



British Society of Paediatric Gastroenterology Hepatology and Nutrition

25th Anniversary

ANNUAL MEETING 2011

26th January - 28th January 2011, Balmoral Hotel, Edinburgh

Local Organisers: Dr David Wilson - Reader in Paediatric Gastroenterology & Dr Peter Gillett - Consultant Paediatric Gastroenterologist

Educational Grants: We wish to thank the following sponsors for their generous support



Caring for young lives
Children's Liver Disease Foundation

Thanks to our Principal Sponsors

On behalf of The Society, we thank you all for renewing your most generous support for our meetings which are an essential element in the partnership we establish in managing children with gastrointestinal, liver and nutritional disorders. It is through mutual respect, understanding and cooperation that we have witnessed such major changes in recent times in the way we deliver education, particularly to our trainees and colleagues within the breadth of our speciality and in the way we deliver quality care to our patients. Long may this relationship continue to flourish.



Thanks to our Silver Sponsor

The Society is extremely grateful that you are willing to participate in our meeting and to offer such generous support. It is through your willingness to share with us your initiatives and ideas that we continue to move forward as a speciality. Thank you.



Thanks to our Bronze Sponsors



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British Society of Paediatric Gastroenterology Hepatology and Nutrition

Welcome address from Local Organising Committee

On behalf of the home team from Edinburgh, we welcome you to the BSPGHAN 25th Anniversary meeting at the Balmoral hotel in the heart of Edinburgh, overlooking Waverley station, at the east end of Princes street.

Edinburgh, the capital city of Scotland, is one of the iconic cities of the world, with the Castle overlooking Princes Street, at the top of the Royal Mile and at the foot of the High Street, the Palace of Holyrood House, Arthur's Seat and the Scottish parliament building. Edinburgh's Old and New Towns are UNESCO world heritage sites- the architecture of Adams, Chambers and Playfair of the 1700s and 1800s were to influence the future look of many European cities.

It's a great social place - to shop, eat and enjoy the sights - Princes Street, George Street and the High street house many stores (eg Jenner's and Harvey Nichols) and great restaurants all within walking distance. For the culturally minded, Edinburgh boasts an array of art galleries - at the Mound (National gallery and Portrait gallery), the City art gallery and gallery of Modern Art (at Dean Bridge) as well as the National museum of Scotland, the Children's museum, the museum on the Mound (in the Bank of Scotland Building), with Britannia now berthed down in Leith at Ocean Terminal. There are 2 Scottish Premier League football teams and top rugby clubs for any potential spectators. Finally, there's theatre- the Usher Hall, the Lyceum, King's, Playhouse and Festival theatres. Edinburgh's International and Fringe Festival, the world's biggest arts festival (in August every year) hosts an eclectic mix of theatre, music, dance and comedy and brings millions of visitors to the city every year. The inglorious saga of the Edinburgh Tram has been the source for many an inspired comic in the last few years!

We hope that the three days you spend with us will be educational, inspirational and most of all enjoyable. The postgraduate day aims to inspire future academic pursuits in PGHAN, and the meeting has a rich blend of clinical and science talks, interspersed with oral and poster presentations from our own members. It's a time to celebrate the Society's history and achievements and to look forward to the next 25 years!

David Wilson & Peter Gillett, on behalf of the Edinburgh Team

<http://www.edinburgh-inspiringcapital.com/visit.aspx>
<http://www.edinburgh.org/>
<http://www.edinburghfestivals.co.uk/>



Front row - Lindsay Bremner (Senior Dietitian), Pam Rogers (IBD and Liver Nurse Specialist), Jenny Livingstone (Senior Dietitian)
 Middle row - Sally Lawrence (GI registrar), Peter Gillett (Consultant), David Wilson (Reader in PGHAN), David Devadason (Consultant)
 Back row - Kat Trueman (Nurse Specialist), David Mitchell (Consultant), Catherine Paxton (Nutrition Nurse Specialist)

Wednesday 26th January 2011

POSTGRADUATE DAY CONFERENCE
10.30 – 17.30

How to do academic work in PGHAN - from absolute beginners to learned professors

8.30 – 10.30

Registration in Walter Scott Foyer

Coffee and Exhibition in Holyrood and Waverley Suite

Session 1

How to get started

Chairs:

Dr Nikhil Thapar - Consultant Paediatric Gastroenterologist
Gastroenterology Unit, Institute of Child Health, London
and
Ms Pam Rogers - IBD and Liver Nurse Specialist
Royal Hospital for Sick Children, Edinburgh

10.30 – 10.35

Welcome and introduction

Dr Peter Gillett
Consultant Paediatric Gastroenterologist
Royal Hospital for Sick Children
9 Sciennes Road
Edinburgh, EH9 1LF

