
32nd Meeting of the

**British Society for
Paediatric Endocrinology
and Diabetes**

10-12 NOVEMBER 2004

Ardoe House Hotel, Aberdeen, Scotland

Programme & Abstracts

32nd Meeting of the
**British Society for
Paediatric Endocrinology
and Diabetes**

10-12 NOVEMBER 2004

Ardoe House Hotel, Aberdeen, Scotland

CONVENOR

Dr Peter Smail, Consultant Paediatrician

BENEFACTORS

**Eli Lilly & Co Ltd, Ferring Pharmaceuticals Ltd, Ipsen UK Ltd,
Novo Nordisk Ltd, Pfizer Ltd, Roche Diagnostics Ltd,
Serono Pharmaceuticals Ltd**

Also supported by the Child Growth Foundation and the Turner Syndrome Support Group

www.bsped.org.uk

Dear All,

Welcome to Aberdeen for the 32nd annual meeting of the BSPED. It is a chastening thought for me that I have only missed one meeting since 1975, though I know there are others who could beat that.

Aberdeen, as well as being the oil capital of Europe is an elegant granite city, the gateway to Royal Deeside and has a base of agriculture and other traditional industries. Its ancient university is over 500 years old and the Regius Chair of Medicine is the oldest Chair of Medicine in the English speaking world. With the other universities and institutes in town such as Rowett Research Institute, Aberdeen has the largest concentration of life scientists in Europe.

This year's meeting is being held at Ardoe House, a well equipped country house hotel and conference centre on the South Deeside Road, just outside the boundaries of Aberdeen. Shuttle buses will be laid on for events in town and for those based at hotels in town. We should also like to invite those of you who wish to visit our magnificent new Royal Aberdeen Children's Hospital which opened in January of this year.

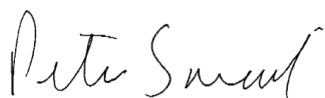
I make no apologies for the programme being a little nationalistic. The main symposium on Thursday will be presented by members of the Scottish Study Group for the Care of Diabetes in the Young which celebrates its 21st anniversary this year. The keynote speaker will be Professor Kevin Docherty, one of the foremost experts on the genetic engineering of insulin producing cells. On the Friday morning there is a programme organised by Faisal Ahmed on behalf of the Scottish Genital Network, a more recent development. It will focus on surgical aspects of intersex. In addition there will of course be oral communication sessions as the main focus of the meeting plus an attended poster session on Thursday. Nursing members will be holding their parallel symposium on Thursday afternoon.

A welcome reception will be held on Wednesday evening in the Maritime Museum which covers the history of Aberdeen's fishing and ship building industries as well as oil developments. There will be a choral and organ recital at St Andrew's Cathedral afterwards. The annual dinner and ceilidh will be held on Thursday night at the Elphinstone Hall at King's College in Old Aberdeen preceded by a drinks reception in the Linklater Rooms.

We look forward to seeing you all on Wednesday 10 November 2004.

With best wishes

Yours sincerely



Peter Smail

Local Organising Chair – BSPED 2004, Aberdeen

Conference Secretariat

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Venue

The 32nd Meeting of the British Society for Paediatric Endocrinology and Diabetes will be held on 10-12 November 2004 in Ardoe House Hotel, South Deeside Road, Blairs, Aberdeen, Scotland AB12 5YP. Telephone number: +44 (0) 1224 860 600 or fax: +44 (0) 1224 861 283

Location

The venue will be the Ardoe House Hotel and Conference Centre, which is situated on the south banks of the River Dee just outside Aberdeen. Some accommodation is available at this venue, but those who prefer the bright lights will be accommodated in the centre of Aberdeen, which has a lively restaurant and club scene.

Aberdeen has good transport links as the airport has frequent British Airways or Eastern Airways flights to 15 mainland destinations. Also there is an Easyjet flight from Luton and a Ryanair flight from Dublin. In addition there is an overnight sleeper train from London. We recommend you take advantage of cheaper flights by booking early.

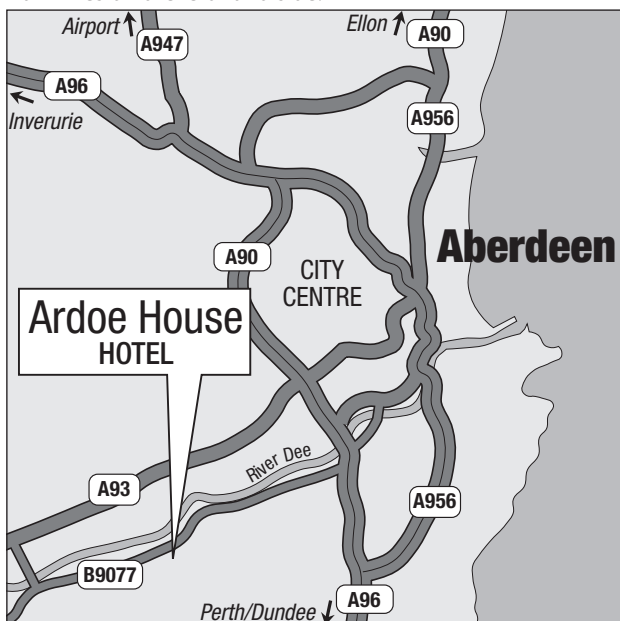
Venue Directions

Ardoe House Hotel is just 4 miles from Aberdeen city centre on the South Deeside Road B9077.

Aberdeen Railway Station is 10 minutes away and the Airport is only 20 minutes away.

Directions by road:

From the North: Ellon - Aberdeen Road, coming into Aberdeen on King Street carry on to Union Street. At the last set of traffic lights at the bottom of Union Street (Bank of Scotland on your left), bear left onto Holburn Street. When you reach the roundabout continue down Holburn Street to the very end. Turn left at the roundabout, across Bridge of Dee. Turn right at the next roundabout (B9077) signposted towards Maryculter. The hotel is approximately two and a half miles on the left hand side.



From the South: Take the main dual carriageway (A90) from Perth/Dundee. You will approach a roundabout as you arrive in Aberdeen. Take the immediate left turn onto the B9077 signposted Maryculter. The hotel is approximately two and a half miles on the left hand side.

From the Airport: Follow the signs for the City Centre on the A96. Turn onto the A90 signposted Dundee/Perth. Follow the dual carriageway over Aberdeen, cross over the Bridge of Dee, turn right at the roundabout (B9077) signposted Maryculter. The hotel is approximately two and a half miles on the left hand side.

From the Train Station: Turn left and left again. At the next junction follow the road until the first roundabout and take the third exit, along Riverside Drive. Follow the road to the next roundabout and turn left over the bridge. At the end of the bridge turn right and at the next roundabout go straight on (B9077). The hotel is approximately two and a half miles on the left hand side.

Programme

A dynamic programme has been planned with a Scottish Study Group for the Care of Diabetes in the Young symposium on diabetes at which the keynote speaker will be Professor Kevin Docherty. There will also be a Scottish Genital Network Symposium and the usual oral, poster and specialist nurses' sessions.

Children's Hospital

At the start of the meeting delegates will have the opportunity to visit the new children's hospital in Aberdeen on the afternoon of Wednesday 10 November. Registration for the meeting will follow this at Ardoe House Hotel.

Registration fees

The registration fee for BSPED members is £250 and for non-members is £280; in addition nurses, trainees and students can register at the reduced rate of £195. There is also a daily rate of £135 and a concessionary rate of £75.00 for local delegates wishing to attend only one session. These fees includes lunch on both 11 and 12 November and the Welcome Reception, but does not include the Annual Dinner.

Name Badges

Name badges will be provided at the registration desk and must be worn for admission to all scientific sessions.

Poster Sessions

Posters will be displayed from 13.00 to 14.30 on Thursday 11 November and on Friday 12 November at 12.00 to 13.30.

There will also be a poster discussion session taking place on Thursday 11 November 2004 at 13.15 to 14.25 during lunch, in the Craigievar Suite. You are encouraged to support this new addition to the programme and we look forward to seeing you there.

The Annual General Meeting of the BSPED

The Annual General Meeting of the BSPED will be held on Thursday 11 November at 16.30 to 17.30 in the Crathes Suite.

Nurses' Session

(GENEROUSLY SUPPORTED BY SERONO PHARMACEUTICALS LTD)

The nurses' session will take place on Thursday 11 November at 14.00-16.00 in the Ogston Suite. A packed session has been scheduled which includes of the following topics:

1. Remote control of diabetic service
2. Transition of care from the paediatric clinic to the adult service
3. Prevalence of overweight and obesity in Aberdeen primary schoolchildren
4. Nurses' business session

CPD Approval

CPD Approval from the Federation of the Royal College of Physicians of the UK has been given for this meeting. Delegates may claim 12 points for full attendance of the meeting. If you want to claim your CPD points you must sign the register on the registration desk at the meeting before 12.30 on Friday 12 November. You will need your GMC number.

Social Programme

The Welcome Reception, generously supported by Pfizer Ltd, will take place on Wednesday 10th November 2004 at the Aberdeen Maritime Museum. All delegates are welcome to join us for a drink and attend a concert at St Andrew's Cathedral.

The annual dinner and ceilidh is taking place at Elphinstone Hall, Kings College, University of Aberdeen. Entertainment will be provided by a band called Real Estate.

Shuttle buses will be provided from the city centre and Ardoe House Hotel to Elphinstone Hall. The price to attend this evening is £45 per person and there may be a limited number of tickets available from the reception desk.

Accommodation

A wide-range of hotels are available in Aberdeen including some within walking distance of the conference venue. A shuttle bus will be in operation to and from Ardoe House Hotel to the following city centre hotels:

Thistle Hotel Caledonian

10-14 Union Terrace, Aberdeen

Copthorne Hotel

122 Huntley Street, Aberdeen

Premier Lodge

Aberdeen City Centre, Invelair House
West North Street, Aberdeen

Brentwood House

101 Crown Street, Aberdeen

A timetable will be available on arrival to either the conference venue or your hotel.

Catering

A buffet lunch will be served on Thursday 11 November and Friday 12 November in the Ballroom Foyer and Craigievar Suite. These are both situated by the main meeting room. Tea and coffee will also be available in these areas during the specified break times.

Ipsen Satellite Symposium

Ipsen Ltd are holding a satellite symposium entitled "Assessment of the GH-IGF-1 axis in paediatric endocrine practice" on Wednesday 10 November from 17.00 in the Crathes Suite.

Benefactors

We are grateful to the following benefactors for their support of the BSPED:

Eli Lilly & Co Ltd, Ferring Pharmaceuticals Ltd, Ipsen UK Ltd, Novo Nordisk Ltd, Pfizer Ltd, Roche Diagnostics Ltd, Serono Pharmaceuticals Ltd.



Wednesday 10 November 2004

	CRATHES SUITE	CRAIGIEVAR SUITE	BALLROOM FOYER
12.00			
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Registration**Ipsen Satellite Symposium:**
Assessment of the GH-IGF-1
axis in paediatric endocrine
practice**Welcome Reception**
at Aberdeen Maritime Museum
*(GENEROUSLY SUPPORTED BY PFIZER LTD)***Concert at St Andrew's Cathedral**

Thursday 11 November 2004

	CRATHES SUITE	OGSTON SUITE	CRAIGIEVAR SUITE	BALLROOM FOYER
08.30	Welcome and Oral Communication 1: Growth/puberty and obesity			
08.45				
09.00				
09.15				
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10.00				
10.15				
10.30			Tea and coffee	
10.45				
11.00	Scottish Study Group for the Care of Diabetes in the Young symposium			
11.15				
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12.00				
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12.45				
13.00			Lunch and Posters	
13.15				
13.30				
13.45			Poster Discussion Session	
14.00				
14.15		Nurses' Session (GENEROUSLY SUPPORTED BY SERONO PHARMACEUTICALS LTD)		
14.30	Oral Communication 2: Reproductive and adrenal			
14.45				
15.00				
15.15				
15.30				
15.45				
16.00			Tea and coffee	
16.15				
16.30	Annual General Meeting			
16.45				
17.00				
17.15				
17.30				
20.00	Annual Dinner at Elphinstone Hall of King's College, University of Aberdeen			

Friday 12 November 2004

	CRATHES SUITE	CRAIGIEVAR SUITE	BALLROOM FOYER
08.30	Scottish Genital Network symposium		
08.45			
09.00			
09.15			
09.30			
09.45			
10.00		Tea and coffee	
10.15			
10.30	Oral Communication 3: Diabetes and thyroid		
10.45			
11.00			
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12.00		Lunch and close of meeting	
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Wednesday 10 November 2004

- 14.00 – 15.30** **Hospital visit**
Delegates will have the opportunity at this time to visit the new children's hospital in Aberdeen. (Coaches depart Ardoe House Hotel 13.00)
- 16.00 – 17.00** **Registration for BSPED Meeting**
BALLROOM FOYER
- 17.00 – 18.00** **Ipsen Satellite Symposium**
Assessment of the GH-IGF-1 axis in paediatric endocrine practice
CRATHES SUITE
- 18.30 – 20.30** **Welcome Reception**
ABERDEEN MARITIME MUSEUM
GENEROUSLY SUPPORTED BY PFIZER LTD
- 19.45 – 20.30** **Concert**
ST ANDREW'S CATHEDRAL
GENEROUSLY SUPPORTED BY PFIZER LTD

Thursday 11 November 2004**08:30 - 10:30 Welcome and Oral Communication 1: Growth / puberty and obesity**

CRATHES SUITE

Chairperson: T Cheetham (Newcastle)

- OC1 08:30 The effects of IL-6, IL-1 beta and TNF alpha on chondrocyte growth during chondrogenesis and terminal differentiation
Cooke VE, Farquharson C & Ahmed SF
- OC2 08:45 The endocrine sequelae of optic gliomas and their therapy
D'Alessio E, Albanese A & Spoudeas HA
- OC3 09:00 Measured versus reported parental height
Cizmeci F, Doherty A, Paterson WF & Donaldson MDC
- OC4 09:15 Increased adiposity in South Asian teenagers is associated with increased dietary fat intake
Atwal P, Ehtisham S & Barrett TG
- OC5 09:30 TW2 or TW3 bone age assessment: Does it make a difference?
Ahmed ML & Warner JT
- OC6 09:45 Hypertriglyceridaemia, increased truncal adiposity and decreased lean body mass in prepubertal leukaemia survivors after bone marrow transplantation
Yeap ML, Cornish J, Oakhill A, Ryan FJ & Crowne EC

10.30 – 11.00 Tea and coffee

CRAIGIEVAR SUITE & BALLROOM FOYER

11.00 – 13.00 Scottish Study Group for the Care of Diabetes in the Young symposium

CRATHES SUITE

Chairperson: P Smail (Aberdeen)

- S1 11:00 Stem cell therapy for diabetes mellitus
Docherty K (Aberdeen), Durward E, Ferguson L, Wareham S, Bogitzopoulou E, Docherty H, Hay C, Barrow J & Bernardo A
- S2 11:45 Epidemiology of diabetes in children: registers and record linkage
Waugh N (Aberdeen)
- S3 12:10 How is information technology supporting diabetes care in Scotland?
Robertson KJ (Glasgow)
- S4 12:35 Diabetes and pregnancy
Pearson D (Aberdeen)

