Endocrinology and diabetes

G1 SELECTING GIRLS WITH PRECOCIOUS PUBERTY FOR BRAIN IMAGING: EUROPEAN VALIDATION OF AN EVIDENCE-BASED DIAGNOSIS RULE


Background: Central precocious puberty (CPP) reveals an occult intracranial lesion (OICL) in 5-10% of affected girls. Systematic brain imaging is recommended but is normal and then not contributive in 90-95% of the cases. Recently, two American groups formulated distinct guidelines to select girls with CPP who require brain imaging. A previous single-center study found those recommendations to lack sensitivity to OICL and had proposed a 100% sensitivity, evidence-based, diagnosis rule, combining two independent predictors of OICL: age at puberty onset [ie, breast development] <6 years, and estradiol (E2) level >45th percentile of girls with idiopathic CPP.

Aim: To validate our previous findings on a large population.

Methods: A retrospective study was performed, including all girls with CPP seen in 7 centers, in 6 European countries during given periods. American recommendations and the stability of our previously derived diagnosis rule were tested.

Results: 443 girls with CPP, including 35 with OICL, were recruited. American recommendations did not identify all OICL. Previously identified independent risk factors for OICL were confirmed: age <6 years (adjusted odds ratio 20.5, 95% CI 8.1–52.1) and E2 >45th percentile (3.0, 95% CI 1.3–7.1). The previously derived diagnosis rule had 100% sensitivity (95% CI 90–100%): all girls with OICL had either an age <6 years or an E2 level >45th percentile. The specificity was 39% (95% CI 34–44).

Conclusions: American recommendations do not seem safe to select European girls with CPP who require brain imaging. In settings where systematic brain imaging is not possible, the proposed diagnosis rule could help safely to avoid more than one-third unnecessary brain imaging.

G2 SLOWING OF GROWTH IN CHILDREN STARTING TREATMENT WITH STIMULANT MEDICATION

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Aims: To establish the timing of the effect of stimulant medication on growth in height. Previous studies over the past 30 years have given conflicting results. None has analysed longitudinal changes in the height velocity. The effect of stimulants on growth remains controversial.

Methods: Growth data from files of all newly treated patients with attention deficit hyperactivity disorder (ADHD) within one paediatric practice were retrospectively reviewed. Seven girls and 44 boys were treated for 6-42 months with either methylphenidate (n=19) or dexamphetamine (n=23). OGH in standard deviation score (SDS) for height velocity, height and weight were analysed using paired t-tests.

Results: There was significant slowing of the height velocity for the first 30 months compared to the age and sex corrected mean from between 0.6 to 1.8 SDS. A further slowing of 0.75 SDS, at 18 yr (n=35) – 0.75, at 18 yr (n=36) – 0.68, and at adult Ht (n=32) – 0.42. Time from onset of symptoms to diagnosis was negatively correlated with Ht at diagnosis (p <0.01). Height SDS was significantly related to Ht SDS at age 16 yrs (p<0.001), 18 yr (p<0.01), and >18 yr (p<0.01), independent of mid-parental height. Jejunal disease was negatively associated with Ht SDS at age 16 yr (p<0.001) and 18 yr, >18 yr (p<0.05). There was no significant effect of St in adolescents with CFS compared to controls.

Conclusion: Delay in diagnosis was related to loss of height and impaired potential for ‘catch up’. Jejunal disease predisposed to growth impairment following diagnosis. These issues should be addressed in the management of paediatric CD.

G3 DELAY IN DIAGNOSIS AND JEJUNAL INVOLVEMENT PREDISPOSE TO GROWTH FAILURE IN CROHN’S DISEASE

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Background: Growth failure is an important feature of paediatric Crohn’s disease (CD) and has been reported to be related to parental height (Ht).

Aim: To identify factors associated with growth failure.