10.35 – 11.05

How to do research in a busy clinical service

Dr David Wilson
Reader in Paediatric Gastroenterology
Child Life and Health
University of Edinburgh
20 Sylvan Place
Edinburgh, EH9 1UW

11.05 – 11.20

Performing research as a nurse specialist

Ms Catherine Paxton
Nutrition Nurse Specialist
Royal Hospital for Sick Children
9 Sciennes Road
Edinburgh, EH9 1LF

WEDNESDAY 26.01.2011

11.20 – 11.35

A trainee's first faltering steps

Dr Paul Henderson
Clinical Research Fellow
Dept of Paediatric Gastroenterology and Nutrition
Royal Hospital for Sick Children
Dept of Child Life and Health
University of Edinburgh
20 Sylvan Place
Edinburgh EH9 1UW

11.35 – 12.00

Academic activities: An NHS consultant's contribution

Dr Mark Beattie
Consultant Paediatric Gastroenterologist
Southampton General Hospital
Tremona Road
Southampton, SO16 6YD

12.00 – 13.00
LUNCH

Session 2
How to keep going

Chairs:

Dr Alastair Baker - Consultant Paediatric Hepatologist
King's College Hospital, London
and
Dr Sally Lawrence - Specialist Registrar
Royal Hospital for Sick Children, Edinburgh

13.00 – 13.20

A dietitian's experience – from audit to PhD

Dr Laura Stewart RD RNutr PhD
Team Lead
Paediatric Overweight Service Tayside
8 Western Ave
Perth Royal Infirmary
Perth PH1 1NX

13.20 – 13.35

Doing a higher degree in PGHAN

Dr Richard Hansen
Clinical Lecturer in Child Health
Child Health
Royal Aberdeen Children's Hospital
Foresterhill
AB25 2ZG

13.35 – 13.50

Running an MSc programme

Dr Nick Croft
Consultant Paediatric Gastroenterologist
Barts and the London NHS Trust
Wingate Institute
26 Ashfield Street
London E1 1BB

13.50 – 14.05

Running a lab

Professor Billy Bourke
Consultant Paediatric Gastroenterologist
Children's Research Centre
Our Lady's Hospital
Crumlin
Dublin 12

14.05 – 14.20

Performing nationwide audit

Dr Richard Russell
Consultant Paediatric Gastroenterologist
Yorkhill Hospital
Dalnair Street
Glasgow, G3 8SJ

14.20 – 14.50

Paediatric surgical research opportunities

Professor Agostino Pierro
Nuffield Professor of Paediatric Surgery and Head of Department of Paediatric Surgery
Institute of Child Health
University College London Medical School.
30 Guilford Street
London, WC1N 1EH

Session 3

Trainee and Allied Health Professionals
Plenary Abstract Session 1

Chairs:

Ms Kate Blakeley - Consultant Clinical Psychologist
Gastroenterology Unit, Institute of Child Health, London
And
Dr Prithvi Rao - Consultant Paediatric Gastroenterologist
Sheffield Children's Hospital, Sheffield

14.50 – 15.00

Severe early-onset colitis due to a mutations in interleukin-10

I. Yeop¹, E. Glocker², B. Grimbacher², M. Elawad¹, K. Lindley¹, N. Thapar¹, N. Shah¹,
¹Paediatric Gastroenterology, Great Ormond Street Hospital, University College London,
²Immunology and Molecular Pathology, Royal Free Hospital & University College London

15.00 – 15.10

The Role of Microaerophilic Colonic Mucosal Bacteria in de-novo Paediatric Inflammatory Bowel Disease

Hansen R^{1,2}, Mukhopadhyay I¹, Russell RK³, Bisset WM⁴, Berry SH¹, Barclay AR³, Bishop J³, Flynn DM³, McGrogan P³, Loganathan S⁴, Mahdi G⁴, Thomson JM¹, Helms PJ², El-Omar EM¹, Hold GL¹

¹Gastrointestinal Research Laboratory, University of Aberdeen

²Child Health, School of Medicine, University of Aberdeen

³Department of Paediatric Gastroenterology, Royal Hospital for Sick Children, Glasgow

⁴Department of Paediatric Gastroenterology, Royal Aberdeen Children's Hospital, Aberdeen

15.10 – 15.20

What about the parents? Parental anxiety and depression is associated with lower quality of life of teenagers with IBD

¹F Scullion, ²J Cossar, ¹C Wesson, ²M Power, ^{3,4}DC Wilson

¹Paediatric Psychology and Liaison Service, Royal Hospital for Sick Children, Edinburgh, UK; Departments of

²Clinical Psychology and ³Child Life and Health, University of Edinburgh, UK; ⁴Paediatric Gastroenterology and Nutrition, Royal Hospital for Sick Children, Edinburgh, UK.