13.00 – 14.30 Lunch & Posters

CRAIGIEVAR SUITE & BALLROOM FOYER

13.15 – 14.25 Poster discussion session

CRAIGIEVAR SUITE

Lead Discussant: T Cheetham (Newcastle). Discussants: R Perry (Glasgow), L Bath (Edinburgh)

14.00 – 16.00 Nurses' Session

OGSTON SUITE

GENEROUSLY SUPPORTED BY SERONO PHARMACEUTICALS LTD

Chairperson: J Reid (Aberdeen)

- N1 14.00 Remote control of diabetic service
E Carnegie (Aberdeen) & A Swaffield (Aberdeen)
- N2 14.30 Transition of care from the paediatric clinic to the adult service
R Elson (Bristol) & N Nicoll (Bristol)
- N3 15.00 Prevalence of overweight and obesity in Aberdeen primary school children
C McDougall (Aberdeen)
- N4 15.30 Nurses' business session
P Musson (Southampton)

14:30 - 16:00 Oral Communication 2: Reproductive and adrenal

CRATHES SUITE

Chairperson: Paula Midgley (Edinburgh)

- OC7 14:30 The relationship between Leptin and Luteinising Hormone as children progress into puberty
Maqsood AR, Trueman JA, Whatmore AJ, Westwood M, Hall CM, Price DA & Clayton PE
- OC8 14:45 Fibroblasts from normal and Turner syndrome children produce similar levels of insulin-like growth factor binding proteins
Tajbakhsh S, Siddals KW, Jones J, Wit JM, Whatmore AJ, Westwood M & Clayton PE
- OC9 15:00 Familial Glucocorticoid Deficiency type 2 is associated with mutations in a novel gene encoding a small single transmembrane domain protein
Metherell LA, Chapple JP, Cooray S, Becker C, Ruschendorf F, Naville D, Begeot M, Huebner A, Cheetham ME & Clark AJL
- OC10 15:15 Abnormalities of clinical and biological pubertal development in paediatric Cushing's disease
Dupuis CC, Storr HL, Perry LA, Ho JTF, Ahmed L, Ong K, Dunger DB, Monson JP & Besser GM
- OC11 15:30 The catecholamine response to fasting in children with adrenal failure
Johnstone HC, Bartlett K, Peaston R & Cheetham TD
- OC12 15:45 Phenotype, genotype and sex of rearing in a cohort of patients with partial androgen insensitivity syndrome
Mason C, Deeb A & Hughes IA

16.00 – 16.30 Tea and coffee

CRAIGIEVAR SUITE & BALLROOM FOYER

16.30 – 17.30 BSPED Annual General Meeting

CRATHES SUITE

from 20.00 Annual Dinner at Elphinstone Hall

ELPHINSTONE HALL OF KING'S COLLEGE, UNIVERSITY ABERDEEN

Friday 12 November 2004**08:30 - 10:00 Symposium 2: Scottish Genital Network symposium**

CRATHES SUITE

Chairperson: Amalia Mayo (Aberdeen)

- S5 08:30 The Scottish Genital Anomaly Network
Ahmed SF (Glasgow)
- S6 09:00 Genital surgery perspective from adult surgery
Deeny M (Glasgow) & Telfer JRC (Glasgow)
- S7 09:30 Scottish Genital Network - the paediatric surgeons perspective
Youngson GG (Aberdeen) & Driver CP (Aberdeen)

10.00 – 10.30 Tea and coffee

CRAIGIEVAR SUITE & BALLROOM FOYER

10:30 - 12:00 Oral Communication 3: Diabetes and thyroid

CRATHES SUITE

Chairperson: Liz Crowne (Bristol)

- OC13 10:30 Does terbutaline reduce the incidence of nocturnal hypoglycaemia in children with type one diabetes - a pilot study?
Wright NP, Ritson S, Clargo H, Mackenzie CA, Price KJ & Wales JK
- OC14 10:45 Inherited non-type 1 diabetes in paediatrics is a heterogeneous disorder
Porter JR, Hattersley AT, Frayling T, Ellard S & Barrett TG
- OC16 11:00 Congenital hypothyroidism in Scotland - twenty four year audit
Jones JH, Perry RJ, Brown AJ, Mackenzie JM & Donaldson MDC
- OC17 11:15 Identification of the transcript encoding IKBE, an inhibitor of NF κ B, as a novel candidate gene in Graves' disease
Owen CJ, Jennings CE, Wilson V, Cheetham TD & Pearce SHS
- OC18 11:30 Birth weight affects screening blood spot thyroid stimulating levels independent of gestational age
Wong SC, Ng SM, Chakkrapani E, Rahman F, Isherwood DM & Didi M

12.00 – 13.30 Lunch and close of meeting

S1**Stem Cell Therapy for Diabetes Mellitus**

K Docherty, E Durward, L Ferguson, S Wareham, E Bogitzopoulou, H Docherty, C Hay, J Barrow & A Bernardo

School of Medical Sciences, University of Aberdeen, Aberdeen, UK.

Since the development of the Edmonton Protocol four years ago, islet transplantation is now seen as a feasible treatment for diabetes mellitus. The problem, however, is in the provision of donor tissue to supply the expected huge demand. Islets of Langerhans are terminally differentiated and do not grow well in culture. For this reason stem cells have been recognised as a potential source of islet tissue for transplantation. A number of recent studies have shown that insulin-secreting cells can be derived from embryonic stem (ES) cells. The basic protocol upon which almost all these studies are based involves selection for nestin-positive neuronal cells followed by manipulations to encourage differentiation towards the endocrine pancreas. Since cells of the endocrine pancreas are of endodermal origin it would make more sense to induce differentiation sequentially through an endoderm stage and then through pancreas to endocrine pancreas, i.e. to recapitulate the events that occur during embryogenesis. Some of the major regulators of gastrulation (e.g. the TGFbeta family member nodal and BMP-4) and transcription factors controlling pancreatic development (e.g. PDX-1, PAX4, Isl-1, MafA, NeuroD/Beta2, etc.) have been identified and provide a logical strategy for achieving this aim.

S2**Epidemiology of diabetes in children: registers and record linkage**

N Waugh

Dept of Public Health, University of Aberdeen, UK.

The Scottish Study Group for the Care of Diabetes in the Young carries out studies of the incidence and outcomes of childhood diabetes, using a register, and record linkage. The incidence of type 1 diabetes has trebled over the last 30 years. The rise probably started in the late 1950s. There are geographical and socio-economic variations, with deprivation providing some protection. SSGCDY has participated in a multi-centre study of mortality in T1 diabetes. The most important finding is an increased risk of heart disease.

S3**How is Information Technology Supporting Diabetes Care in Scotland?**

KJ Robertson

Diabetes Service, RHSC, Glasgow, UK.

The paucity of support for true clinical information technology in the NHS has spawned numerous, often home-made, solutions including Access databases, spreadsheets and commercial systems. Apart from the wide variations in functionality, the major flaw in this approach has been the lack of information standards. Scotland has grasped the thistle by tackling the problem from both the content and system perspectives. The Scottish Care Information Diabetes Collaboration (SCI-DC) is a managed programme of work which has developed and promulgated a core dataset for use throughout NHS Scotland and software to support direct care and improved information flow between those involved in this care. At the core of the development is a shared diabetes care record which can be accessed only by those caring for the patient. All Health Boards in Scotland have adopted the central diabetes record element which should quickly improve the quality of aggregated and anonymised information available for service planning as well as highlighting deficiencies in the care of individual patients. Scotland is also implementing a single system for retinopathy screening which will interface with SCI-DC in a standard manner. The challenges and opportunities of this approach will be discussed along with the impact of wider information management and technology initiatives in Scotland and England.

S4**Diabetes and Pregnancy**

D Pearson

Good outcomes can be achieved by meticulous glycaemic control prior to and during pregnancy; however, national and regional audits confirm the challenges in achieving optimal results in comparison to the background population. Despite efforts by mothers and their diabetes care teams, the babies are often large for gestational age (Mean birth weight 3427g, 86% > 50%ile, 55% > 90%ile) and are delivered early (median gestational age 37weeks) by caesarian section (64%). Specialist neonatal support, which has contributed so much to the improved outcomes of recent decades, is still required for some neonates.

Perinatal mortality (27.8 per 1000) has fallen, but offspring still have more congenital abnormalities (Congenital anomaly rate 60-97 / 1000 vs. 28 / 1000). The risk of stillbirth (18.5 - 25 / 1000) and infant mortality ((14.2 - 58.5 / 1000) remain well in excess of the non diabetic population.

Animal studies show that the metabolic environment of the developing fetus and fetal genes influence the malformation rate. In clinical practice a comprehensive pre-pregnancy care package, to address all risk factors for malformation, will reduce congenital anomalies and other adverse outcomes. The management of acute (e.g. severe hypoglycaemia 40%) and chronic complications (e.g. proliferative retinopathy 22.5%) are challenging. Controlled trials are underway to investigate interventions to reduce adverse maternal outcomes. An understanding of the interrelationships between maternal diabetes, placental and fetal development has helped to guide good clinical practice.

S5**The Scottish Genital Anomaly Network**

SF Ahmed

Paediatric Endocrinology, RHSC, Yorkhill, Glasgow, UK.

Patients with complex genital anomalies (CGA) require help from multiple agencies either directly in a specialist centre, in partnership with local hospitals through a shared care or outreach arrangement, or in children's own homes through a specialist outreach team. They are, therefore, heavily dependent upon tertiary services within the UK health care delivery system. In view of the comparative rarity and complex issues involved in treating children with complex genital anomalies, the British Society for Paediatric Endocrinology and Diabetes (BSPED) recommends that endocrine problems relating to intersex should be managed by specialists in tertiary paediatric endocrinology and the British Association of Paediatric Surgeons (BAPS) recommends their early referral to the nearest regional surgical centre for both immediate and continuing management by a multidisciplinary team. There is a constant drive towards continuous improvement in access and quality of health care. At the same time, such a low-volume highly-specialised, multidisciplinary service needs to be sustained by a, comparatively, small number of professional staff. Taking into account Scotland's unique demography and geography, it is unrealistic to expect that every major children's centre should be able to deliver a comprehensive service from its own base. In this respect, the Scottish Genital Anomaly Network (SGAN) is a network of a multidisciplinary group of health care professionals that was formed in 2002 with the primary longer term aim of providing an optimal level of care to affected patients through the development of a managed clinical network (MCN), thus preserving services within all localities, whilst maintaining access to national expertise.

S6**Genital Surgery Perspective from Adult Surgery**

M Deeny [1] & JRC Telfer [2]

[1] Department of Gynaecology, Stobhill Hospital & Glasgow Royal Infirmary, Glasgow, Scotland.; [2] Canniesburn Plastic Surgery Unit, Glasgow Royal Infirmary, Glasgow, Scotland..

Genital reconstruction raises several complex issues. Whilst the surgery itself may be demanding, it can be most rewarding for patient and surgeon alike. However, surgery is only part of the management of this group of patients and operative intervention should only be embarked upon with a full knowledge of the short and long term implications, possible complications and limitations of the various procedures. A dogmatic surgical approach is no longer acceptable and an awareness of the needs and expectations of the patient is paramount. The preoperative evaluation of the patient from both a physical and psychological perspective, the timing of any intervention, the choice of techniques and calculation of risk versus benefit, have to be made on an individual patient basis.

In Glasgow, as adult rather than paediatric surgeons, our aim is to provide continuity of care for these patients as they develop from child to adult. We present our philosophy of approach to female genital reconstruction, discussing the type of surgery available, the implications of previous surgery, the management of coexisting gynaecological problems, continence issues, psychological concerns, sexual function and fertility, illustrated with some clinical cases.

S7**Scottish Genital Network - The Paediatric Surgeons Perspective**

GG Youngson & CP Driver

Department of Paediatric Surgery, Royal Aberdeen Children's Hospital, Aberdeen, Scotland.

Outcome analysis in surgical practice often includes several assumptions, one being a direct relationship with the volume of surgery performed. This presentation will analyse the acquisition of skills used to perform genitoplasty and other procedures in reconstructive surgery of children with intersex states and genital anomalies. There are several influences affecting experiential learning and acquisition of skills in surgeons in training, and these are presented. Moreover, the options in configuring surgical services such that access, continuity of care, and yet exposure to the appropriate expertise are also presented. The current arrangements and configurations of patterns of care amongst surgeons operating in Scotland are discussed.

The development of evidence based medicine, patient advocacy and the internet have increased the pressure points acting on a surgeon when making a decision regarding surgical reconstruction in the intersex patient. Male genital reconstruction is relatively straightforward in both the timing and nature of surgery but the female equivalent is an ethical minefield. The nature and timing of clitoral and vaginal surgery has been questioned by several publications looking at long term outcome of procedures performed in childhood. While this has opened up a truly worthwhile debate on what should be done and when, the evidence base is incomplete and the surgeon is left picking his way through the information and guidance available - not all of which can be considered impartial. A truly informed discussion via repeated discussions with the parents seems the way forward, while simultaneously avoiding procedures that offer little in childhood but which are better suited to patient choice when at an age they can absorb the pertinent facts.

OC1**The effects of IL-6, IL-1 beta and TNF alpha on chondrocyte growth during chondrogenesis and terminal differentiation**

VE Cooke [1, 2], C Farquharson [2] & SF Ahmed [1]

[1] Bone & Endocrine Research Group, Royal Hospital For Sick Children, Glasgow, UK; [2] Roslin Institute, Roslin, UK.

Abnormal growth patterns are commonly observed in children suffering from chronic inflammatory diseases such as Juvenile Idiopathic Arthritis (JIA) and Inflammatory Bowel Disease (IBD). These disorders are associated with the increased production of pro-inflammatory cytokines, which may influence growth through a local effect in the growth plate. To test this hypothesis we determined the effects of IL-1 beta, IL-6 and TNF alpha on the growth of the ATDC5 chondrogenic cell line. Cytokines (0.1-100 nanograms per millilitre) were added individually or in combination to the ATDC5 cells during periods of both chondrogenesis and terminal differentiation.

Chondrocyte proliferation (tritiated thymidine uptake), differentiation (alkaline phosphatase (ALP) activity) and proteoglycan synthesis (alcian blue uptake) were determined.

IL-6 (+10 nanograms per millilitre of IL-6 soluble receptor) had little effect on proliferation, differentiation or proteoglycan synthesis. At 10 and 100 nanograms per millilitre, TNF alpha significantly reduced proliferation (more than 70% decrease) and proteoglycan synthesis (more than 40% decrease) at both time points. A significant increase in relative ALP activity (nanomoles per milligram of protein) was observed during chondrocyte terminal differentiation at 10 and 100 nanograms per millilitre TNF alpha (55 percent and 156 percent increase respectively, both P-value less than 0.05). At all concentrations, IL-1 beta significantly reduced proliferation (more than 80 percent decrease) and proteoglycan synthesis (at least 30 percent decrease) during chondrogenesis and chondrocyte terminal differentiation (all P-value less than 0.05 versus control). Adding the cytokines in combinations (all 10 nanograms per millilitre) produced no synergistic or reductive effects on any of the growth parameters.

