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Patch testing in children, a useful investigation

P.E.BEATTIE AND M.S.LEWIS JONES

Dept. of Dermatology, Ninewells Hospital, Dundee, UK

Allergic contact dermatitis in children, until recently considered rare, appears to be increasing in incidence. This may however reflect an increased tendency to patch test children. The reported rate of positive patch test reactions in children varies from 14–70% and of relevant reactions from 20–92%. Most studies have involved limited patch testing.

A retrospective case study of all children under the age of 16 years who had been patch tested over a 3-year period in our department was carried out. The children had a variety of indications for patch testing including uncontrolled atopic dermatitis, non-atopic dermatitis in localised areas such as the foot, scalp and oral region or a history of reacting to foodstuffs or local anaesthetic creams.

There were 118 children (69 girls and 49 boys) aged from three to 15 years (median 11, IQR 8–14 years). Overall 67 (57%) children had positive reactions that were of current or past relevance or uncertain relevance. Testing to the standard series had been carried out in 111 children, of whom 58 (52%) had a positive reaction. Sixty children had been patch tested to medicaments of whom only six had a positive reaction. None of the children patch tested to corticosteroids ($n = 47$), shoe series ($n = 15$), fragrance series ($n = 12$), cosmetic series ($n = 10$) or rubber series ($n = 5$), had a positive reaction. One of five children tested to sunscreens reacted to Uvistat and one of two tested to the dental battery reacted to Palladium. Four children were tested to latex and did not react. Thirteen children were tested to their own creams and five to their own shoes (one positive). Open patch testing to food additives was indicated in ten children, with positive reactions in all. Nickel was the most common allergen (29%), as reported previously, followed by cobalt (9%), fragrance (7%), lanolin (5%) and rubber chemicals. An irritant reaction to cobalt was seen in 17%.

Our incidence of nickel allergy is higher than reports from Glasgow¹ and Sheffield² and may reflect an increased incidence of body piercing and nickel exposure at a young age or a higher pick-up rate. Patch testing is a useful and worthwhile investigation in a paediatric setting. The incidence of positive reactions is high and avoidance of clinically relevant allergens may be a useful adjuvant to topical therapy.

References

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Psychological problems and childhood atopic eczema

W.K.WOO, A.HIGGINS*, JR CORBETT AND E.A.BINGHAM

Department of Dermatology, *Department of Clinical Psychology, Royal Victoria Hospital, Belfast, UK

This is a preliminary report of a series of twelve children with 'difficult to control eczema' where psychological interventions helped. The children aged 2–12 years (mean age 6.3; five females)

were identified for psychological intervention on the basis that an excessive itch-scratch cycle was associated with adjustment difficulties (e.g., treatment non-compliance; behavioural problems; peer relationship difficulties; anxiety). Psychological interventions used included relaxation and distraction techniques, hypnosis, social skills training, cognitive behaviour therapy, reinforcement schedules and behaviour management strategies. Not only did these interventions have benefits for the proximal psychological problems outlined above, but also for eczema control. In eight of the twelve cases there were improvements. Two cases showed partial and unsustainable improvement and were referred to community services because of non-illness related factors (i.e., Attention Deficit Hyperactivity Disorder). There was an attrition rate of two out of twelve across treatment. Our findings indicate the potential importance of clinical psychology provision to paediatric dermatology services and the need for more controlled systematic investigation.

Atopic dermatitis and the hygiene hypothesis: a case control study

S.GIBBS*, H.SURRIDGE¶, R.ADAMSON¶, B.COHEN§, G.BENTHAM† AND R.READING¶

*Dermatology Department, Ipswich Hospital, Ipswich IP4 5PD, ¶School of Medicine, Health Policy and Practice, University of East Anglia, Norwich, NR4 7TJ, §PHLS Central Public Health Laboratory, Colindale, London NW9 5HT, †Department of Environmental Science, University of East Anglia, Norwich NR4 7TJ

The notion that a reduced exposure to microbial pathogens in early life increases the chances of the expression of atopic disease has come to be known as the hygiene hypothesis¹. It has arisen from observations of the rapidly rising prevalence of atopic diseases in recent decades, the lower prevalence of atopy in lower socio-economic groups and the lower prevalence of atopy with rising birth order. Direct evidence for the hypothesis to date has been inconsistent.