Methods: We retrospectively identified 96 cases, 60 males, 36 females, with CD diagnosed before age 15 yrs. All had parental Hts recorded and had no other growth-inhibiting conditions. Hts were converted into standard deviation scores (SDS). Univariate analysis was undertaken of factors postulated to affect Ht: length of delay from onset of symptoms to diagnosis, pre/post pubertal onset of symptoms, site of disease activity (jejunal, ileal, terminal ileal), sex, systemic steroid therapy, mid-parental Ht SDS. Positive factors were entered into regression models at diagnosis, 16 yr, 18 yr, and at ‘adult’ (>18 yr) final height.

Results: Median age at diagnosis was 11.6 yrs (range 4.2-15) after a median 1.0 yr (range 0.1-4.0) delay from onset of symptoms. 22% had jejunal involvement. 67% had 1 course of systemic steroids. Mean Ht SDS were: at diagnosis (n=96) – 0.67, at 16 yr (n=63) – 0.75, at 18 yr (n=36) – 0.68, and at adult Ht (n=32) – 0.42. Time from onset of symptoms to diagnosis was negatively correlated with Ht at diagnosis (p <0.01). Ht diagnosis was significantly related to Ht SDS at age 16 yrs (p<0.001), 18 yr (p<0.01), and >18 yr (p<0.01), independent of mid-parental height. Jejunal disease was negatively associated with Ht SDS at age 16 yr (p<0.001) and 18 yr, >18 yr (p<0.05). There was no significant effect of steroids. Mean ‘adult’ (>18 yr) Ht deficit was –3.3 cm (95% CI -5.6 to -0.9) compared to mid-parental height.

Conclusion: Delay in diagnosis was related to loss of height and impaired potential for ‘catch up’. Jejunal disease predisposed to growth impairment following diagnosis. These issues should be addressed in the management of paediatric CD.

G4 DISTURBED ADRENAL FUNCTION IN ADOLESCENTS WITH CHRONIC FATIGUE SYNDROME

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Aims: The symptoms of the chronic fatigue syndrome (CFS) are similar to those of hypocortisolaemic states. Adult studies have shown abnormal adrenal function in some patients, probably of central origin, however little information is available on children and adolescents. We used the low-dose Synacthen test to study adrenal function in adolescents with CFS compared with controls.

Methods: 23 adolescents with CFS by CDC criteria (11 males; mean age 13.9 years) and 17 age and sex matched controls (8 males; mean age 13.2 years) underwent a low dose Synacthen test at 1400hrs. Cortisol levels were estimated every 5min from 0-45 minutes. Androgens, 17OHP and prolactin were estimated at baseline. Peak cortisol and time to peak were identified. Cortisol rise in adolescents with CFS compared to controls.

Results: 9% of cases had minimally abnormal DST compared with nil controls. CFS patients had significantly lower mean cortisol levels at 0, 15, 20 and 25 minutes. CFS cases had significantly lower peak cortisol (t=2.33 p<0.025), longer time to peak cortisol (t=2.1 p<0.05) and lower AUC (t=3.0 p<0.005). There were no significant differences between cases and controls in androgens, 17OHP, and prolactin.

Conclusions: Adolescents with CFS have subtle alterations in adrenal function compared with age-matched controls. Our findings of a blunted cortisol response are similar to adult studies and may suggest a chronic reduction in central stimulation of the adrenal glands.
**Abstract G6**

**WHY ARE WELL CHILDREN WITH GH AND CORTISOL DEFICIENCY SUSCEPTIBLE TO HYPOGLYCAEMIA?**

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Introduction: Children and adolescents with pituitary hormone deficiency (PHD) can become hypoglycaemic when well. We have therefore studied the metabolic response to fasting in patients with a range of endocrinopathies to establish factors that might influence susceptibility.

Methods: 14 children with PHD including GH deficiency (7 ACTH sufficient - ACTHS; 7 ACTH insufficient -ACTHD) and 6 with primary adrenal failure (PAF) were studied during a 14 hour overnight and morning fast on their normal treatment regimen and after the omission of a single dose of GH +/− hydrocortisone. ACTHD patients on glucocorticoid replacement were taking 8.8 ± 0.9 mg/m² and PAF 11.3 ± 1.2 mg/m² hydrocortisone daily (p=0.01). Blood glucose (BG), GH and cortisol concentrations were measured at 20 minute intervals from 0700; insulin was measured hourly and ketone bodies (KB) and NEFAs measured at 0700, 1100, and 1200hrs.