The inhibitory effect of IL-1 beta and TNF alpha on chondrocyte growth suggests that these cytokines may influence the growth of children with JIA and IBD through their local effect on the growth plate chondrocytes.

OC2**The Endocrine Sequelae of Optic Gliomas and their Therapy**

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*[1] Department Paediatric Endocrinology, St George's Hospital, Tooting, London UK; [2] London Centre Paediatric Endocrinology, University College and Great Ormond Street Hospitals, London UK.***Objectives:**

We sought to characterise endocrinopathies resulting from mass effects or anti-tumour therapy in low grade optic tumours

Patients and Methods:

We identified 40 (12M; 28F) survivors of optic nerve (n16), chiasmatic/optic pathway (n22) or hypothalamic (n2) gliomas, attending two centres. 16 underwent resection (12 complete), 10 required VP shunts and 19 progressed despite chemotherapy (n12), radiation (n12) or both (n11); 5 were observed. Growth and endocrine data were retrospectively collected.

Results:

Patients were all diagnosed before 11 years (4.1 <0.3 to 10.9>) and followed for 5.2 (0.1 to 19.0) years. Precocious Puberty (PP) requiring therapy occurred in 14 (35%), 1.0 (-1.0 to 8.2) year after diagnosis, two (14%) subsequently developing hypogonadism. 14 (40%) had no pituitary deficiency, 12 (30%) had isolated GH (with PP in 75%), 8 (20%) had two and 4 (10%) had three hormone deficits. Excepting the one child with diabetes insipidus (DI), GH deficiency (27/40) was always the first and most (65%) common deficit, especially (90%) after radiation, with (10/11) or without (11/12) chemotherapy, but also (7/12) after chemotherapy alone (57%) and simple observation 1/5 (20%) despite a shorter follow up. 8 (20%) patients each received sex steroids or thyroxine, 6 (15%) received hydrocortisone and 1 (2.5%) DDAVP. 23/27 GHD patients received GH therapy, 4.0 (1.3-10.4) yrs after diagnosis for 2.3 (0.5 to 10.4) yrs and 13 have achieved an adult height [-0.8 (-2.8 to 1.6)sds], appropriate for midparental height [-0.4 (-2.4 to 1.3)sds], but with greater BMI [2.5(-0.1 to 0.4)sds].

Summary:

PP is common but may evolve to LH/FSH deficiency. DI is rare. The evolving hierarchical endocrinopathy echoes their common developmental signalling cascade (GHD, TSH, LH/FSH, ACTH), and eventually involves ACTH. Omitting radiation does not prevent it. Despite hormone substitution, there is a tendency to obesity.

Conclusion.

All children with optic tumours, regardless of therapy, should be referred for endocrine surveillance at diagnosis, to limit ultimate short stature, obesity, subfertility and life-threatening pituitary failure.

OC3**Measured versus reported parental height**

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Introduction: Parental height is central to the assessment of growth in children. A number of studies have documented inaccuracy in self-reported heights. At the Yorkhill Growth Clinic, we have formed the impression that men tend to overestimate their height and women to underestimate. We have tested this hypothesis by comparing measured versus reported parental heights.

Methods: Standing height of parents was measured by a single observer (FC) using a Holtain Stadiometer and compared with reported heights. Age and source of reported height were recorded. Height estimation was considered accurate if reported height (RHt) was within 0.5 cm of measured height (MHt). Ethical approval and informed consent were obtained.

Results: 200 parents (100 M; 100 F), mean age 37.8 (range 20.8-69.3) years, participated. 83 subjects guessed RHt while 117 had been measured previously (74 in a medical setting, 37 in a non-medical setting, 6 did not recall where. Height was reported accurately by 31 subjects (13 M, 18 F), of whom 16 had been measured in a medical setting. 40 females overestimated height by mean (SD), range 2.1 (1.4), 0.6-6.4 cm, while 42 underestimated by 2.2 (1.5), 0.7-6.2 cm. 63 males overestimated height by 2.3 (1.2), 0.6-5.2 cm, while 24 underestimated by 1.5 (0.7), 0.6-3.3 cm. Using regression analysis, gender and age were significant predictors of the difference between RHt and MHt. Males significantly overestimated height, with a mean difference between RHt and MHt of 1.09 cm (95% CI 0.698, 1.476, $p < 0.001$). For females, the average difference between RHt and MHt was 0.09 cm (95% CI -0.564, 0.376, $p = 0.693$). Overall there was a small positive correlation between age and RHt-MHt ($r = 0.251$, $p < 0.001$).

Conclusions: Our results reinforce the need for accurate measurement of parents in clinical practice and confirm our hypothesis that males overestimate their height, but refute that that females underestimate.

OC4**Increased adiposity in South Asian teenagers is associated with increased dietary fat intake**

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Healthy South Asian teenagers have higher levels of body fat, with more central adiposity than their White European peers. The aim of this study was to determine whether these ethnic differences were associated with ethnic differences in diet.

A cohort of healthy White European and South Asian teenagers in whom body composition analysis had been undertaken underwent dietary evaluation using three methods: a 3-day food diary, a 24-hour food recall and a food frequency questionnaire, which had been adapted to accommodate Asian diets. The results were analysed using CompEat software. Groups were compared using T tests. Ethical approval was obtained.

24-hour food recalls were obtained for 98 children of whom 73 also completed 3-day food diaries. Boys consumed more calories than girls (2416 kcal vs. 1948 kcal, $p < 0.001$). Overall the South Asian children consumed the same amount of calories per day as the White European children (2186 kcal vs. 2103 kcal, $p = 0.53$), but derived a higher percentage of their dietary energy from fat (41 vs. 35%, $p < 0.001$), and less from carbohydrate (44% vs. 49%, $p < 0.05$) and protein (13% vs. 15%, $p < 0.005$). South Asian children derived a higher percentage of their energy and fat from meat and less from dairy products than White European children. There was a significant correlation between percentage dietary energy derived from fat and percentage total body fat on DXA scan (boys: $r = 0.49$, $p < 0.05$, girls: $r = 0.41$, $p < 0.05$). Similar correlations were seen with measures of central adiposity but not with BMI SDS. Fat intake was also highly correlated with Townsend deprivation score ($r = 0.53$, $p < 0.001$).

Healthy South Asian teenagers have a similar calorie intake to their White European peers, but have a higher consumption of fat, which correlates with their increased level of adiposity. Appropriate dietary modifications may help to reduce their diabetes risk.

OC5**TW2 or TW3 Bone Age Assessment: Does it Make a Difference?**

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Background: Skeletal maturity/bone age is used to provide information on growth potential and/or to aid decisions about management of various endocrine conditions. The Tanner-Whitehouse 2 (TW2) method is the most widely used system in the U.K. Recently, the TW3 method was published to address the possibility of earlier maturation. This new technique has not been widely publicised or much used in the U.K.

Aim & Methods: To compare TW2 and TW3 in children undergoing bone age estimation as part of a diagnostic workup or as part of growth monitoring. 215 children from 3 regional paediatric endocrine centres had TW2 & TW3 estimations made. 73 (37 girls) had congenital adrenal hyperplasia (CAH), 69 (24 girls) had idiopathic short stature (ISS) and/or constitutional delay in growth and puberty (CDGP), and 73 (42 girls) 'others' were a mixed group of diagnoses (early/precocious puberty, poor growth, GH deficiency).

Results: TW3 estimates were significantly younger than TW2 for each of the three diagnostic groups ($p < 0.0005$), although the differences (0.7, 0.5 and 0.8 years respectively for CAH, ISS/CDGP and 'others') were not significant between groups, $p = 0.07$. Bland Altman plots showed a significant positive relationship for the difference between the two techniques and the mean for boys and girls which was diagnosis independent. A difference of > 1.0 year between TW3 and TW2 was reached at 11.5 years in boys and 10.3 years for girls.

Conclusion: TW3 differs significantly from TW2, particularly in older children, independent of the diagnosis. The difference between girls and boys probably reflects pubertal tempo and may reflect secular trends in age of onset of puberty. Caution should be taken in any changeover from TW2 to TW3 since ages are not interchangeable in an individual child and the variation between the two assessments increases with age.

OC6**Hypertriglyceridaemia, increased truncal adiposity and decreased lean body mass in Prepubertal Leukaemia Survivors after Bone Marrow Transplantation**

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Previous studies identify increased adiposity in childhood Leukaemia survivors but not its regional distribution, although it is visceral adiposity that confers increased risk of future cardiovascular morbidity.

Aim: Determine body composition and metabolic risk factors in childhood Leukaemia survivors.

Methods: With ethical approval and written consent 21 BMT (Group1), 29 ALL (Group2) and 29 Control (Group3) prepubertal children (5-12 years), more than 1 year off treatment were recruited. Height, weight, BMI, waist, hip circumferences, fasting serum triglycerides and insulin were measured. Body composition was determined by Bioimpedance analysis (TANITA) and DEXA scan (LUNAR PRODIGY).

Results: Mean BMI SDS for Groups 1, 2 and 3 were 0.07, 0.86 and minus 0.012 respectively. Group2 was significantly increased ($p = 0.009$) but not Group1 as they were significantly shorter, (Height SDS Group1 minus 1.04 versus Group3 minus 0.22 ($p < 0.001$)). Mean total body percentage fat by DEXA was increased in both Group1 and 2 versus Group3 (28.6% versus 20.0% ($p = 0.001$)) and (27.5% versus 20.0% ($p = 0.001$)). Mean fat free mass index in Group1 corrected for height was significantly reduced vs Group3 (13.72 versus 16.19kilogrammes per metre squared ($p = 0.018$)). Waist hip ratio was increased in Group1 and Group2 compared with Group3 (0.895 versus 0.817 ($p < 0.001$); 0.862 versus 0.817, ($p = 0.019$) respectively). TANITA identified increased truncal to peripheral fat ratio in Group1 and Group2 versus Group3 (0.819 versus 0.755 ($p = 0.005$); 0.782 versus 0.755 ($p = 0.036$)). Triglyceride levels were elevated in Group1 versus Group3 (0.94 and 0.66millimoles per litre ($p = 0.009$)). Fasting insulin levels were higher in Group1 versus Group3 (4.0 and 2.8milliinternational units per litre), but this did not reach statistical significance.

Conclusion: Prepubertal BMT and ALL Leukaemia survivors have increased truncal adiposity and BMT survivors decreased lean body mass, hypertriglyceridaemia and higher fasting insulin levels. Prepubertal childhood Leukaemia survivors already demonstrate markers indicating increased risk of the metabolic syndrome.

OC7**The relationship between Leptin and Luteinising Hormone as children progress into puberty**

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An increase in leptin levels coupled with decreased leptin binding activity has been proposed as a metabolic signal to allow pubertal progression. Studies of individuals with rare mutations in the gene for leptin or its receptor also indicate that functional leptin is required for normal puberty. In primates, nocturnal leptin is reported to rise just prior to an increase in Luteinising Hormone (LH) pulse amplitude, though the validity of this relationship is controversial. This study aimed to test the hypothesis that leptin is related to LH secretion as children progress towards and into puberty.

20 children (13 boys and 7 girls, mean ages 12.2 and 12.6 respectively), with a range of growth disorders, who were either prepubertal (n=7) or progressing into puberty (n=13) were studied. First morning urine samples were collected on 3 consecutive days per month for 6 months, and leptin and LH were measured in pooled monthly samples by an IRMA and a fluorimmunoassay respectively.

Urinary leptin was higher in girls than boys in both pre (5.27 ± 4.2 vs 2.11 ± 1.9 ng/L, $p < 0.05$) and pubertal groups (9.79 ± 6.3 vs 4.86 ± 5.2 ng/L, $p < 0.05$). In the group as a whole leptin correlated positively with LH (Spearman's, $r = 0.285$, $p < 0.01$), though the correlation was greater in the prepubertal group ($r = 0.371$, $p < 0.05$) than the pubertal group ($r = 0.227$, $p = 0.052$). When analysed by pairing LH levels with leptin for the preceding month, there was no significant correlation for the whole group or the pubertal group, however leptin correlated significantly with LH, ($r = 0.437$, $p < 0.05$) in the prepubertal group.

Nocturnal leptin and LH excretion in prepubertal children are significantly associated. In this group the strength of this relationship is increased when assessing leptin as a lead to LH. These data support the concept that leptin influences LH secretion in children.

OC8**Fibroblasts from normal and Turner syndrome children produce similar levels of insulin-like growth factor binding proteins**

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Turner syndrome (TS) is associated with short stature. Many girls are treated with growth hormone (GH), though the clinical response to such therapy is variable. We hypothesised that this may relate to aberrations in the GH / insulin-like growth factor (IGF) axis; thus we assessed potential differences in IGF bioavailability by comparing IGF binding protein (IGFBP) production by skin fibroblasts from children with and without TS.

Cells from normal (n=5) and TS (n=5) subjects were seeded at 1×10^4 on day 0 and treated plus/minus GH (200 nanograms/millilitre) or IGF-I (100 nanograms/millilitre) on days 0, 2, 4, and 6. Conditioned medium (CM) was harvested on days 1, 3, 5, and 7 for analysis of IGFBP production.

Western ligand (125I-IGF-I) blotting of CM from normal fibroblasts under basal conditions demonstrated the presence of four binding proteins with molecular weights consistent with IGFBP-3 (43-45kDa), IGFBP-2 (34kDa), IGFBP-5 (30kDa) and IGFBP-4 (24kDa); IGFBP-3 followed by IGFBP-4 appeared to be the most abundant IGF binding species. Medium from TS cells revealed a similar IGFBP profile.

ELISA measurement of IGFBP-3 and -4 levels demonstrated increased production over the culture period. On day 7, CM from TS cells contained similar levels of IGFBP-3 (0.0514 plus/minus 0.045 milligrams/litre) and IGFBP-4 (21 plus/minus 12 nanograms/millilitre) to those observed in CM from normal fibroblasts (0.02 plus/minus 0.022 milligrams/litre and 30 plus/minus 21 nanograms/millilitre respectively). Neither GH nor IGF-I affected the IGFBP profile or levels of IGFBP-3 and -4 produced by normal or TS fibroblasts.

Fibroblasts isolated from children with TS are comparable to fibroblasts from normal children with respect to IGFBP profile, IGFBP-3 and -4 production and response to GH / IGF-I treatment. These findings suggest that the short stature associated with TS can not be explained by altered IGF-I bioavailability due to differences in IGFBP levels.

OC9**Familial Glucocorticoid Deficiency type 2 is associated with mutations in a novel gene encoding a small single transmembrane domain protein**

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Familial Glucocorticoid Deficiency (FGD) or hereditary unresponsiveness to adrenocorticotropin (ACTH) (OMIM 202200) is an autosomal recessive disorder resulting from resistance to the action of ACTH on the adrenal cortex to stimulate glucocorticoid production. Affected patients are deficient in cortisol but not mineralocorticoids and, if untreated, are likely to succumb to hypoglycaemia and/or overwhelming infection in infancy or childhood. Mutations in the ACTH receptor (melanocortin 2 receptor, MC2R) account for approximately 30% of FGD cases. Patients with a normal MC2R are referred to as having FGD type 2 (FGD2). We previously identified one candidate locus for FGD2 at 8q12.1 - 21.2 in one large kindred but many consanguineous FGD2 families exist whose disease cannot be mapped to either the MC2R or chromosome 8 locus. In one such family (A) whole genome SNP analysis using the GeneChip Human Mapping 10K Array from Affymetrix revealed a single candidate region on chromosome 21. Here we report identification of disease-associated mutations in an uncharacterised gene located within this interval. Homozygous mutations were detected in affected individuals in both families, IVS3ds+1 G to T in family A and IVS3ds+1 G to C in family B. In addition the IVS3ds+1 G to C mutation was detected in a second family, a further splice mutation (IVS3ds+3 ins T) was identified in three families and a homozygous nonsense mutation of the initiator methionine residue (ATG to ATA) was identified in 5 families. In conclusion we have identified a causative gene for FGD2 which is co-expressed in tissues with MC2R and encodes a small single transmembrane domain protein. Further work will reveal the frequency of mutations in this gene in FGD2 patients and the mechanism by which it leads to adrenal failure.