This case-control study involving 602 children aged one to four years in Norfolk, UK was designed to test the hypothesis with respect to atopic dermatitis (AD). Cases and matched controls were selected randomly from primary care databases and carefully defined using the UK Diagnostic Criteria for AD. Exposure to infection during infancy was measured with a range of direct and indirect methods including assays of salivary antibodies to Epstein Barr virus and Varicella Zoster virus, data extracted from primary care records and a questionnaire administered to parents. Odds ratios (OR) for the effect of these measures on AD were calculated using logistic regression with adjustment for possible biological and social confounding factors.

Reduced odds of AD were associated with rising birth order (OR for one older sibling 0.59, 95% CI 0.42 to 0.84 and for two or more older siblings 0.49, 95% CI 0.31 to 0.77). None of the measures of exposure to infection reduced the odds of AD, either in the unadjusted or adjusted analyses. Some measures showed a weak association between exposure and greater odds of AD, in the opposite direction to that predicted by the hygiene hypothesis.

These data confirm a significantly reduced risk of AD in second and subsequent siblings but this 'sibling effect' of reduced odds with rising

birth order does not appear to be explained by exposure to infection in early life. More generally, these data cast doubt on the hygiene hypothesis as a causal explanation for AD in young children.

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Contact urticaria to play dough: a possible sign of dietary allergy

S.E.BARON AND C.MOSS

Department of Dermatology, Birmingham Children's Hospital, Steelhouse Lane, Birmingham

A 3-year-old boy, one of triplets, with eczema from 4 months of age suffered a severe reaction at nursery. Whilst playing with play dough his hands and forearms became immediately erythematous, swollen and intensely itchy. The contact urticaria took 2 hours to subside. There was no concomitant flaring of his eczema. Cautious re-exposure identified red play dough as the cause. Because of the possibility of allergy to red dyes in foods and medicines (to which he had never been exposed), and future exposure to play dough, further tests were carried out to identify the precise allergen.

Information about constituents of their products was obtained from the manufacturers of Playdo[®], Early Learning Centre Soft Stuff[®], Play Stuff[®] and Ivanhoe[®] play dough, Smarties[®] and coloured antibiotic syrups. The child then underwent open patch testing. Smarties[®] and Smartie-sized pieces of play dough were applied to the forearm under micropore[®] adhesive tape. Cotton wool soaked in the antibiotic syrups was applied to the back under micropore[®] adhesive tape. After 20 minutes there was acute contact urticaria to the red Playdo[®], the red Smartie[®] and the red Cefaclor syrup. At 40 minutes there was a milder reaction to the orange Playdo[®] and orange Smartie[®]. The child was given oral chlorpheniramine and the reactions settled over the next hour. The common ingredient of red and orange Playdo[®] and red and orange Smarties[®] is the colourant E124. Cefaclor syrup contains E129 as a colourant.

Open patch testing is widely used as a test for dietary allergy. Therefore, in view of the positive tests, we advised avoidance both topically and orally of all products containing E124 and E129. This is the first report to date of a child presenting with contact urticaria to these two additives. A history of play dough allergy may thus provide useful information about dietary allergy.

Hydroxychloroquine therapy for Hydroa vacciniforme

V.S.RAMRAKHA-JONES AND D.BILSLAND

Department of Dermatology, Southern General Hospital, Glasgow

Hydroa vacciniforme is a rare idiopathic photodermatosis which typically starts in childhood. It presents with an exposed-site blistering eruption, which eventually heals with crusting and scarring. Although spontaneous improvement occurs with age, the mean duration of the disease is 9 years, and tends to be longer in males¹. Thus, it can severely impair the child's quality of life particularly in the summer months.

We report a case of a 10 year old boy with an 8 year history of hydroa vacciniforme characterised by severe summer flare-ups, with haemorrhagic blistering on the face and hands, often secondarily infected. These disease flares failed to respond to various photoprotective measures including sunscreens, dietary fish oils, beta-carotene, and narrowband UVB desensitisation.

For 4 months over the summer of this year (May to August) he was treated with hydroxychloroquine at a dose of 100 mg daily

(3 mg/kg). This drug was tolerated well and has markedly reduced the extent and severity of his blistering. Hydroxychloroquine has been used in other photodermatoses, and there is one report of its use in the treatment of hydroa vacciniforme.²

While the amount of ambient ultraviolet radiation is a variable factor which can influence disease expression, we have been sufficiently impressed with the therapeutic response to report this case.

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Childhood onset systemic lupus erythematosus and complement deficiency

S.L.WALKER AND M.JUDGE

Dermatology Centre, Hope Hospital, Manchester

A 15-year-old boy presented with a 2-month history of lethargy and a rash affecting his cheeks, nose and ears. His exercise tolerance had diminished and he complained of painful knees, mouth ulcers and scalp hair loss. Anorexia led to 6 kg weight loss. He was off school. There is no significant past medical history. His mother's cousin and her son have systemic lupus erythematosus. His mother incidentally has lichen planus.