Results: Patients with ACTHD had the lowest mean BG levels with 3 becoming hypoglycaemic (BG < 3.6 mmol/l) off treatment in contrast to the ACTHS and PAF patients. Cortisol levels were higher after GH had been omitted in the ACTHS group (p=0.02) and daytime GH levels were higher in the PAF group in comparison to those with PHD (p=0.03). Morning cortisol levels were uniformly low or unrecordable in patients with PAF and ACTHD despite the lower cortisol dose in those with PHD. Cortisol replacement resulted in higher morning levels than those produced endogenously in the ACTHS (p=0.02). Children with ACTHD were more insulin sensitive when treatment was omitted (HOMA; p=0.05). There was no difference in KBs and NEFAs between groups.

Conclusions: ACTHS PHD individuals counter-regulate when medication is missed and patients with PAF may be protected from hypoglycaemia by endogenous GH release. A lack of GH pulsatility coupled with very low cortisol levels and enhanced insulin sensitivity is associated with an inappropriate ketogenic response and hypoglycaemia in patients with GH and ACTH deficiency. Our data do not suggest that patients with ACTHD need a lower glucocorticoid dose than patients with PAF.

**Abstract G7**

**ETHNIC AND GENDER DIFFERENCES IN BODY COMPOSITION IN BRITISH SCHOOLCHILDREN**

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There is an increased incidence of obesity in British children which coincides with the emergence of Type 2 diabetes. Previous research has demonstrated that obese teenage South Asian girls are at highest risk. South Asian adults have an increased risk of Type 2 diabetes compared to Caucasians, which is related to differences in insulin resistance and body composition.

Aims: The aim of this study was to determine if ethnic and gender differences in body composition can be seen in childhood and at what age they first become apparent.

Methods: A cohort of 1099 healthy British schoolchildren aged 5-18 years consisting of 3 ethnic groups (South Asian [AS], Afro-Caribbean [AC] & Caucasian [C]) had whole body DXA body composition scans performed to assess fat and fat free mass. Mean (SE) differences in % body fat were analysed using ANOVA with and without adjustment for body weight.

Results: There were clear ethnic differences in % body fat, which were apparent from the age of 5 years with girls having significantly higher values which increased with age. There was a trend for South Asian children to have higher % body fat from the age of 5 years, which became highly significant once % body fat was adjusted for weight (p<0.001). The greatest differences were seen between the South Asian and Afro-Caribbean children with Caucasian children being an intermediate group. (See Table).

Conclusions: There is clear evidence of gender and ethnic differences in body composition apparent from an early age. These differences are consistent with the increased risk of Type 2 diabetes seen in obese South Asian teenage girls and suggest the potential for preventative measures.

**Abstract G8**

**HEIGHT, WEIGHT, & BODY MASS INDEX (BMI) OF ETHNIC MINORITY CHILDREN AND YOUNG PEOPLE IN ENGLAND: COMPARISON WITH BRITISH 1990 CENTILES**

J.S. Ponnampalam, T.J. Cole, N.K.S. Thalange. Norfolk & Norwich University Hospital, Norwich; Institute of Child Health, London

Aim: To compare height, weight and BMI of ethnic minority children living in England with the British 1990 growth reference (UK90).

Methods: Height, weight and BMI for 4034 subjects aged 2-23 years (2017 males), from the Health Survey for England 1999 which focussed on ethnic minorities, were obtained from the British Data Archive. SD scores were calculated and compared with UK90.

Results: See table. Black subjects were significantly taller, and Asian and Chinese subjects shorter than UK90. Chinese and Asian females were particularly short. White and Black subjects had significantly higher BMI than UK90, particularly Black Caribbean females.

Conclusions: It is important to consider ethnic origin in the interpretation of growth data when using UK90 growth charts.