OC10**Abnormalities of clinical and biological pubertal development in paediatric Cushing's disease**

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Virilization is said to be frequent in paediatric Cushing's disease (CD) and may be related to ACTH-stimulated adrenal androgen secretion. Serum androstenedione (A4), DHEA-S, testosterone (T) and SHBG, LH, FSH were therefore measured at diagnosis in 29 CD patients (18m, 11f; median (range) age 13.4 yr (6.4-17.8)). Virilization was present as hirsutism (63% of patients) and acne (45% of patients). Pubertal development was assessed for normal consonance of stages and considered abnormal when axillary hair, pubic hair or genitalia stages were advanced compared to breast stage or testicular volume (TV). On this basis, puberty was abnormal in 14/29 patients (48%, median (range) age 10.5yr (6.4,13.7)) and normal in 15/29 (52%, age 15.2yr (10.8,17.8)). Androgen levels were converted to SDS from data in 647 normal subjects aged 8.5-16.5 yr. In the whole group of patients (n=29), median (range) SDS values were not significantly elevated for any of the adrenal androgens; A4 +0.82 (-1.85,9.06; n=25), DHEAS -0.4 (1.92,1.46; n=27) and T +0.89 (-3.78,311.75; n=29). However, median (range) A4 SDS was higher in patients with abnormal compared with normal puberty +2.38 (0.4,9.06) versus +0.52 (-1.85,3.91) respectively (P=0.03 Mann-Whitney U test). Pubertal boys (TV 4ml, n=8) had median (range) T SDS -1.77 (1.09,11.7) (prepubertal boys n=10, T was 0.58 (-1.09,11.75)) associated with low LH, FSH median (range) values of 2.1 (0.3,4.6), 1.0 (0.7,6.3) mU/L. Pubertal girls (Br stage 2, n=9) also had low LH and FSH; 1.1 (0.3,7.4), 3.0 (0.3,4.4) mU/L. Normal pubertal values in both sexes are LH >2.0 and FSH >3.0 mU/L. In the whole group median (range) SHBG was low; -1.93 SDS (-4.32,0.86) (n=19), and negatively correlated with the elevated BMI (BMI SDS median 2.4, range 0.5-5.1) (r=-0.49). In conclusion, many patients with paediatric CD had abnormal puberty. When virilization was present this was associated with a raised A4; SHBG is lowered associated with the increased BMI. Disturbance of pituitary-gonadal function was demonstrated in many pubertal patients.

OC11**The Catecholamine Response To Fasting In Children with Adrenal Failure**

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*[1] Department of Paediatrics, Royal Victoria Infirmary, Newcastle Upon Tyne; [2] SCMS, University of Newcastle Upon Tyne; [3] Department of Clinical Biochemistry, Freeman Hospital, Newcastle Upon Tyne.***Introduction**

The adrenal medulla requires intramedullary glucocorticoids for normal development and function and catecholamine concentrations are reduced in children with congenital adrenal hyperplasia (CAH). We hypothesised that ACTH sufficient children with GHD would have altered catecholamine production compared to children with primary or secondary adrenal insufficiency (AI).

Methods

25 children were studied following ethical approval. 5 children were GH deficient/ ACTH sufficient (PHDCS), 7 had GH and ACTH deficiency (PHDCD), 6 had salt-losing CAH and 6 had primary adrenal failure excluding CAH (PAF). An additional child with CAH was studied following adrenalectomy. Children were admitted twice and fasted for 14h from 2200h. Medication was given as normal on one occasion and a single dose of evening GH and/or morning hydrocortisone omitted on the other. Plasma glucose concentrations were measured every 20 minutes, catecholamines hourly from 0700 hrs and NEFAs / ketones at 1200hrs. Morning adrenaline and noradrenaline production was calculated using area under the curve (AdAUC / NAUC).

Results

There was no difference in the AdAUC between our 4 groups of patients, on or off treatment. PHDCS children had higher NAUC off treatment than those with AI ($p=0.04$). Patients with PHDCD and PAF (but not CAH or PHDCS) demonstrated evidence of counterregulation with a negative relationship between AdAUC and glucose nadir ($r=-0.77$; $p=0.04$ and $r=-0.79$; $p=0.06$), a positive relationship between AdAUC and NEFAs ($r=0.78$; $p=0.04$ and $r=0.92$; $p=0.01$) and ketones ($r=0.60$; $p=0.15$ and $r=0.83$; $p=0.04$). Catecholamine levels were no different to other CAH patients post-adrenalectomy.

Conclusions

There was no overall difference in fasting adrenaline production between patients with primary or secondary AI and isolated GHD despite variations in hypoglycaemic susceptibility. However cortisol deficiency may result in reduced circulating noradrenaline levels. Adrenaline production does form part of the counter-regulatory response in patients with early and late onset adrenal insufficiency.

OC12**Phenotype, genotype and sex of rearing in a cohort of patients with Partial Androgen Insensitivity Syndrome**

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Partial androgen insensitivity syndrome (PAIS) is a heterogeneous group of intersex disorders characterised by a typical perineoscrotal hypospadias/micropenis phenotype, and a normal androgen-producing testis. Only a minority is explained by a mutation in the androgen receptor (AR). Phenotypic expression is widely variable and there are no agreed guidelines to determine the sex of rearing in individuals with borderline masculinisation.

The aim of the study is to quantitatively assess the external genital phenotype in relation to AR genotype and sex of rearing.

Mutation positive PAIS patients were identified from the Cambridge Intersex Database. Details about mutations and sex of rearing were recorded. Phenotype was defined using an external masculinisation score (EMS), based on scrotal fusion, presence of micropenis, positions of the urethral meatus and the gonads. The normal score is 12. Sex of rearing was compared in cases with similar mutations reported on the International McGill database.

29 mutation positive patients were identified. 18 patients were raised male, in whom the median EMS was 5. The median EMS was 3 in 11 patients raised female. All patients with EMS of 4 or more were raised male. However, 8 patients with EMS of 3 or less were also raised male.

2 patients with identical mutations (Arg840Cys) had an EMS of 2 and 11, yet were both raised male. 2 mutations (Glu211Glu, Ser703Gly) were reported previously in patients with complete AIS and one mutation (Gly214Arg) has even been reported in a normal male.

The external genital phenotype in PAIS is extremely variable and is rarely predicted by the AR genotype. Sex of rearing is not entirely dependent on the EMS. Cultural issues, other modifying genes and response to androgen trials might be influencing factors. Further studies are needed to clarify how decisions about sex of rearing are taken in patients with lower range EMS.

OC13**Does terbutaline reduce the incidence of nocturnal hypoglycaemia in children with type one diabetes - a pilot study?**

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Asymptomatic nocturnal hypoglycaemia is extremely common in children with diabetes. It has been estimated that 30 to 40% of children will suffer an episode of hypoglycaemia on any one night. There is evidence that the beta agonist terbutaline may prevent hypoglycaemia in children by enhancing the counter-regulatory responses to hypoglycaemia. We undertook a pilot study to assess the feasibility of using the terbutaline as a therapeutic option to prevent hypoglycaemia at night.

Methods: Fifteen children, with diabetes for at least a year, each received a single dose orally at bedtime, in random order and on separate occasions, of placebo, low dose (<7yrs 15mcg/kg, >7yrs 0.5mg) and standard dose (<7yrs 75mcg/kg, >7yrs 2.5mg) terbutaline. Overnight venous glucose profiles were performed at home on separate occasions to monitor the effect on blood glucose. Regular capillary glucose measurements were made the day before and day after the study medication. Hypoglycaemia was defined as a blood glucose <3.5mmol/l.

Results: The incidence of hypoglycaemia was reduced on the nights the children received standard dose terbutaline (2/15) compared to the nights they received either placebo (6/15) or low dose terbutaline (7/15). There was no difference in the mean blood glucose on the following day between the occasions the children received standard dose terbutaline (mean = 11.1 mmol/l) and the occasions they received placebo (mean = 10.9 mmol/l).

Conclusions: Terbutaline appears to reduce the incidence of nocturnal hypoglycaemia in children with diabetes without having an adverse effect on their blood sugar the following day.

OC14**Inherited non-type 1 diabetes in paediatrics is a heterogeneous disorder**

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In a UK survey of non-type 1 diabetes in childhood, we identified families with non-type 1 diabetes inherited as an autosomal dominant trait, in whom the most common MODY mutations had been excluded (Ehtisham et al. Archives of Disease in Childhood 2004;89(6):526-9.). We hypothesised that childhood onset autosomal dominant non-type 1 diabetes would be genetically homogeneous due to the young age of presentation compared with adult onset diabetes, and would be a valuable resource for identifying penetrant new diabetes genes.

We aimed to clinically, biochemically and genetically characterise families with childhood onset non-type 1 diabetes and autosomal dominant inheritance.

Recruitment was from 3 sources: follow up of the UK survey of childhood diabetes; the UK MODY database; and direct contact with consultant paediatricians. Families were visited at home and all available members were bled and measured.

19 families have been visited (20 probands). The median age of the index case at diagnosis of diabetes was 10.9 years (range 0-15); median HbA1c = 6.4% (4.1-11.4). 8 were insulin treated, 4 with oral agents and 8 with diet alone. Rather than being homogenous these families form 5 groups; probable autoimmune diabetes (n=2, median BMI-SDS - 0.4, triglyceride 0.65 millimoles per litre, c-peptide 244 picamoles per litre); probable MODY (n=9, median BMI-SDS 0.2, triglyceride 0.64 millimoles per litre, c-peptide 638 picamoles per litre); probable type 2 diabetes (n=5 median BMI-SDS + 2.1, triglyceride 1.65 millimoles per litre, c-peptide 815 picamoles per litre); probable syndromic diabetes (n=2, median BMI-SDS + 2.7, triglyceride 3.62 millimoles per litre, c-peptide 1479 picamoles per litre); and neonatal diabetes (n=1).

Inherited childhood non-type 1 diabetes is a heterogenous group of disorders that can be differentiated on clinical and biochemical findings. This clinical and biochemical classification should help guide a candidate gene approach to further characterisation of these families.

OC15

ABSTRACT WITHDRAWN

OC16**Congenital Hypothyroidism in Scotland - twenty four year audit**

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*[1] Department of Child Health, Royal Hospital for Sick Children, Yorkhill, Glasgow, UK; [2] Scottish Newborn Screening Laboratory, Royal Hospital for Sick Children, Yorkhill, Glasgow, UK.***Introduction**

Screening for congenital hypothyroidism (CHT) began in Scotland in 1979. Efficiency data up to 1993 (Period 1) have been published previously. We present a summary of the data from 1994 - 2003, comparing efficiency with Period 1.

Results

The subjects comprise 246 infants who had abnormal Guthrie TSH results between 1/1/94 and 31/12/2003. The diagnosis of CHT was definite in 139 (56.5%), probable in 16 (6.5%), uncertain in 42 (17.1%), transient in 34 (13.8%) and indeterminate in 15 (5.7%). The mean annual incidence of true CHT (definite and probable) was 1:3727 (1:4350, Period 1).

Median age at Guthrie was 6 days for true CHT (7 in Period 1) and 7 days for the transient/uncertain group (5 - 14 days, Period 1).

Age at Guthrie was 10 days or more for 6.5% of the cohort (10.5%, Period 1).

Median age at notification for true CHT was 10 days (11 in Period 1).

Median age at start of treatment was 11 days (11 - 15 days, Period 1). The median time between notification and treatment starting, where appropriate, was 0 days. However the range was wide (-16 to 179 days), with 14 patients starting treatment more than 6 days after notification of whom 12 had normal T4 and 11 moderately raised TSH on first venous sample. Interestingly 10 of the 14 were eventually classified as true CHT.

Seven patients had an older sibling with dysmorphogenesis but only three had cord blood TFTs. We would expect 100% cord blood testing in this situation.

Thyroid scanning was carried out in 102 patients and was of diagnostic value in 89%.

Conclusion

All parameters compared showed improvement. It is worth noting that 16 neonates had their first Guthrie at 10 days or later. All neonates should have a Guthrie test by day 6, regardless of their feeding status.

OC17**Identification of the transcript encoding IKBE, an inhibitor of NFkB, as a novel candidate gene in Graves' disease**

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Introduction

Up to 80% of susceptibility to Graves' disease (GD) is thought to be genetic. However, little progress has been made using linkage and association analysis in identifying new GD susceptibility genes. We have taken a novel functional genomic approach to attempt to identify GD susceptibility genes.

Methods

We performed microarray analysis of CD4 positive lymphocyte RNA to identify differential gene expression between 4 male patients with inactive GD and 4 age-matched controls. Candidate gene expression was confirmed by quantitative real-time RT-PCR in 30 GD patients and 30 controls. Ethical approval was obtained.

Results

Of the 12,632 transcripts examined by microarray, 6131 were expressed in CD4 positive cells, and 7 were differentially expressed between GD patients and controls ($p < 0.05$). Of these 7 transcripts one mapped to a previously identified locus of GD linkage, and this was nuclear factor for kappa light chain gene enhancer in B cells inhibitor, epsilon (NFKBIE), located at 6p21.1. The NFKBIE transcript was expressed at a mean of 1.83 fold higher in GD patients compared to controls ($p = 0.036$). By RT-PCR the mean NFKBIE mRNA expression level in the GD patients was 2.22plus/minus0.20 versus 1.60plus/minus0.11 in the controls ($p = 0.005$), confirming the differential expression.

Seven informative single nucleotide polymorphisms (SNPs) in NFKBIE were then genotyped by PCR/RFLP or mass spectrometry genotyping, in a local case-control cohort of 531 GD probands and 555 controls. One of these SNPs, located in the 3'UTR, has shown association with GD, with the minor A allele being found in 272 of 1076 GD alleles (25.3%) compared to 228 of 1110 control alleles (20.5%) (Chi-squared=6.96, $p = 0.008$, Odds ratio=1.3). Conclusion

NFKBIE plays an important regulatory role in immune cell development and T-cell regulation. Our study provides novel evidence that NFKBIE, which maps to an area of GD linkage, may have an important role in GD.

OC18**Birth weight affects screening blood spot thyroid stimulating levels independent of gestational age**

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Background: Thyroid stimulating hormone (TSH) levels are thought to be lower in preterm infants compared to those born at term. Cut-off for re-examination of screening blood spot TSH is the same for all babies regardless of gestation and birth weight. Previous studies of TSH levels from fetal and live birth studies are based on small numbers.

