nephrolithiasis may be due to CYP24A1 mutations that reduce the patient’s ability to metabolise 1,25-dihydroxyvitamin D.

Comment (CJ): In a previous report in regard to infantile hypercalcaemia (N Engl J Med 2011;365(9):410-21; http://dx.doi.org/10.1056/NEJMoa1103964) the culprit has been shown to be inactivating mutations of the CYP23A1 in infants i.e. they became hypercalcemic with vitamin D supplementation, as a result of poor ability to deactivate vitamin D. This case report expands this to the adult realm where the point is that: 1) chronic high calcium with high urine calcium may be lack of ability to deactivate vitamin D; and 2) this can be improved with normalisation of calcium with ketoconazole, an inducer of the CYP enzyme system.

Reference: J Clin Endocrinol Metab 2014; published online Jan 13
Abstract

Hyperthyroidism increases brown fat metabolism in humans

Authors: Lahesmaa M et al.

Summary: This study examined the impact of hyperthyroidism on brown adipose tissue (BAT) metabolism in humans. 10 patients with overt hyperthyroidism and 8 healthy controls had glucose uptake and perfusion of BAT, white adipose tissue, skeletal muscle, and thyroid gland measured using positron emission tomography imaging. Hyperthyroid patients had 3-fold higher BAT glucose uptake (p=0.013), 90% higher skeletal muscle glucose uptake (p<.005), 45% higher energy expenditure (p<0.005), and a 70% higher lipid oxidation rate (p=0.001) than healthy controls. Hyperthyroidism had no effect on BAT perfusion. The differences between hyperthyroid patients and controls were reversible after restoration of euthyroidism. In conclusion, hyperthyroidism increases glucose uptake in BAT independently of BAT perfusion.

Comment (CJ): In case you had missed the news, not all fat is bad. Recently ‘rediscovered’ brown fat is still present in adults, in small amounts, and activated by cold. Investigations are underway as to whether this may be a key to those slim humans who can eat anything and not get fat (do they have increased brown fat and can simply burn it off?). The reason I included this study is that in hyperthyroidism one of the key symptoms is feeling ‘hot’ and this is often the case once the Free T4 is normalised. Well it appears that the patient is right, they have upregulated their brown fat, and this persists for some time, even when the thyroid function is normalised. Although it has not been studied, I wonder if the reverse is the case i.e. in hypothyroidism, people still feel cold as their brown fat is down-regulated even when their free T4 is normalised.

Abstract

Independent commentary by Dr Diana Purvis

MChB (Otago), MRCPCH (London), FRACP (Paediatrics) and (Dermatology)

Diana is both a paediatrician and a dermatologist, with experience in adolescent health, neonatology, allergy and rheumatology. She trained in New Zealand and at Great Ormond Street Children’s Hospital in London. Diana is a dermatologist at Starship Children’s Hospital and is currently a lead in the development of National Network for the Treatment of Childhood Eczema.

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**Effect of inhaled glucocorticoids in childhood on adult height**

**Authors:** Kelly H et al., on behalf of the CAMP Research Group

**Summary:** This study investigated the effect of inhaled glucocorticoids in childhood on adult height. 1041 participants in the Childhood Asthma Management Program were randomised at the age of 5–13 years to receive budesonide 400µg, nedocromil 16mg or placebo daily for 4–6 years. Adult height was measured in 943 participants at a mean age of 24.9 years. Mean adult height was 1.2cm lower in the budesonide group than in the placebo group (p=0.001) and 0.2cm lower in the nedocromil group than in the placebo group (p=0.05). A larger daily dose of inhaled glucocorticoid in the first 2 years was associated with a lower adult height (~0.1cm per µg/kg; p=0.007). In conclusion, the initial decrease in attained height seen with the use of inhaled glucocorticoids in prepubertal children persisted into adulthood.

**Comment (CJ):** This was a study commented on in a number of leading journals. The concern from endocrinologists is that inhaled steroids are systemically absorbed, they do get further than the lungs, and there are small but subtle defects in growth. The importance is that, as several commentaries have stated, it is better to be alive with asthma and 1cm shorter than to die from asthma. The study itself is important in that the authors have clearly demonstrated a dose-dependent effect of inhaled steroids on adult height. The authors highlight the importance of treatment of atopic eczema in early life with systemic glucocorticoids, but that such treatment should be limited to children with severe disease.


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**The adverse health consequences of the use of multiple performance-enhancing substances – a deadly cocktail**

**Authors:** Perera N et al.

**Summary:** This case report described the harmful consequences of abuse of performance-enhancing substances (PESs) in a recreational weight lifter/physical trainer. The previously healthy man had been using multiple PESs, stimulants, and masking agents long term and presented to a tertiary-care hospital with jaundice and mild hepatitis. This progressed rapidly into liver and multisystem organ failure. The toxicity was found to be arsenic-related. This cautionary case reinforces the need to increase awareness of surreptitiously or self-administered cocktails of potential PESs.

**Comment (CJ):** I included this as the acronym of PES (performance enhancing substances) was a new one, and also to highlight the polypharmacy and contaminants that are becoming rife in certain sporting circles. It also highlights that the contaminants in these substances are often the culprit for severe complications, and that those that impair, infect or absorb these agents are setting themselves up for severe long term consequences, or in this case, severe short term demise. Again, important to know one’s poison, and that as far as the gym and body building goes: no pain, no gain. Unfortunately anecdotal use of steroid availability and use in gyms even in late adolescence is common, and in the USA is a huge problem especially with the financial rewards available in the professional sports.

**Reference:** J Clin Endocrinol Metab 2013;98(12):4613-8

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**Independent commentary by Dr Craig Jefferies**

**BHB, MBCHB, Dip Paeds, FRACP, MD.**

Craig has been a Paediatric Endocrinologist based at the Starship Children’s Hospital since 2005, where he is the current Clinical Director of the Paediatric Endocrinology Service. He attended medical school at Auckland, and received the majority of his Paediatric training in Starship before completing a fellowship in Paediatric Endocrinology at the Hospital for Sick Children, Toronto, Canada. His current roles include: inpatient and outpatient care for Endocrinology and Diabetes at the Starship, as well as visiting outreach clinics in the North Island including Taranaki, Tauranga, Rotorua and Gisborne. He is an honorary senior lecturer at the Liggins Institute.

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**CLICK HERE to read about Methylprednisolone aceponate 0.1% ointment/cream with commentary by Dermatologist Jennifer Pilgrim.**

This review discusses the evidence in support of the use of methylprednisolone aceponate 0.1% ointment/cream, a fourth-generation, non-halogenated topical corticosteroid approved for use in New Zealand for the management of atopic eczema.

**Disclaimer:** This publication is not intended as a replacement for regular medical education but to assist in the process. The reviews are a summarised interpretation of the published study and reflect the opinion of the writer rather than those of the research group or scientific journal. It is suggested readers review the full trial data before forming a final conclusion on its merits.

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