**Abstract G8**

**INSULIN RESISTANCE IN CHILDREN BORN PREMATURELY: ARE PERINATAL EVENTS IMPORTANT?**

F. Regan, M. Mcgregor, P. Hofman, E. Robinson, W. Cutfield. Liggins Institute, University of Auckland, New Zealand

Aims: Children born prematurely have decreased insulin sensitivity (S). The objective of this study was to determine whether pre or post-natal glucocorticoids, postnatal nutrition or maternal gestational proteinuria and hypertension (GPH) have an effect on insulin sensitivity.

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Methods: 27 Prepubertal children aged 5-8 years born prematurely (≥32 weeks) were studied. All subjects underwent a fasted 90 minute frequently sampled intravenous glucose tolerance test. Bergman’s modified minimal model was used to calculate $S_1(10^{-7} \muU/ml)$. Medical notes were examined to determine exposure to steroids, total parenteral nutrition, oral nutrition and reason for delivery.

A group of 11 short normal children born at term were used as controls.

Results: See tables 1 and 2.

Conclusions: Children born prematurely have decreased insulin sensitivity compared to those born at term. This $S_1$ is not influenced by pre or postnatal glucocorticoids. Premature babies delivered because of maternal GPH had greater $S_1$ than those that were delivered for other reasons. Nutritional parameters were not correlated with $S$ however all babies received inadequate protein in the first four weeks of life followed by excess fat which may contribute to decreased $S$.

Abstract G8, Table 1

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<td>14 ± 1</td>
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Values expressed as mean ± SEM.

Abstract G8, Table 2

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<tr>
<td>$S_1$</td>
<td>13 ± 1</td>
<td>15 ± 2</td>
</tr>
</tbody>
</table>

Values expressed as mean ± SEM.

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G9 PHYSICAL ACTIVITY IS IMPORTANT FOR THE METABOLIC HEALTH OF PRIMARY SCHOOL CHILDREN, BUT THE AMOUNT OF TIMETABLED PE DOES NOT SEEM TO MATTER (THE EARLYBIRD STUDY)


Introduction: Insulin resistance is believed to underlie type 2 diabetes and cardiovascular disease. Physical activity is an independent determinant of insulin resistance in adults, but little is known of its impact in children. Opportunity for physical education (PE) in schools varies, and our aim was to determine its impact on total activity levels and metabolic health.

Methods: Total physical activity over seven days (CSA accelerometer), anthropometry, insulin resistance (HOMA-IR) and its metabolic correlates were measured in 215 children (mean age 9.0±0.9yrs) from three schools offering widely different timetabled opportunity for PE (S1: 12h/week, S2: 2.5h/week, S3: 1.5–2h).

Results: 1. Surprisingly, there were no differences in total physical activity (units/week) between schools among the girls and, despite far less timetabled PE (S1: 12h/week, S2: 2-2.5h, S3: 1.5–2h), total activity among the boys was higher in S2 (39.1) than in S1 (34.7, p=0.02). 2. There were no differences in insulin resistance according to school. 3. The girls undertook less total physical activity than the boys (p=0.007), were more insulin resistant (p<0.001) and had higher triglycerides (p=0.04). 4. In girls, there were modest inverse associations between their total physical activity and insulin resistance ($r=-0.27$, $p=0.02$), triglycerides ($r=-0.24$, $p=0.04$) and cholesterol/HDL ratio ($r=-0.26$, $p=0.03$). In boys, there were associations between total physical activity and fat percentage ($r=-0.29$, $p=0.008$) and cholesterol/HDL ratio ($r=-0.23$, $p=0.04$). 5. Insulin resistance was closely related to triglyceride levels in both sexes (girls: $r=0.41$, boys: $r=0.39$, p<0.001).

Conclusions: 1. Physical activity clearly impacts on the metabolic health of children at primary school age. 2. It is of concern that young girls undertake significantly less physical activity and already have higher insulin resistance and triglyceride levels than boys. 3. It doesn’t seem to matter how much PE is timetabled at school, as the child seems to compensate out of school. 4. These findings may be important to the allocation of limited time and resources at school.