Aim: To assess the effect of birth weight and gestation at birth on screening blood spot TSH levels.

Methods: All blood spots TSH submitted to 1 single Regional Neonatal Screening Laboratory over a 6 weeks period were included in the study. Screening was performed using capillary blood spot samples taken after day 5 of life. Blood spot TSH levels were measured using a time resolved fluoroimmunoassay (Delfia TM Neonatal hTSH).

Results: We included 3547 infants (283 preterm infants). Median gestational age at birth was 40 weeks (Range 24-43) and median birth weight was 3496 gram (range 565-5500). Significant inverse relationships (Spearman's correlation co-efficient) were identified between screening TSH with gestation at birth ($R = -0.07$, $p < 0.001$) and birth weight ($R = -0.09$, $p < 0.001$). Multiple linear regression analysis identified birth weight as the only independent factor influencing blood spot TSH (Beta coefficient = -0.063, $p < 0.0001$). Mean blood spot TSH was significantly higher ($p = 0.01$) in very low birth weight infants (1.8, SD 2.7) compared with infants with birth weight 1500 grams or greater (1.2, SD 2.4). 1.69% of infants screened had TSH levels over 5 milliunits per litre.

Conclusion

Birth weight rather than gestational age at birth is an independent factor influencing blood spot TSH level.

P1**Home Use of Betahydroxybutyrate Meters for Diabetic Children**

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*[1] Dept of Paediatrics, Altnagelvin Area Hospital, Londonderry BT47 6SB, N Ireland; [2] Dept of Clinical Chemistry, Altnagelvin Area Hospital, Londonderry BT47 6SB, N Ireland.***Background**

Increased blood betahydroxybutyrate (OHB) indicates loss of metabolic control in type 1 diabetes mellitus. Home measurement may be beneficial.

Objective

To assess accuracy and usefulness of parental measurement of diabetic childrens' OHB.

Methods

Parents were instructed in use of the Abbott Medisense OHB meter by a diabetic nurse and advised to use it if their child was unwell, pyrexial or had a capillary blood glucose >15millimoles per litre. Written advice was given on interpretation of results and appropriate action: OHB <0.6millimoles per litre - nil; 0.6-1.5 - retest in 2 to 4 hours; 1.5-3.0 - contact the diabetes team; >3 - go to hospital. Sheets were given to record timing of measurements, indications and action taken. Accuracy of measurement was assessed by asking parents to measure OHB on 4 quality assurance samples. Ethical Committee approval was obtained.

Results

84 OHB measurement episodes (mean 4, range 1-23) were recorded by 20 parents over 6 months. Indications: high capillary glucose alone 42%; high glucose and unwell 21%; unwell alone 19%; high glucose, pyrexial and unwell 4%; recheck 2%; 12% inappropriate reason with one family representing over half of these. OHB results were <0.6millimoles per litre - 75%; 0.6-1.5 - 16%; 1.5-3.0 - 7% and >3 - 2%. Action was inappropriate in 14% with inappropriate undertreatment 9% and inappropriate overtreatment 5%.

Interindividual coefficient of variation for OHB measurement on quality assurance samples was 7.2%, 11.7%, 7.7% and 9.7% at target concentrations of 2.8, 1.7, 3.9 and 3.1millimoles per litre respectively. 5 readings fell outside 3 standard deviations of the truncated mean.

Conclusions

Most OHB measurements were precise with appropriate interpretation. If education is adequate home OHB measurement may improve diabetic control.

P2**Review of immobilisation induced osteopenia in children**

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Prolonged immobilisation increases the risk of low bone mineral density (BMD) and low trauma fractures in children with cerebral palsy (CP).

Aim: To identify the characteristics of patients with osteopenia caused by immobilisation due to other aetiologies.

Methods: Retrospective review of case notes and BMD scans of immobile patients (duration >3 months) referred for bone density assessment. Children with osteogenesis imperfecta were excluded.

Results: Of 19 identified, 3 were excluded due to poor scan quality. Aetiologies identified were spinal cord injury (5), cerebral palsy (3), spinal muscular atrophy, dysmorphic syndrome, encephalopathy, Intracerebral bleed, spina bifida, sacral agenesis, muscular dystrophy and Hypomelanosis of Ito.

14 children were wheelchair dependant, while 2 walked with support at home but used wheelchair outdoors.

During physiotherapy, 6 used standing frames, 3 tilt table, and 2 walking frame. Median age was 9.4years (range 5 to 13.5). 13 had sustained low trauma fractures. Median duration of immobility prior to first fracture was 5years (0.3 to 11.5). Median number of fractures was 3 (1 to 4). Commonest bone involved was femur (61%).

Median Body mass index Standard Deviation score (SDS) was 0.86(-2.9 to 3.0). Median height SDS was -1.2(-5.21 to 1.55). Median lumbar spinal BMD Z score was -2.92(-4.8 to 0.8). Median lumbar Bone mineral apparent density (BMAD) Z score was -2.29(-4.87 to 0.14), Median Whole Body BMD (WBM) Z score was -0.84(-4.4 to 0.67). Some patients had normal lumbar spinal BMD(4), BMAD(6) and WBM(12) Z scores. There was a linear relationship between lumbar spinal BMD and duration of immobility ($r = -0.68$, $p=0.005$). This maybe due to poor growth with increased immobility duration.

Conclusion: Children with immobility due to aetiologies other than CP are also at risk of low BMD. Although BMD is significantly reduced in most immobilised children, some sustain low trauma fractures despite normal spinal and whole body BMD values. Alternative approaches for assessing BMD in such children need to be considered.

P3**Constitutional Delay of Growth and Puberty (CDGP) is associated with the GPR54 gene but not leptin (L), Leptin Receptor (LR) and Cocaine and Amphetamine Regulated Transcript (CART) genes**

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CDGP is a common growth disorder, often showing dominant inheritance but with variable penetrance. Thus genetic association is very likely. There are many candidates: we have assessed the possible contribution of L, LR genes (mutations in each cause very delayed or absent puberty), CART (mediates the effect of L on GnRH pulse generation), and GPR54 (a hypothalamic G-protein coupled receptor, which is mutated in familial hypogonadotropic hypogonadism) genes.

Ethical approval was obtained from the Salford and Trafford local research ethics committee. Two approaches were undertaken: (1) Genotyping for recognised polymorphisms (L - 3' CTTT repeat, LR - Gly>Arg substitution in exon 6, and (2) screening the whole gene by denaturing high performance liquid chromatography (DHPLC, WAVE) for CART and MassARRAY for GPR54. Analysis was undertaken in 89 CDGP subjects and their parents and in 113 healthy controls. Association was tested both by genotype frequency in cases versus controls and by transmission disequilibrium testing (Tdt).

The frequency of the L CTTT repeat (short versus long) and the LR alleles did not differ between cases and controls, nor was there significant bias in the Tdt. An adenine deletion was identified in exon 3 of CART; its frequency in CDGP was 12% and 7% in controls ($p=0.1$). However in the GPR54, polymorphic markers 15kB upstream of the coding sequence showed preferential transmission of one allele at a 2:1 ratio in males ($p=0.03$ and 0.06 for the 2 linked markers).

Sequence variations in the L, LR and CART genes are not associated with CDGP. Polymorphisms upstream of the GPR54 gene may be linked to CDGP and may contribute to the tempo of growth and pubertal development, but this needs confirmation in other cohorts.

P4**Environmental Factors in the Aetiology of Septo Optic Dysplasia and Congenital Hypopituitarism**

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Congenital hypopituitarism (CH) and Septo Optic Dysplasia (SOD), are thought to be due to an insult occurring in critical brain development during early fetal life. Whilst some patients have genetic defects (eg. HESX-1 Pit-1 & PROP1), in most cases no cause is found.

Within our regional hypopituitary database, background details are available on 31 SOD patients and 30 CH patients. Genetic screening in 42% (including 6 familial cases), identified 1 Pit-1 mutation. No differences in maternal smoking or alcohol consumption during pregnancy were seen. Drug abuse during pregnancy, including cocaine, was reported in 4 SOD mothers (12.9%), but not in CH mothers. There was also an increase in maternal first trimester bleeding in SOD compared to CH (33% vs 17% [ns]).

Both SOD (3.19kg) and CH (3.20kg) patients had reduced mean birth weight ($p<0.05$) using UK population means. SOD patients had reduced maternal age (22.6 years) ($p<0.05$) compared to the UK population (28.6 years) and CH patients (26.8 years). There is a substantial over representation of SOD children of Afro-Caribbean and mixed/Afro-Caribbean origin compared to the local population (26.8% vs. 3.4%), and no SOD children of Asian origin (0% vs. 7.3%). There are also more Afro-Caribbean and mixed/Afro-Caribbean CH patients (17.1%), although there are CH patients of Asian origin (10.3%).

More SOD patients were born in autumn and winter (32.2% and 29.0%) compared to the local population (25.3% and 23.9%) and CH patients (17.2% and 30.0%). Possibly reflecting environmental insults during early pregnancy.

The increased risk of bleeding during pregnancy and vasoactive drug usage in SOD mothers, suggests a vascular insult is more likely in SOD. As very few genetic mutations were identified in our group, it would appear that environmental factors have a more significant role in the aetiology of SOD compared to CH.

P5**Age and Intellect Appropriate Levels of Patient/Parent Educational Information for Endocrine Disorders**

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BACKGROUND It is well established that verbal communication alone may be insufficient in educating patients, as they may forget up to 50% of the information provided in a consultation within minutes of leaving. Endocrine conditions are often complex and poorly understood. Written information can aid in recall of the material. This study aims to explore how well the information caters for varying adult intellect levels and childhood age groups. **METHODS** Twenty leaflets were analysed for design according to a twenty-point criteria created by the authors. Readability was assessed by using the OFSTED Basic Skills Agency SMOG scores. Leaflets with SMOG scores of less than or equal to 5 are generally understood by the majority of the population. **RESULTS** According to the design criteria leaflets scored in the range of 11.5-19.5 (maximum 20), mean/median score 14.5. (SD 2.2). According to the SMOG readability grading, the leaflets scored in the range of 8.0-13.7, with a median score of 10.9 and a mean of 10.7 (SD 1.7). Specific endocrine/diabetes leaflets fared worse with a mean design score of 14.2 and SMOG score 11.7. **DISCUSSION:** This study indicates that a high proportion of written information available to patients is inappropriate for the audience targeted. Information for adults of differing intellect levels and children in distinct age groups are required. Guidelines have been created for production of patient/parent information. Examples relating to congenital hypothyroidism, short stature and precocious puberty have been produced.

P6**Is there a role for metformin in the management of childhood obesity?**

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Introduction.

Over the last decade there has been an increase in the global prevalence of childhood obesity associated with the emergence of type 2 diabetes in children (T2DM). Obesity is a risk factor for T2DM and we have reported a 26% incidence of impaired glucose tolerance (IGT) and 7% incidence of T2DM in 42 obese (BMI > 98th centile) children aged 4.6 to 17 years.

Metformin has been reported to reduce the risk of developing T2DM by 31% in a large study of obese adults but there are no large studies in children.

Aim.

To review the clinical outcomes in metformin-treated obese children at a single centre.

Methods.

A retrospective case note review was performed of 9 (1 male, 8 female) obese children with IGT aged 8.7 to 16.5 years, treated with metformin 500 milligrams two or three times per day. Auxological and biochemical data were assessed at baseline and between 6 months and 12 months after starting metformin treatment.

Results.

There was a mean reduction in BMI SDS of minus 0.4 (range minus 1.81 to plus 1.86) at 6 months and minus 0.8 (minus 0.06 to minus 1.95) at 12 months. There was a mean reduction in fasting insulin of 20 milli international units per litre (minus 5.1 to minus 43) and a mean reduction in fasting glucose of 0.4 millimoles per litre (minus 0.7 to plus 0.1) at between 6 and 12 months. There was a mean reduction in a measure of insulin resistance (HOMA-IR) of 4.8 (1.2 to 5.4) at between 6 and 12 months.

Conclusions.

Metformin improved BMI SDS and insulin glucose status. A larger scale, prospective, randomised placebo controlled trial is needed to evaluate the therapeutic benefit of metformin in obese children and to determine whether it may have a role in reducing the risk of developing T2DM.

P7**Designing a Diabetes education programme : involving families and teachers in the development of a Paediatric DAFNE course**

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Objective: The aim of the study is to develop a structured education course for children with Type 1 Diabetes, which meets the needs of young people and which is delivered using recognised educational techniques. The views of young people, their parents and secondary school teachers have therefore been sought to influence the development of a DAFNE course for 11-16 year olds. Methods Local Research Ethics Committee approval was obtained. Focus groups were attended by 24 children and 29 parents. Semi-structured group discussion focussed on intensive insulin management, perceptions of current diabetes education, and recommendations for course design. Discussions were tape-recorded and transcribed, before qualitative analysis.

Secondary school teachers worked with the research team focussing on their areas of expertise - mathematics, food technology and personal, health and social education.

Results: Participants identified several potential problems with the DAFNE approach, including self-management at school and the need for greater understanding of diabetes by school staff. Their views strongly influenced course design, which now includes the involvement of friends and the development of a school resource pack. Teachers designed lesson plans, work sheets and practical sessions based on the National Curriculum. They have advised on educational techniques and helped address issues such as management of diabetes at school.

Conclusions: Qualitative methodology has allowed patient involvement in course design. Teachers have worked with the research team to ensure the curriculum is appropriate for this age group and will be involved in training health personnel as educators.

P8**Effect of Insulin Glargine on glycaemic control in children with type 1 diabetes mellitus**

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Objective:

To see if there is an improvement in HbA1c with insulin Glargine (IG).

Method:

41 children were commenced on IG either as part of four (QDS) or three (TDS) injections per day regimen between November 2002 and April 2004. In a retrospective review their preIG and serial HbA1c available till July 2004 were noted. Data were analysed for the whole group as well as the QDS and the TDS groups separately.

Results:

21 boys and 20 girls were started on IG at a mean age of 14.3 years (range 8 to 18 years). 30 children were on a QDS (lispro preprandially and IG nocte) and 11 on TDS (Humalog mix 25 prebreakfast, Lispro/Novorapid pretea and IG nocte) regimen.

Whole group (41)

Mean plus/minus 2SD preIG HbA1c was 9.2 plus/minus 3.8 percent (95 percent CI 8.6-9.7)

On follow-up (32) mean plus/minus 2SD postIG HbA1c after 10.2 months was 8.5 plus/minus 3.0 percent (95 percent CI 8.0-9.0, p less than 0.005)

In the QDS group (30) 17 children who were already on a QDS regime with NPH insulin (Insulatard) showed a significant improvement in HbA1c with IG.

Mean plus/minus 2SD preIG HbA1c (17) was 9.4 plus/minus 4.6 percent (95 percent CI 8.2-10.3).

On follow-up (14) mean plus/minus 2SD HbA1c after 11.3 months 8.0 plus/minus 4.2 percent (95 percent CI 6.9-9.1, p less than 0.01).