Examination revealed discrete, livid infiltrated plaques on the cheeks, nose and ears. There was associated hyperpigmentation. He had a reticulate rash on the flexor aspects of his arms, vasculitic lesions affecting the tips of his digits and brown, annular macules on both palms. General examination including the musculoskeletal system was normal.

The differential diagnosis was that of systemic lupus erythematosus (SLE) with sarcoidosis a possibility.

He had a normochromic normocytic anaemia with a b 11.7, WCC 3.3 and a mild thrombocytopenia 129. ESR 24. Renal, liver, thyroid function and a serum ACE level were normal. Antinuclear antibody (ANA) was strongly positive 1/10 000 speckled. Ro antibody positive. Double stranded DNA antibodies were borderline. Both C3 and C4 were markedly reduced 0.31 and 0.06 g/l respectively. C1 esterase inhibitor, C1q and CH50 were all normal. Anticardiolipin and antineutrophil cytoplasmic antibodies were negative. Urinalysis was negative and has remained so throughout follow up. A skin biopsy was performed which demonstrated features suggestive of lupus.

He was commenced on prednisolone 40 mg daily, topical beta-methasone and sun block. His symptoms improved somewhat and hydroxychloroquine 200 mg daily was added in as the steroid dose was reduced. His symptoms have resolved, his ESR is normal and his ANA titre is currently 1/1000. The hyperpigmentation persists but he no longer requires a topical steroid. At 9 months follow up he is on prednisolone 2.5 mg daily and hydroxychloroquine 200 mg daily.

The incidence of SLE among children under 15 is approximately 0.5 per 100 000 with a female to male ratio of 2:1 before puberty.

Heparin skin necrosis in a child

A.TAKWALE, K.BATTA, P.MILLER* AND C.MOSS

*Department of Dermatology & Cardiology, *Birmingham Children's Hospital, Birmingham*

Heparin-induced skin necrosis is a rare but potentially serious side effect of anticoagulants. Dermatologists may be familiar with coumarin skin necrosis in adults, but this adverse effect is less

common with heparin and in children. We report a girl who developed skin necrosis 3 hours after an intra-arterial heparin injection given for a routine procedure.

A 5-year-old girl with an asymptomatic patent ductus arteriosus (PDA) and a small ventricular septal defect underwent routine catheterisation for closure of the PDA. She had been born at 29 weeks gestation and required numerous interventions as a neonate, but was now well apart from mild eczema. She received intra-arterial sodium heparin (monoparin) 800 i.u. at the beginning of the procedure, which lasted for 90 minutes. Other drugs included: midazolam, propofol, cisatracurium, fentanyl citrate and cefuroxime. Three hours later she developed two very painful, purple, angular, clearly demarcated areas on the buttocks. Immediate treatment included topical betamethasone valerate, iv hydrocortisone and Chlorpheniramine maleate. The central area of the larger lesion subsequently blistered and appeared necrotic. The lesions gradually healed over the next two weeks with minimal scarring and no recurrence.

When first examined by a dermatologist at 24 hours, the lesions were thought to represent acute thermal burns. However investigation of the operating theatre revealed no possible contact with a heat source. A local vasculitic or thrombotic process was suggested by the lesional morphology and heparin seemed the most likely cause.

Heparin may induce platelet-aggregating immunoglobulins in susceptible individuals causing a type III Arthus reaction manifesting as thrombocytopenia, skin necrosis and thrombosis. Heparin IgG antibodies and heparin-platelet factor 4 levels are usually raised but were negative in our patient. Cutaneous necrosis secondary to heparin administration may serve as a warning of the potentially lethal complications of iv use. This child is likely to require anticoagulation for future procedures. Fortunately alternative anticoagulants are available such as danaparoid sodium or r-hirudin.

Congenital linear porokeratotic eccrine ostial dermal duct naevus

L.A.MURPHY AND D.J.ATHERTON

Paediatric Dermatology, St Johns Institute of Dermatology, London

Porokeratotic eccrine ostial and dermal duct naevus (PEODDN) is a rare hamartomatous malformation centred on the eccrine sweat duct. The distinctive histological feature is the presence of well-formed cornoid lamellae in close association with eccrine sweat ducts. The term porokeratotic eccrine ostial and dermal duct naevus (PEODDN) was coined by Abel & Read (1980) to describe this clinical entity¹.