G10 VACCINATION IN DIABETIC CHILDREN: ARE WE? SHOULD WE? WHO KNOWS?

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Aims: To audit rates of vaccination against influenza and pneumococcus in children with diabetes, in line with Department of Health (DoH) guidelines, and to ascertain implementation and knowledge amongst hospital paediatricians and diabetes nurse specialists (DNS) of these guidelines.

Methods: Structured telephone interview of (1) the parents of all children with diabetes attending Bedford Hospital Diabetes clinic and (2) the DNS and the lead diabetes consultant in each hospital in the Eastern Region.

Results: Of 75 children eligible, there were 15 non-responders (response rate 80%). 14/56 children with a diagnosis of diabetes for over 1 year were vaccinated against influenza in 2001 and 27/60 children were planning vaccination in 2002. 1/60 children had been vaccinated against pneumococcus. There was no significant difference in the self-reported rates of flu in the previous year (p=0.32). 8/15 DNSs and 11/17 consultants advise vaccination for influenza and 3/15 and 2/17 respectively advise pneumococcal immunisation. In 7/15 hospitals the DNS and the consultant give differing advice. 15/32 specialists are aware of the DoH guidelines.

Conclusions: DoH guidelines state that all patients (without age limit) with diabetes should be vaccinated against influenza and pneumococcus. This is based on studies which give a theoretical risk in the adult population. 44% of children in Bedford were immunised in 2002. 19/32 specialists advise vaccination for influenza and 5/32 for pneumococcus. A literature search found no further evidence to support the guidelines. Unnecessary immunisation programmes may have wide ranging ethical, public relation, and medicolegal implications. Whether there is sufficient evidence base to recommend immunisation in children is unclear, and a clear UK paediatric consensus is needed. Each hospital needs to clarify local policy.

G11 TESTING FOR AUTOIMMUNE DISEASES IN CHILDREN WITH TYPE 1 DIABETES: NATIONAL SURVEY OF PRACTICE, OPINION AND PREVALENCE

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Aims: Children with type 1 diabetes are predisposed to other auto-immune diseases including coeliac and thyroid disease. The UK prevalence of these complications is unknown, and the need for and frequency of screening tests is controversial. A survey and an economic analysis addressed these questions.

Methods: We undertook a postal questionnaire survey of all consultants caring for diabetic children, through the clinical trials unit of the British Society for Paediatric Endocrinology and Diabetes. We then used a decision analytical model to estimate the costs and benefits of a single screening episode.

Results: The response rate was 166/260, 64%. Reported prevalence in children with type 1 diabetes was: coeliac disease, 2.0 per 100 (95% CI 1.8–2.2); hypothyroid disease, 3.2 per 100 (95% CI 2.9–3.4); and hyperthyroid disease 0.2 per 100 (95% CI 0.2–0.3).

Nearly half used antibody tests for coeliac disease at diagnosis in all children with 77% testing later, but with little agreement on the interval. 75% felt there should be routine testing. Iga endomysial antibodies were the most frequently used. Nearly half of the consultants used microsomal antigen/thyroid peroxidase in all children at diagnosis, with 14% testing symptomatic children. Subsequently, 47% tested all children, however, 40% thought there should not be routine autoantibody tests. 83% felt there should be routine thyroid function tests.

The use of coeliac antibody testing with confirmatory biopsy is cost-effective, with cost/QALY estimates from £12,250, and a cost per case detected from £6,190.