TDS group:

Mean plus/minus 2SD preIG HbA1c (11) was 9.3 plus/minus 3.7 percent (95 percent CI 8.2 -10.3)

On follow-up (9) mean plus/minus 2SD HbA1c after a mean of 10.8 months was 8.5 plus/minus 1.7 percent (95 percent CI 7.9-9.0, p less than 0.005)

Conclusion:

An improvement in glycaemic control was noted with IG on short-term follow-up. Children who were already on a basal bolus regimen with NPH insulin (Insulatard) also showed a significant improvement in their HbA1c after switching over to IG. There was an improvement in HbA1c in both the QDS and the TDS groups. This suggests that TDS regimen is a viable option in children who are not ready for the QDS regimen yet.

P9**A prospective evaluation of Growth Hormone Treatment (GHT) for Quality of Life (QOL) in children**

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We report a longitudinal study of QOL from baseline (before beginning GHT=Time 1) to 6 months after commencing treatment for growth hormone deficiency (GHD=Time 2). LREC approval was obtained. 26 consecutive referrals (16 males: age range = 7.87-16.21 years, mean age 11.27 years (SD=2.71)) beginning GHT including children with isolated idiopathic and acquired GHD (malignancy N=15) were recruited. At both time points, height, weight, sitting height, body mass index, subischial leg length, and skinfold thickness were recorded. Children and parents completed standardised measures of QOL. Children also completed a brief estimate of IQ and the Shuttle test as an indicator of energy.

Children completed an increased number of runs on the shuttle test, indicating improved energy (M=69.8, 79.4, $p<0.05$). Child QOL increased according to parent report (M=54.0, 61.5, $p<0.05$), especially in relation to psychosocial (M=54.0, 61.6, $p<0.05$) but not physical QOL (M=54.7, 61.2, $p=0.10$). Children reported improvements in their own QOL, physical and psychosocial QOL, although none reached significance. There were no changes in IQ. Separate analyses for children with idiopathic GHD compared with cancer related GHD were not significant for IQ or QOL.

Our findings provide preliminary evidence for the QOL implications of GHT in children. Limitations include the small sample size and brief follow-up period. Although the primary reason for GHT is to increase children's height, these preliminary data provide supportive evidence of the additional benefit of an improvement in QOL.

P10**A tertiary care experience of obesity investigations**

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The increasing prevalence of obesity in children has resulted in rising numbers of referrals for evaluation of underlying medical causes.

Aim: To ascertain the nature and results of investigations performed in these children in order to develop an evidence-based protocol.

Methods: Retrospective case-note analysis of obesity referrals to an endocrine clinic.

Results: 41 children (mean age 8.3 years, range 0.3, 18) referred for evaluation of obesity over a 5 year period (August 98-August 03). Mean Body Mass Index (BMI) standard deviation score (SDS) was +3.99 (range +1.98, +11.8). The commonest investigations performed were thyroid function tests (TFTs) (71%), blood pressure (BP)(60%), bone age (51%), fasting insulin (41.5%), fasting plasma glucose (37%), and lipid profile (39%). Other tests including Dexamethasone suppression tests, serum gonadotrophins and neuroimaging (MRI/CT head) were performed if indicated by history and physical examination. No child in our group had abnormal TFTs. Other investigations showed some abnormalities: raised BP (64%), raised fasting insulin (35%), altered lipid profiles (6%) and bone age advanced by over 2 years (19%). An underlying endocrine cause was not detected in any child, but one had associated hypogonadism. The yield of the tests was higher with a BMI SDS cut off of +3. Hyperinsulinaemic (HI) children were not more obese than non HI ones (median BMI SDS +3.6 vs +4.0).

Conclusions: Endocrine causes of obesity are uncommon and investigation should only be undertaken when clinically indicated. The investigations with greatest yield were those looking for co-morbidities and complications. More abnormalities are found when a higher BMI SDS (i.e. +3) is used. There is a need for an evidence based protocol for evaluation of obese children which should be primarily directed at assessing cardiovascular risk, reinforcing the emphasis on changing lifestyle in the long term management of obesity.

P11**Thyrotoxicosis: outcome and choice of definitive therapy**

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Introduction

Thyrotoxicosis usually requires life-long therapy although the treatments - antithyroid drugs (ATD), surgery (S) and radioiodine (RI) - are utilised in different ways. We have assessed outcome in a unit where families are encouraged to discuss the therapeutic options with surgeon and radiotherapist when ATD are stopped.

Methods

All children under 18 years of age with thyrotoxicosis managed in our unit between 1997 and 2003 were identified from our paediatric endocrine database. Clinical details including age, height at diagnosis and clinical course were collected. Remission was defined as euthyroidism 12 months off ATD.

Results

32 patients were identified (28F, 4M). One female patient was excluded (McCune Albright syndrome). The remaining 31 patients had autoimmune thyroid disease. The average age at diagnosis was 12.1 years (range 3.5-17.0) and most were tall (+1.0 SD versus a parental target of +0.2 SD; $p < 0.01$). Co-morbidity (other autoimmune disease, chromosomal defects, dysmorphism) was common (30%). 5 patients are currently being treated with their first course of ATD and of those who completed a course of treatment, 23% are in remission. RI was used as initial therapy in 2 children with learning difficulties. S or RI were used for poor compliance (2 patients), drug side-effects (2 patients) as well as relapse. 46% of patients have now had S and 23% RI (excluding those on first ATD course). Complications of S and RI were infrequent. Sodium iodopodate was an effective way of rendering the patient euthyroid pre-surgery.

Conclusions

Hyperthyroidism is present for some time pre-diagnosis. Around a quarter of young people with autoimmune thyrotoxicosis remit after a single course of ATD. Most patients opt for thyroidectomy or are treated with RI within 4 years of presentation when these options are available. RI may be particularly useful in the poorly compliant or in those with learning difficulties.

P12**Hypercalcaemia in relapsed medulloblastoma 8 years post diagnosis; evidence to support PTHrP production by medulloblastoma cells**

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Introduction

A 19 year old male presented with symptomatic hypercalcaemia as the first manifestation of relapsed metastatic medulloblastoma. Management at the time of the initial presentation 8 years earlier was with surgical excision and craniospinal radiotherapy. His biochemistry at the time of relapse and studies of medulloblastoma cell lines have provided information about the pathogenesis of his hypercalcaemia.

Methods

PTHrP was measured by immunoradiometric assay in blood, and in conditioned and control media from three medulloblastoma cell lines following 72 hours growth.

Results

The histology at initial presentation (11 years of age) and at the time of relapse (with bone marrow infiltration and widespread bony metastases) demonstrated medulloblastoma cells. Ionised calcium concentrations were 2.89 millimoles per litre and serum PTHrP levels were increased at the same time (2.7 picomoles per litre; normal range 0.7-1.8 picomoles per litre). There was evidence of PTHrP production by one cell line (MHH-MED-8A, 4.4 picomoles per litre, normal range 0.7-1.8 picomoles per litre), while results for both other lines tested were below the limit of detection (less than 0.7 picomoles per litre). Our patient was managed with a combination of steroids, bisphosphonate therapy (pamidronate 1 milligram per kilogram x 3 doses) and haemodialysis, and made a steady clinical and biochemical recovery. In view of the diagnosis of widespread late recurrence of medulloblastoma a decision was taken to use palliative chemotherapy with radiotherapy to the cervical spine.

Conclusions

Relapse 8 years after diagnosis is unusual in medulloblastoma and for this relapse to be manifest as hypercalcaemia is also very uncommon. Our investigations suggest that the clinical picture was a reflection of abnormal PTHrP production by medulloblastoma cells.

P13**Introduction of Insulin Glargine(Lantus) into mainly thrice daily insulin regimens in children and adolescents with diabetes**

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Introduction: Glargine is a new basal analogue insulin which has a more prolonged and predictable duration of action than isophane/NPH insulin.

Method: A retrospective study of patients attending the Diabetes Clinic who had been on Glargine for 6 months or more at the time of study and whose duration of disease exceeded one year. Indications for Glargine treatment and various outcome measures were examined 6 months before and after Glargine treatment.

Results: 42 children(19 boys) were included in the study. 2 children with duration of disease <1y were excluded. Age ranged from 5.7 to 17.2 with a mean of 12.7 y (s.d. ,Standard deviation, 3.3 y); Mean duration of disease was 6.2y (s.d. 3.5y). Indications for Glargine treatment included night-time hypoglycaemia (43%) and hyperglycaemia before breakfast (36%). 37/42 (88%) patients were on thrice daily insulin injection regimens pre-Glargine. After 6 months, the number of daily injections were 4 or 5 (14%), 3 (83%) and 2 (2%). 3 teenage-girls were switched back to a twice daily insulin regimen because of adherence difficulties. Daily mean insulin dose was 1.18U (s.d. 0.35U) and 1.05U (s.d. 0.28U) per kg per day, 6 months before and after Glargine treatment respectively. The mean decrease of 0.13 (s.d. 0.23) U per kg per day was highly significant ($p=0.0008$). HbA1c did not change significantly ($p=0.8$): mean change of 0.05% (s.d. 1.17%) after 6 months glargine treatment. The BMI-SDscore did not change either (mean change -0.03, s.d. 0.37, $p=0.7$). Over the 6 month periods before and during glargine treatment, severe hypoglycaemias (1 or 2 episodes) occurred in 7 and 4 children and diabetic ketoacidosis (1 or 2 episodes) occurred in 1 and 1 child respectively. At the end of the study, 39/42 (93%) children remained on Glargine treatment.

Conclusion: The introduction of insulin Glargine into mainly thrice daily insulin regimens was acceptable, safe and well tolerated by patients. Daily insulin requirements fell on Glargine treatment whilst HbA1c remained unchanged.

P14**Trends in Childhood Diabetes in Wessex 1996 To 2002**

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Aim - To audit data collected for children with diabetes <16yrs in the Wessex Region and assess significant trends from 1996 to 2002.

Method - Audit data was collected annually by questionnaire from each of the 10 districts on: clinic staff numbers, occurrence rates, length of stay (LOS) and incidence of Diabetic Ketoacidosis (DKA) at presentation, re-admission rates with DKA and mean clinic HbA1c.

Results - The number of consultants per 100 patients varied between 5.5 and 0.9 across the districts in 1996 and between 2.3 and 0.7 in 2002. The paediatric diabetes nurse specialist ratio (PDNS) per 100 patients varied between 1.4 and 0.2 in 2002. All districts except one have had a dietitian with diabetes experience in their clinics.

There is a significant trend of increasing incidence and prevalence of diabetes over the study period ($p=0.04$ for incidence, $p<0.001$ for prevalence). The LOS for new patients (not in DKA) has shown a decrease (from 3.3 to 1.8 days), and varies between districts. This variation may be related to PDNS cover per patient ($r = -0.54$, $p =0.11$). The incidence of DKA at presentation and re-admission has remained constant (averages of 22.3% and 5.7% respectively). However the incidence of DKA re-admissions varies considerably between districts from a mean of 2.6 to 10.6%, but is not directly related to PDNS cover per patient ($r = -0.06$, $p=0.88$). Mean HbA1c levels varied between districts but different assays hinder comparison.

Conclusions - The incidence and prevalence of childhood diabetes is increasing in the Wessex region. Fewer consultants are looking after more diabetic children. PDNS cover remains poor in some districts and may explain variation in LOS of new patients but not readmission with DKA rate. Audit allows collection of useful data and comparisons between districts, which may lead to changes in service provision.

P15**Persistent hyperinsulinaemic hypoglycaemia of Infancy : Patient clinical and molecular genetic characteristics**

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Recent advances in molecular genetics and membrane physiology have elucidated the mechanisms of glucose-stimulated insulin release and identified the pathogenesis of persistent hyperinsulinaemic hypoglycaemia of infancy (PHHI). The clinical goal, in PHHI, is to achieve euglycaemia by pharmacological and sometimes surgical intervention. Different mutations in the SUR/Kir6.2 gene are associated with focal or diffuse disease and the advantage of preoperative radiological identification of focal disease would be to limit surgery and avoid rendering the infant diabetic.

The aim of this study was to review the recent experience of PHHI at our centre by performing a retrospective case note study of the last eight subjects.

Median age at presentation was 13 hours, although one presented at 6 months. Five required intensive or high dependency care. Mean peak insulin concentration was 21mU/L with corresponding mean glucose of 1mmol/l. The mean peak glucose requirement was 25mg/kg/minute, with intravenous dextrose for mean 17.7 days and polycal in feeds for mean 51.5 days. Mean doses of diazoxide and chlorthiazide were 8.5 and 9.9 mg/kg/day, respectively for 33.3 days (11-67). Two cases were transient (11 and 62 days). Two remain on treatment beyond 5 months. Four required surgery, but preoperative radiology was not performed. Mean age at surgery was 63 days, one required further surgery within 24 hours and another after 107 days. Diffuse disease was present in 3 and mixed focal/ diffuse in one. Paternal deletions (N=2) and one homozygous mutation in the SUR/Kir6.2 gene were identified in 3 subjects, all of whom underwent surgery. Three developed post-operative diabetes and one subject demonstrates neurodevelopmental impairment but he had other complex problems.

The intensive multidisciplinary care of these infants has been associated with good clinical outcomes. Accurate pancreatic imaging using PET scan, combined with rapid molecular genetic diagnosis would significantly enhance clinical and surgical management.

P16**GNRH therapy for precocious puberty causes weight gain**

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Endocrinology; Birmingham Children's Hospital; Birmingham.

INTRODUCTION

Precocious puberty is defined as the onset of puberty before the age of 8 years in girls and 9 years in boys. Where it seems appropriate, pubertal progression can be halted by regular administration of GNRH analogues, and therapy discontinued when it is suitable for the child to continue into puberty. Such treatment is not usually associated with any significant adverse effects. An observation by some parents of excessive weight gain on GNRH analogue therapy prompted us to audit patients on GNRH therapy.

AIM

To identify whether goserelin administration leads to increased weight gain.

METHOD

Auxology data was collected on 17 children receiving GNRH analogue, Goserelin, for at least 1 year. These children received either goserelin 3.6mg 3-4 weekly or goserelin 10.8mg 8-10 weekly subcutaneously.

Height and weight data was collected pre treatment and then at 6months and 1 year after treatment. Body mass index (BMI) was calculated and all measurements were converted into a SDS using British reference data.

RESULTS

All patients were female with a median age of 7.25 years (range 1.81-9.67 years), Weight SDS increased from 1.69 pre treatment to 1.88 at 6months and 2.11 at 12 months, both significant [$p<0.05$]. The mean BMI SDS also increased from 1.23 pre treatment to 1.52 at 6 months [$p<0.05$] and then to 1.87 at 12 months [$p<0.01$]. There were no significant changes in height SDS. Using IOTF criteria, 29% were obese, 29% were overweight and 42% were of normal weight pre treatment. At 12 months of therapy, 47% were obese and 29% were overweight.

CONCLUSION

Goserelin therapy for precocious puberty significantly increases weight and BMI, during the first year of therapy. It is important to make parents and the child aware of this risk during goserelin therapy.

P17**Another genetic cause for septo-optic dysplasia**

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Septo-optic dysplasia consists of a triad of optic nerve hypoplasia, hypopituitarism and midline brain defects. The exact cause is unclear, although genetic causes, eg HESX- 1, have been reported.