We report a patient with PEODDN who exhibited a long linear hyperkeratotic lesion on the left lower limb which developed during the weeks after birth, and which extended from the buttock to the proximal nail fold of the great toe. In addition there were scattered hyperkeratotic lesions on the left palm, comprising groups of comedo-like papules. The child was systemically well and had been a full-term normal spontaneous delivery; parents were nonconsanguineous and there was no relevant family history.

Two distinctive types of lesion are recognised clinically in PEODDN, both of which are demonstrated in our patient: palmo-plantar papules resembling comedones, whose central pits are occluded with keratin plugs, and hyperkeratotic plaques which resemble linear verrucous epidermal naevi. Histologically the hallmark of the condition is the close association of cornoid lamellae with eccrine sweat apparatus.

This rare hamartoma is considered to arise from the eccrine duct². It has been suggested that PEODDN could represent an abnormal keratinizing epidermal invagination rather than an abnormally dilated and parakeratotic acrosyringium and dermal duct.

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A case of lipid proteinosis with molecular diagnosis

T.HAMADA, RAJ EADY AND J.A.MCGRATH

Department of Cell and Molecular Pathology, St John's Institute of Dermatology, St Thomas' Hospital, London, UK

Lipoid proteinosis (OMIM 247100) is a rare, autosomal recessive disorder characterized by skin scarring and infiltration as well as vocal cord thickening leading to hoarseness. Histologically, there is widespread deposition of hyaline material and disruption/reduplication of basement membrane. Recently, we have mapped the disorder to 1q21 and identified the gene for lipid proteinosis as the extracellular matrix protein 1 gene, *ECM1*¹. Ten different homozygous mutations have now been identified in patients from a number of different countries. In each case, the sequence changes comprise nonsense, frameshift, or internal deletion mutations leading to loss-of-function of *ECM1*¹.

We report here the case of a 14-year-old Pakistani boy with consanguineous parents, whom we have followed at St Thomas' Hospital since early childhood. He has had progressive hoarseness since early infancy. Skin signs are relatively mild. There is diffuse skin thickening, which also affects the tongue, and pitted scarring on the face and upper trunk. Molecular analysis revealed a homozygous C>T transition at nucleotide 1036 in exon 7 of *ECM1*; the mutation is designated Q346X, which is predicted to result in loss of function of the *ECM1a* isoform.

Although the precise function of *ECM1* is not known, molecular analysis of *ECM1* not only improves diagnostic accuracy and make feasible carrier screening and DNA-based prenatal diagnosis in lipoid proteinosis, but also indicates the potential importance of *ECM1* in several aspects of normal skin biology, including wound healing.

Reference

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“Transient” Bullous Disease of the Newborn may be severe

S.E.BARON*, F.SHAH*, RAJ EADY† AND C.MOSS*

**Department of Dermatology, Birmingham Children's Hospital and †St John's Institute of Dermatology, St Thomas's Hospital, London*

Transient bullous disease of the newborn is a rare form of recessive dystrophic epidermolysis bullosa in which type VII collagen is initially retained in epidermal cells, only later reaching its normal position at the dermo-epidermal junction. Affected infants have a relatively good prognosis, often with complete resolution of blistering by 12 months of age. However, as our patient illustrates, the neonatal presentation can be very severe.

A full-term female infant, born to consanguineous Pakistani parents, presented at birth with extensive skin loss affecting knees, shins, forearms and feet. She had normal nails and a normal cry. Over the first week she developed further blisters on the abdomen and buttock and later in her mouth. A diagnostic shave biopsy of a rubbed area of unaffected skin, taken at 7 days, showed widespread separation along the dermo-epidermal junction under light microscopy.

Electron-microscopy showed that the split was immediately beneath the lamina densa, with perinuclear inclusions in numerous basal keratinocytes. Immunoelectron microscopy identified the inclusions as type VII collagen, while the normal linear staining for type VII collagen at the dermo-epidermal junction was absent. Laminin 5 (GB3) staining was normal and linear. These changes are characteristic of transient bullous disease of the newborn. The denuded areas of skin healed over the first two months, with minimal further blistering.

Transient bullous disease of the newborn was first described by Hashimoto in 1985. Whilst in the early neonatal period the blistering and erosions can be severe (fatal in one case), by 12 months of age the infants are usually free of blisters. Sequential skin biopsies of such children show a gradual progression of type VII collagen from its

early intraepidermal position to a more normal unbroken band at the dermo-epidermal junction, mirroring the clinical improvement. It is therefore necessary to take an early biopsy, preferably within the first 2 weeks of life in order to recognize this variant of dystrophic epidermolysis bullosa.

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