Conclusion: Thyroid antibodies do not offer a significant advantage over thyroid function tests when used as a screening test. The model suggests testing for coeliac disease may be cost effective.
G12 AWARENESS OF ORAL COMPLICATIONS OF DIABETES IN PAEDIATRIC DIABETES CARE TEAMS IN YORKSHIRE

V. Clerehugh1, F. Campbell2, J. Csikar1, S.A. Williams1, M. Gilthorpe3.
1Leeds Dental Institute, 2St James Hospital, 3Biostatistics Unit, University of Leeds

Destructive periodontal (gum) disease has been proposed as the sixth complication of diabetes (Löe 1993) and dental reports acknowledge that poorly controlled diabetes is a risk factor for periodontal disease. Rees (2000) suggested that an increased risk of dental caries (tooth decay) relates to increased glucose in the saliva and gingival crevicular fluid in poorly controlled diabetic patients. Periodontal infection can adversely affect diabetes control. Type 1 diabetes accounts for around 10% of diabetes cases and often manifests acutely in childhood and adolescence. Control of diabetes can be problematic in these youngsters and periodontal problems can develop in children and adolescents. It is unclear whether Diabetes Care Teams are aware of the potential for oral problems relating to diabetes control.

Aim: Therefore a pilot study was set up in the Yorkshire Region to determine the awareness amongst Paediatric Diabetes Care Teams of possible periodontal/dental complications of diabetes.

Methods: Questionnaires (n=62) were distributed to all 17 Paediatric Diabetes Care Teams in Yorkshire comprising 9 questions covering: possible complications of diabetes; annual review checks; advice given to patients; referral services available; training to identify problems; confidence in identifying problems. There were 3 mailings in September 2002.

Results: There was a 79% response rate (24% Consultants, 20% Dietitians, 56% Nurse role). Reassuringly, 98–100% were aware of nephropathy, neuropathy, retinopathy, ischaemic heart disease, stroke, foot problems and poor pregnancy outcome as possible complications of diabetes; a less well recognised complication was coeliac disease (68%) and only 30–40% were aware of potential periodontal or dental problems. Very few included oral screening in the Annual Review (<10%) and there was least confidence in referring patients for treatment of gums or teeth (20–30%) in contrast to the 98% who would refer to a dietitian; 78% would like training in oral problems.

Conclusion: There is relatively low awareness of oral complications of diabetes in Paediatric Diabetes Care Teams in Yorkshire.

G13 THE NATIONAL PAEDIATRIC DIABETES AUDIT: DATA FROM 2001

A.H.K. Smith1, J.A. Edge2, on behalf of the Project Steering Committee.
1Diabetes UK, 10 Parkway, London NW1 7AA; 2John Radcliffe Hospital, Headington, Oxford OX3 9DU

Aims: The National Paediatric Diabetes Audit aims to facilitate a national audit mechanism to develop a cycle of continuous quality improvement in paediatric diabetes care throughout the UK.

Methods: Anonymous demographic data and simple intermediate outcomes in the year 2001 for children aged 0–16 were collected and aggregated centrally. Data was collected from 110 centres in England & combined with aggregate data from Wales, creating a cohort of 10 029 patients. The outcomes were death during the year, number of readmissions with diabetic ketoacidosis (DKA), number of severe hypos, and the latest HbA1c result.

Results: The mean age was 11.14 years ± 3.60 (n=9950), the mean duration of diabetes was 4.04 years ± 3.45 (n=9686), & the mean age at diagnosis was 6.69 years ± 3.90 (n=9675). 74.8% (n=7504) had ethnicity recorded & of these, 91.1% (n=6839) were white. 48.2% were female. 95.7% (n=9602) had type of diabetes recorded. Of these, 98.7% had Type 1 diabetes (n=4386). 7147 DCCT-standardised HbA1c results were analysed. 57.7% (n=5785) had a record of admissions for DKA and 55.6% (n=5573) had a record of the number of severe hypos. The mean HbA1c was 9.07% ± 1.69. Significant associations with increasing HbA1c level were found for centre (p<0.0001), ethnicity (non-white v white, p<0.0001), deprivation (the most deprived 40% of the cohort vs. the least deprived 40% of the cohort, p<0.0001), increasing age (15-16 years v 0–4 years, p<0.0001) and duration of diabetes (9 years v 1 year duration, p<0.0001). The rate of readmission with DKA by centre varied between 0 and 32%.

Conclusions: Older children, who have had diabetes for longer, are socially deprived and from minority ethnic groups are more likely to have higher HbA1c levels. These results have been fed back to participating centres, allowing them to focus their care.