Recently mutations in the SOX2 gene have been reported to be associated with anophthalmia. These patients were reported to have bilateral/unilateral anophthalmia; some also had learning difficulties and genital anomalies. We report a case of anophthalmia and hypopituitarism with a SOX2 mutation.

EM was born at 35 weeks gestation, following antepartum haemorrhage, with a birth weight of 2.28 kg. He was ventilated initially, and during his 4-week stay on the neonatal unit, anophthalmia and micropenis were noted. There was no hypoglycaemia or jaundice during the neonatal period. MRI scans have confirmed absent of optic nerves, cavum septum pellucidum and a thin corpus callosum. The pituitary gland had a normal appearance.

He is now 4 years old and endocrine testing has confirmed GH-insufficiency on 2 tests (Peak 7.7mU/l and 12.6mU/l); he has now been commenced on growth hormone therapy. There is also evidence of gonadotrophin deficiency. Free thyroxine levels have been low normal (10.8-13.5 pmol) although the stimulated cortisol response is normal. Other problems include feeding difficulties, for which he requires a gastrostomy, developmental delay and deafness due to middle ear disease.

Anophthalmia is a severe form of optic nerve hypoplasia. Together with male genital tract anomalies in this patient and previously reported patients with SOX2 mutations, this may represent a variant of hypopituitarism/septo-optic dysplasia.

P18**WATCH IT - A New Approach to Managing Childhood Obesity**

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Background

Despite the increasing prevalence of childhood obesity, there are limited resources available to support obese children and their families. Locally, there is no specialist paediatric clinic, no hospital dietetic service for obese children and community dietitians can only offer 1 or 2 appointments and a phone call.

Aim

To develop a community-based service for obese children and teenagers in Leeds, run by non-health professionals.

WATCH IT! provides a family-centred flexible and individual programme for obese children and teenagers aged 8 - 16 years with a Body Mass Index above the 98th centile. Families and children may self refer or be referred by any other agencies.

The programme has 3 components:

- a) Frequent individual appointments (initially weekly) offering encouragement, support and motivational counselling.
- b) HELP (Healthy Education Lifestyle Programme) - a toolkit of resources taking a solution-focussed approach towards eating behaviour, physical activity, nutrition and emotional well being.
- c) WATCH IT! group activity sessions

The programme is delivered by 4 community workers chosen for their personal qualities and communication skills. They have received basic training in nutrition, physical activity, mental health, child protection, auxology and motivational and behavioural change techniques. They receive regular supervision from a dietitian, psychologist and sick children's nurse.

Evaluation

The effectiveness of the programme is monitored through auxology and qualitative questionnaires which are undertaken 3 and 6 months respectively. Over 50 children attended during the development phase of the Programme. 34 children have enrolled since January 2004 with 80 percent attendance and a fail to attend rate of only 6 percent. Body Mass Index standard deviation scores have decreased by 0.2 (95 percent confidence interval 0.06, 0.31) (p less than 0.001) (a comparison group of hospital referred children increased by 0.1 standard deviation). Independent interviews with families indicated high satisfaction.

Conclusion

This structured approach in community settings shows some success in promoting reduction in overweight, and is well received by motivated families.

P19**How Practical Is Waist Circumference as a Clinical Measure of Obesity?**

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Abdominal girth in adulthood is an important measure associated with cardiovascular risk. Waist circumference charts have now been published for use in children. As 3 anthropometric methods have been recommended for use, we decided to explore how they differed and whether any 1 method might be superior.

Aim: To ascertain the variation between 3 different methods of measuring waists for children of a range of weights and Body Mass Index.

Methods: 41 children (31 girls, 10 boys) aged 3.6 - 18.8 (mean plus or minus standard deviation

12.4 plus or minus 3.3 years) attending a paediatric endocrinology clinic were weighed and measured by the same expert auxologist. Waist measurements were taken at the:

- a) mid point between the lowest rib and iliac crest
- b) crease on lateral flexion
- c) 4 centimetres above the umbilicus

Children were asked which method most approximated their waistline. The measures for each child were compared and Bland Altman plots drawn.

Results: Body Mass Index standard deviation ranged from minus 1.7 to plus 4.22 (mean plus or minus standard deviation 0.98 plus or minus 1.6). There was wide variation in measures for each child up to 8 centimetres. 6 had more than 6 centimetres and 16 more than 3 centimetre difference between any 2 measures. Only 8 of these were obese, and only 15 showed a difference of less than 1 centimetre between the 3 measurements. Bland Altman plots showed no consistent difference between the measures. Only 3 children felt their waists were either at a) or b). 12 felt that c) was accurate, but 19 thought their waist was at or below the umbilicus.

Conclusion: Measuring waists by 3 different methods produced great variation in waist circumference. No single method was superior in terms of its correlation with Body Mass Index standard deviation score. Further work is needed before waist circumference can be regarded as a useful anthropometric measure. Currently, we would recommend using method c) as this is the simplest to measure.

P20**South Asian teenagers have intrinsically lower adiponectin concentrations independent of body composition**

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Low concentrations of the adipocytokine adiponectin predict future development of diabetes. Adiponectin concentrations are inversely correlated with insulin resistance in adults, and adiposity in both adults and children. We have previously shown that South Asian teenagers have more body fat and are less insulin sensitive than White European teenagers; however there is little data on ethnic differences in adiponectin concentrations.

We aimed to test the hypothesis that South Asian children have lower adiponectin concentrations that can be explained by ethnic differences in insulin sensitivity and body composition.

We undertook analysis of body composition (DXA and anthropometry), insulin sensitivity (HOMA) and fasting adiponectin, in a cohort of 129 healthy White European and South Asian teenagers. Statistical analysis was by T test and analysis of covariance. Linear associations were assessed by Pearson correlation.

Girls had higher adiponectin concentrations than boys (mean 10.6 vs. 7.6 micrograms/ml, $p < 0.001$). Adiponectin was weakly correlated with HOMA insulin sensitivity in girls ($r = 0.29$, $p < 0.05$) but not in boys. Adiponectin had a stronger inverse correlation with measures of central adiposity (waist circumference $r = -0.37$, $p < 0.001$, waist:thigh ratio $r = -0.41$, $p < 0.001$) than with measures of total body fat. South Asian children had lower adiponectin concentrations than White European children (boys: 6.9 vs. 8.4 micrograms/ml, $p = 0.05$, girls: 9.2 vs. 12.0 micrograms/ml, $p < 0.05$), in keeping with their reduced insulin sensitivity and increased central adiposity. However ethnic differences in adiponectin were still present when covariate analysis was undertaken with total body fat (girls: 9.1 vs. 11.9 micrograms/ml, $p < 0.05$), or with measures of truncal adiposity.

Adiponectin is inversely related to adiposity and insulin resistance in children, however South Asian children have intrinsically lower adiponectin concentrations than White UK children, even after allowing for ethnic differences in body composition. Lower adiponectin concentrations may contribute to increased diabetes risk in South Asians.

P21**Refractory neonatal hypocalcemia secondary to maternal Vitamin D deficiency**

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Introduction: Maternal vitamin D deficiency is well recognised as a cause of late (5-10days age) and late-late (2-12 weeks age) neonatal hypocalcemia. In the UK, the Department of Health (DoH) recommends vitamin D supplements in pregnancy for high risk women eg. Asians. However, this guideline is mostly ignored. We report a case series of refractory neonatal hypocalcemia secondary to maternal vitamin D deficiency.

Method: Retrospective case notes review over a 2 year period from 2001-2003 in one centre for neonatal hypocalcemia (late and late-late).

Results: Four cases were identified, all males, presenting between the ages of 6 days and 12 weeks with focal seizures. 3 were South Asians (Indians) and 1 was Arab muslim (Libyan). There was no pattern of seasonality. 3 were bottlefed with formula milk and 1 was exclusively breastfed (presented at 12 weeks age).

Significant hypocalcemia was confirmed in the neonates and vitamin D deficiency was demonstrated biochemically in the mothers. Other investigations including metabolic screen, head ultrasound and ECG were normal. None of the mothers had Vitamin D supplementation in pregnancy.

All 4 cases received intensive calcium supplementation with intravenous calcium gluconate boluses, oral calcium gluconate, calciferol and 1 alpha cholecalciferol according to maximum prescribable doses. 2/4 cases also received intravenous calcium infusion, magnesium supplementation, pyridoxine as well as anticonvulsant therapy. Mothers were supplemented with oral vitamin D and calcium supplements.

The seizures resolved in 2 days in 2/4 cases but persisted for 7 and 14 days in the other 2 cases. Biochemical hypocalcemia was more refractory to treatment ranging from 5-21 days before normocalcemia was achieved.

Conclusion: This case series highlights the refractoriness to treatment of neonatal hypocalcemia secondary to maternal vitamin D deficiency. The exact cause for this refractoriness remains unclear. It may be that current treatment guidelines need to be revised and it is essential that DoH guidelines are implemented to prevent this problem.

P22**Children with Diabetes have Elevated Blood Pressure**

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Objective: To determine blood pressure (BP), and its determinants in a population of children with diabetes.

Approval: Ethical approval for the study was sought, but deemed unnecessary by East Norfolk & Waveney LREC.

Introduction: BP is a key determinant of macro- and microvascular complications, and consequent morbidity and mortality in people with diabetes. The development of normative BP reference data for children in Great Britain has allowed us to determine whether children with diabetes have elevated BP.

Methods: Repeated oscillometric blood pressure measurements (Dinamap 8100, Johnson & Johnson, Seattle, USA) were recorded in 140 children with diabetes aged 4-16y attending diabetes clinics. BP was transformed into SD scores using the LMS Method, based on normative oscillometric BP data for Great Britain. Relationship between BP and BMI, HbA1c, microalbuminuria and duration of diabetes was analysed by multivariate analysis.

Results: Systolic BP, was initially below the mean, but rose with duration of diabetes, whereas diastolic BP was consistently elevated regardless of duration of diabetes. Multivariate analysis showed the rise in Systolic BP was strongly correlated with BMI SDS ($p=0.002$) and diastolic BP ($p=0.008$), but not HbA1c or microalbuminuria.

Conclusions: Children with diabetes have elevated diastolic BP, even shortly after diagnosis. This elevation in diastolic BP may be a consequence of peripheral hyperinsulinism. Systolic BP rises with duration of diabetes; this rise being explained by the concomitant increase in BMI. Intensive insulin regimens necessary to achieve optimal glycaemic control also result in increased BMI, and consequently elevated BP. The use of intensive insulin regimes needs to be accompanied by intensive dietetic support to mitigate the rise in BMI and hence SBP.

P23**A survey of the use of continuous subcutaneous insulin infusion in paediatric diabetes practice in the United Kingdom, 2003-2004**

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Aim: To survey the use of continuous subcutaneous insulin infusion (CSII) among paediatric diabetologists in the UK in 2003-2004. **Background:** Guidelines for the use of CSII for patients with Type 1 diabetes (T1DM) were published by the National Institute of Clinical Excellence in 2003. It was anticipated that 1-2% of patients would be suitable for such treatment yet no data are available as to how many children are using CSII in the UK.

Methods: Members of BSPED were asked to complete a postal survey. Paediatricians were questioned about their experience of CSII with an emphasis on service provision and funding.

Results: 149 centres participated with a response rate of 39%. Centres managed a median 100 (range: 3-400) children under 16 years of age. 201 children were identified as being on CSII, an estimated 1.1% of children with T1DM. The median number of patients on CSII per centre was 0 (0-26). The major indication for initiation of CSII was to improve glycaemic control (52%) but 38% of children were started on CSII at the request of the family. 62% of patients were being funded by local primary care trusts with only 15% of patients self funding. Only 38% of centres felt confident to initiate CSII without specialist help and insulin pump companies were supporting CSII provision in 57% of centres. 57% of centres did not use CSII therapy. Those centres not using CSII stated that concerns regarding funding (64%) and lack of expertise (65%) were the main reasons for the reluctance to start CSII.

Conclusion: CSII is not widely used by UK paediatricians. This may increase as greater experience is gained in their use but is likely to be limited by lack of appropriate resources. It is anticipated that this survey will be repeated before the next NICE appraisal in 2006

P24**Does giving patients a free choice of their growth hormone device help improve their compliance with therapy?**

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Aim: To evaluate whether giving patients a free choice of their growth hormone (GH) device improves compliance

Background: In December 2000, our unit took over the budget for prescribing GH from the local health authority. Hospital prescribing facilitated hospital tracking of prescriptions. Additionally, a home delivery service ensured that drugs were delivered and allowed fridge counts to assess compliance with therapy. Since January 2001 patients started on GH at our unit have been offered a free choice of their GH device.

Methods: In December 2000, 115 patients were being prescribed GH by our unit. Clinicians decided which GH device these patients should be given. 125 patients were started on GH between January 2001 and May 2004. Of these 50 (40%) have had their GH prescribed through our pharmacy unit. Our pharmacy department routinely collects compliance data by comparing the expected usage of GH with the actual GH used (based on delivered GH vials and fridge counts of leftover GH vials).

Results: The median compliance with GH therapy from patients who were not given free choice of their delivery device was 89%. This broke down to 88% compliance for needle less devices and 91% for pen devices. This compares with a median compliance of 95% (84%-105%) for all devices when patients were given a free choice (ns). This broke down to 96% (93%-100%) for needle less devices and 87% (84%-105%) for pen devices.

Conclusion: The levels of compliance have been improved with the home delivery system to quite high levels within our unit. There is a tendency to improve compliance with free choice. However, no statistically significant improvement in compliance between patients being offered free choice of growth hormone device and those in whom GH device is determined by the clinicians can be demonstrated.

P25**Metformin is Effective in the Treatment of Severe Childhood Obesity**

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Introduction: The prevalence of severe childhood obesity is increasing. It is associated with adverse health outcomes, including the future development of cardiovascular disease and diabetes, partly mediated through insulin resistance. Consequently, metformin has been recommended for children with severe obesity.

Objective: To determine whether metformin was effective in reducing BMI SDS in severely obese children (BMI SDS above 2.0).

Methods: Retrospective case-note review of 15 Severely obese children (BMI SDS +2.1 - +3.9, 9-16y, 7 males), who underwent an oral glucose tolerance test (OGTT) to evaluate insulin resistance, defined as high fasting insulin, excessive insulin rise on OGTT, and/or late hypoglycaemia. Insulin resistance was quantified using Whole Body Insulin Sensitivity Index (WBISI). Insulin resistant subjects were offered metformin treatment. Parents and children were counseled about possible side-effects. Children were initially started on Metformin 250mg tds, increased as tolerated to a maximum of 1g tds.

Results: All 15 children were found to be insulin resistant. No child had diabetes, although one had impaired glucose tolerance. There was a significant correlation between presenting BMI SDS and WBISI ($r=+0.52$, $p=0.048$). Fourteen children commenced metformin, with one declining treatment. No child subsequently withdrew from treatment. Follow-up data are available for 11 treated children after 4-24 months therapy. All treated children had a reduction in BMI SDS (mean -0.4 SDS, $P=0.001$). There was a non-significant trend to greater reduction in BMI SDS in the less severely insulin resistant children, measured by WBISI ($r=-0.38$, ns).

Conclusions: All severely obese children studied were insulin resistant, and the severity of insulin resistance was correlated with the elevation in BMI SDS. Metformin treatment was generally well tolerated, and no child withdrew from treatment. All metformin treated children followed-up to date had a reduction in BMI SDS. Metformin is effective in the treatment of severely obese children.

P26**Slipped upper femoral epiphysis at presentation of thyrotoxicosis: a previously unreported association**

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Slipped upper femoral epiphysis (SUFE) is associated with multiple endocrinopathies including hypothyroidism. Here we report 2 cases of thyrotoxicosis presenting with SUFE, a previously unreported association. Case 1: A 15 yr old girl presented to the orthopaedic surgeons with tall stature and an 18 month history of hip and lumbar spine pain. SUFE was diagnosed radiologically with displacement of capital epiphysis of both femora. A 3 month history of anxiety, goitre, hyperphagia, hyperhidrosis and tiredness was elicited. Heart rate (HR) was 90 bpm and blood pressure (BP) 120/70 mm Hg. Height was 2.23 SD (target height - 0.18 SD) and BMI -0.17 SD. Serum TSH was 1.7 microunits/millilitre (NR 1.7 - 10.2) and T4 215 nanomoles/Litre (NR 60 - 140). Colloid and microsomal antibodies were positive. Isotope scan demonstrated a cold nodule. Fine needle aspiration cytology showed no evidence of malignancy. The nodule was sclerosed using sodium tetradece. Clinical and biochemical remission was achieved with carbimazole (CBZ) and maintained with CBZ and thyroxine. Thyroid carcinoma was diagnosed 20 years after initial presentation.

Case 2: A 15 yr old boy presented with a 3 month history of hip pain. SUFE was diagnosed radiologically requiring screw fixation. His mother reported deteriorating behaviour, agitation and restlessness. He was clinically and biochemically thyrotoxic: HR 100 bpm, BP 140/90 mm Hg, hyperreflexia, serum TSH < 0.03 milliunits/Litre (NR 0.3-3.8) and T4 295 nanomoles/Litre (NR 69-141). Thyroid receptor antibodies were present (15units/Litre, NR 0-10). Height was 0.84 SD (target height -0.68 SD) and BMI -1.22 SD. Ultrasound showed a multinodular goitre. Clinical and biochemical remission was achieved and maintained with CBZ.

P27**Auxology and clinical features at presentation of thyrotoxicosis in childhood and final adult height: prepubertal versus pubertal children**

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Paediatric thyrotoxicosis is heterogenous condition. It was our impression that prepubertal differed from pubertal children with thyrotoxicosis. We report auxology and clinical features at presentation in a cohort of 44 children of whom 20 girls, presenting in puberty, have reached final adult height (FAH).

Methods: A retrospective study of 44 children presenting with thyrotoxicosis. Children with other conditions likely to affect auxology were excluded. Children were defined as pubertal according to the criteria of Tanner et al. Height (Ht) and body mass index (BMI) SDS were derived from the 1990 growth standards.

Results: 15 children were prepubertal (M:F 1:2.4) and 29 pubertal, (1: 4.8). Family history was common in both groups (40% vs 55%). BMI was significantly lower in prepubertal children (-0.90 plus/minus 0.90 SD vs 0.09 plus/minus 0.93 SD, $p < 0.05$) but Ht was similar (0.56 plus/minus -1.21 SD vs 0.78 \pm 1.03 SD). Duration of symptoms (7.8 plus/minus 6.6 months vs 9.5 plus/minus 16.7 months) did not correlate with either Ht or BMI in either group.

FAH in 20 girls presenting in puberty was significantly less than Ht SDS at presentation (0.65 plus/minus 0.98 SD vs 0.91 plus/minus 1.10 SD, $p < 0.05$), however mean FAH was above the population mean.

Prepubertal children were more likely to present with hyperphagia and weight loss (66% vs 51% and 73% vs 35% respectively).

Dominant symptoms in pubertal children were neck swelling, tiredness and polydipsia (33% vs 55%, 0% vs 30% and 13% vs 30%). Goitre and eye signs were common in both groups (86% vs 96% and 73% vs 55% respectively).

P28**Usefulness of hCG test in differentiating hypogonadotrophic hypogonadism from pubertal delay**

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Pubertal delay occurs in 5% of boys aged 14 years. The differentiation of hypogonadotrophic hypogonadism (HH) from the much commoner Constitutional Delay of Growth and Puberty (CDGP) can be difficult.

Objectives

To compare the testosterone (T) response to 3 day (3d) and 3 week (3w) hCG testing in HH and CDGP using Receiver Operating Characteristic (ROC) methodology.

Patients, methods and design

Retrospective analysis of data from 58 children and adolescents who underwent 3d and 3w hCG stimulation tests. Patients were divided into 2 groups on clinical data: HH [n = 36; mean age at investigation 8.1yrs (SD 5.5)], and CDGP [n=22; 11.6yrs (SD 4.8)].

Results

Mean delta 3 d T was lower in HH [2.9(SD 3.4)nmol/L vs 14.8(13.9) in CDGP], as was mean delta 3w T [7.3(5.4) vs 18.9(10.3) in CDGP]. Similar trend seen in basal T [0.87(0.49) vs 3.37(1.28) in CDGP], and mean peak 3d and 3w T, as well as lower mean (3w-3d) T in HH [5.1 (3.7) vs 8.2(7.2) in CDGP]. All differences highly significant ($p < 0.001$).

Delta 3d T < 3 nmol/L has a positive predictive value (PPV) 89 percent for HH; delta 3d T > 9 has PPV 100 percent for CDGP.

ROC analysis suggested an optimal cut-off delta T of 5 nmol /L at 3 d and 12.5 at 3 w. Area under ROC was 0.88 for 3d test and 0.80 for 3w test.

Discussion

Mean values in both groups for delta and peak 3 d and 3 w T are significantly different but with wide scatter. Delta 3 d T < 3 very suggestive of HH whilst delta 3 day T > 9 very suggestive of CDGP. 70 percent of sample accurately diagnosed using these cut-offs.

The area under ROC analysis implied that the 3 day test performed best and that little was gained by extending the test to 3 weeks.

P29**Body composition in children with chronic renal failure and the effect of rhGH treatment**

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In a LREC-approved observational study, Body Mass Index(BMI) was compared to Fat Mass(FM) and Lean Body Mass(LM) using DXA in 25 children with chronic renal insufficiency(CRI)(median age:11yrs,10th,90thcentiles:5.8,13.3) and 19 post-transplant patients(Tx) (median age 15yrs (10.7,17.6)). Seven children with CRI and 4 Tx children received rhGH.

RESULTS: In the CRI group, median HtSDS and BMISDS were -1.6(-2.7,1.3) and -0.1(-1.4,1.7), respectively. Median calorie intake was 95%(81,118) and the protein intake was 100%(93,129) of recommended. Median %FMSDS was 0.8(-0.5,1.2) and LMSDS was -1.8(-3.5,-0.5). In the Tx group, the median duration post-tx was 3.3yrs(3.8,8.8). Median HtSDS and BMISDS were -1.4(-3,0.2) and 0.5(-1.8,2.5) respectively. Median calorie intake was 107%(90,122) and protein intake was 113%(101,152). Median %FMSDS was 1.4(0.3,2.4) and LMSDS was -2.3(-4.7,-0.8). The median BMISDS for the whole group at 0.5(-1.7,1.7) was significantly lower than the %FMSDS, 1.1(-0.1,2.5), and significantly higher than the LMSDS, -1.89(-4.2,-0.5)($p < 0.005$). There was a significant relationship between energy & protein intake, and BMISDS & %FMSDS but not with LMSDS in the Tx group($r = 0.6$, $p < 0.05$). This was not evident in the CRI group. In the Tx group, there was an inverse association between BMI and time since Tx($r = 0.5$, $p < 0.05$). LM was low in the CRI group and remained so post-transplant. In the CRI group, rhGH patients had a median %FMSDS of 0.27(-0.55,1.55) and LMSDS of -1.11(-1.89,-0.4) compared to 1.05(0.25,2.5) and -1.83(-3.5,-0.35) respectively in the patients not on rhGH. In the Tx group, rhGH patients had a median %FMSDS of 1.16(0.76,2.02) and LMSDS of -1.46(-3.76,-0.2) compared to 1.6(0.25,2.5) and -2.77(-4.72,-1.09), respectively in patients not on rhGH.

CONCLUSIONS: BMI is not an accurate representation of body composition in children with chronic renal disease who appear to have a relatively high FM and a low LM. The effect of rhGH on body composition in chronic renal failure and, especially, post transplant requires further study.

P30**Appropriate Dose of Insulin in the first hour of Diabetic Ketoacidosis Management**

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Insulin dosage in the first hour of Diabetic ketoacidosis management.

Background:

European Society of Paediatric Endocrinology and Diabetes United Kingdom recommend the use of insulin of 0.1 units per kilogram per hour, in the first hour of Diabetes ketoacidosis management, in children above 5 years. However there is insufficient evidence whether lower doses of insulin could be used effectively and much safely.

Aim:

To study the effect of two different doses of insulin on the blood glucose values, acidosis and any clinical symptoms of cerebral oedema.

Method:

We retrospectively reviewed the case notes of all children who presented with diabetic ketoacidosis, over a six-year period, to our hospital. In the initial hour, patients were administered insulin at either 0.05 unit per kilogram per hour as per our unit guideline (group1) or 0.1unit per kilogram per hour as per diabetes UK guideline (group 2), depending on individual physician's choice.

Results:

23 episodes of diabetic ketoacidosis occurred in 14 children between 7 to 14 years. 10 of these patients were administered insulin at 0.1unit per kilogram per hour and 18 were administered insulin at 0.05unit per kilogram per hour. For a similar degree of acidosis and mode of fluid administration the drop in blood glucose value was higher in group 2 (range 10.2 to 22) compared to group 1(range 2.4 to 7.4 millimoles per decilitre). Data regarding the change in acidosis was available in four patients and was less than 0.3 units in all 4 patients (3 from group 2). One patient had signs suggestive of raised intracranial pressure. Three patients complained of mild headache. All four patients were from group 2.

Conclusion:

Use of lower dose of insulin seems to be safer, especially in patients with Ph of less than 7.1 and when fluid boluses are needed for dehydration.

P31**Does HbA1c at presentation and the quality of diabetic control within the first year after diagnosis influence long-term glycaemic control? Is glucose toxicity to the beta cell a factor?**

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It has been suggested that children who obtain good early of their diabetes maintain better long-term control. We sought to confirm these anecdotal observations by examining children's glycosylated haemoglobin (HbA1c) in the first year after diagnosis and their long term HbA1c. We also examined the link between HbA1c at diagnosis, mode of presentation and long-term HbA1c. Glucose has a direct toxic effect on beta-cells. One might expect that children who had the highest HbA1c levels at presentation or who presented with ketoacidosis would have poorer long-term control.

Methods: All HbA1c measurements within our diabetic clinic are routinely entered into a database. The records of 155 children with type 1 diabetes were examined. The relationship between HbA1c at presentation, mean HbA1c within the first year and long-term rolling mean HbA1c were examined.

Results: HbA1c in the first year following diagnosis was highly correlated with HbA1c levels throughout the rest of the child's diabetic career ($r = 0.43$, $p < 0.001$). Whether or not a child presented with ketoacidosis had no effect on long-term rolling HbA1c values. HbA1c at diagnosis (measured in 43 children) was also correlated with long-term control ($r = 0.35$, $p < 0.001$). Multiple regression suggested that the best predictor of lifetime HbA1c was mean HbA1c in the first year following diagnosis ($r^2 = 0.37$). Including HbA1c at diagnosis in the model improved its ability to predict longterm HbA1c ($r^2 = 0.54$).

Conclusions: Attaining good diabetic control in the first year after diagnosis is a strong predictor that the individual will maintain good diabetic control thereafter. Whilst psychosocial factors are doubtless important the correlation between HbA1c at diagnosis and subsequent control raises the possibility that achieving good early control may reduce the toxic effect of hyperglycaemia on the beta cell and preserve endogenous insulin secretion.

P32**The Psychological Impact of Genital Anomalies on Parents: Preliminary Results of the Scottish Audit of Genital Anomalies (SAGA)**

A E Robson, on behalf of the Scottish Genital Anomaly Network (SGAN)

AE Robson

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There is scarce information on how parents cope with children with genital anomalies. SAGA is an MREC-approved, prospective survey of the clinical care of such children in Scotland. Assessment of the parents was performed by psychometric tests to evaluate stress (Parent Stress Index, PSI) and three patterns of coping (Coping Health Inventory for Parents, CHIPs; I: maintenance of family integrity, co-operation and optimism; II: social support, self-esteem and psychological stability; III: understanding of the medical situation through communication with other parents and clinical staff) and a semi-structured interview for qualitative analysis. Out of 25 eligible cases, consent was obtained from the parents of 17 boys with male undermasculinisation with a median age at referral to SAGA of 4 months (range, 5days to 2.6yrs) and a median external masculinisation score of 9 (6 to 10). The raw Total Stress Score as assessed by the PSI was within the normal range (<85th centile) in 9 out of 10 parents who were assessed and in one parent it was above the normal range at 85th centile denoting increased stress. Assessment by CHIPs showed that only one parent had an abnormal score for pattern III, denoting increased coping burden. Semi-structured interview analysis revealed general satisfaction with the clinical service but concerns were raised about the lack of knowledge about the imminent surgery and the lack of written information that could complement the time-restricted contact with the clinical team. On the whole, the parents reported a desire for an opportunity to discuss concerns regarding their child and used the interview for this purpose.

In this group of boys with relatively mild forms of XY undermasculinisation, parents do not display clearly abnormal levels of stress or burden of coping. The semi-structured interview complements this objective assessment and highlighted the need for more effective exchange of clinical information.

P33**Audit: Prescribing Growth Hormone according to NICE guidelines**

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Aim: To audit how well the prescribing of growth hormone (GH) in our unit from January 2003 to July 2004 adhered to the guidelines set out by the National Institute of Clinical Excellence (NICE) in May 2002.

Background: NICE has issued guidelines on selection of patients for GH therapy. Isolated GH deficiency should be diagnosed on the basis of two provocation tests but in specified circumstances, one test will suffice. We decided to audit how well our prescribing of GH adhered to the NICE guidelines.

Methods: Patients started on GH and those having provocation tests were identified from records kept by the endocrine specialist nurses. The patients' notes and biochemistry results were reviewed.

Results: 60 children were started on GH during the 18-month period. 85% were prescribed for NICE approved indications (Turner's syndrome 13%, GH deficiency 52%, Chronic renal insufficiency 12%, Prader Willi syndrome 3%, small for gestational age 5%). The remainder included patients with dysmorphic syndromes, cystinosis and rheumatological conditions. Of 31 patients with a diagnosis of GHD, 12 had isolated GHD of whom 6 only had one provocation test. Of the other 19 patients, 6 had multiple pituitary hormone deficiencies, 2 had defined CNS pathology and 11 had received cranial irradiation.

Conclusion

85% of our prescribing is consistent with NICE guidelines. However, only 50% of patients with isolated GHD underwent 2 provocation tests. This audit has identified a need to increase the proportion of patients with isolated GHD having 2 provocation tests. In addition, we need to review our practice of GH prescribing in non-approved conditions.

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