15.20 – 15.30

Osteoporosis in paediatric Crohn's disease:

Influence of immune cells on proliferation of the osteoblast like cell line Saos2

Dr G Penman, Clinical Fellow, Academic Unit of Child Health, Sheffield University; Dr D Campbell, Consultant Paediatric Gastroenterologist, Sheffield Children's Hospital; Professor A.G. Pockley, Department of Oncology, University of Sheffield.

15.30 – 15.40

A fat lot of good: An 8 year longitudinal study of the balance and trends in fat intakes in children with cystic fibrosis.

C. Smith¹, A. Winn², P. Seddon³, S. Ranganathan^{3,4}

¹Department of Nutrition and Dietetics, Royal Alexandra Children's Hospital; ²Department of Computing, Mathematics and Information Sciences, University of Brighton; ³Respiratory Medicine, Royal Alexandra Children's Hospital; ⁴Brighton and Sussex Medical School. Brighton

15.40 – 15.50

The value of faecal calprotectin in the investigation of suspected early-onset inflammatory bowel disease

Casey A¹, Henderson P^{1,2}, Rogers P¹, Gillett P¹, Wilson DC^{1,2}

¹Department of Paediatric Gastroenterology, Hepatology and Nutrition, Royal Hospital for Sick Children, Edinburgh. ²Child Life and Health, University of Edinburgh, Edinburgh.

15.50 – 16.15
AFTERNOON TEA

Session 4
Tricks of the trade

Chairs:

Dr Mark Dalzell - Consultant Paediatric Gastroenterologist,
Alder Hey Children's Hospital, Liverpool
and

Dr Aniela Tybulewicz - Consultant Paediatrician
St John's Hospital, Livingston West Lothian

16.15 – 16.35

Expert groups – how to start and succeed

Dr Dan Turner

Consultant Paediatric Gastroenterologist

Shaare Zedek Medical Center

Jerusalem

16.35 – 17.00

Qualitative research: techniques and tools

Dr Rachel Taylor

Research Associate

Dept of Children's Nursing

Isleworth

Middlesex TW7 6HW

17.00 – 17.30

Mentoring and promoting clinical research

Professor Anne Griffiths

Division Head

Dept of Paediatrics, University of Toronto

Hospital for Sick Children

Division of Gastroenterology, Hepatology and Nutrition

555 University Avenue

Toronto, M5G 1XB

17.30

Close

17.30 – 20.30

Professional and working group meetings

Associates'

Trainees

1900 meet for game 1930
FOOTBALL: Consultants versus Trainees (again)

21.00
MEET THE SPONSORS ICE BREAKER DINNER
Café Andaluz
77B George Street, Edinburgh

Thursday 27th January 2011

25TH ANNUAL MEETING OF THE
BRITISH SOCIETY OF PAEDIATRIC
GASTROENTEROLOGY, HEPATOLOGY
AND NUTRITION

08.00 – 09.45

Professional and Working group meetings

Hepatology
Nutrition
Research
Paediatricians with an Interest
Education

08.00 – 10.00
Registration

Session I - Hepatology

Chairs:

Dr David Devadason - Consultant Paediatric Gastroenterologist
Royal Hospital for Sick Children, Edinburgh
and
Dr Emer Fitzpatrick - Specialist Hepatology Registrar
King's College Hospital, London

10.00 – 10.05

Introduction

Dr David Wilson
Reader in Paediatric Gastroenterology
Child Life and Health
University of Edinburgh
20 Sylvan Place
Edinburgh, EH9 1UW

10.05 – 10.25

Paediatric hepatology – Looking back

Professor Deirdre Kelly
Consultant Paediatric Hepatologist
Liver Unit, Birmingham Children's Hospital
Steelhouse Lane
Birmingham, B4 6NH

10.25 – 10.45

Alpha-1 antitrypsin deficiency

Dr Dino Hadzic
Consultant Paediatric Hepatologist
Dept Child Health
King's College Hospital
Denmark Hill
London SE5 9RJ

10.45 – 11.05

Stem cell therapy and the liver

Professor Stuart Forbes
Professor of Transplantation and Regenerative Medicine
MRC Centre for Inflammation Research
University of Edinburgh
The Queen's Medical Research Institute
47 Little France Crescent
Edinburgh, EH16 4TJ

11.05 – 11.35

Is cirrhosis actually reversible?

Professor John Iredale
Professor of Medicine
MRC Centre for Inflammation Research
University of Edinburgh
The Queen's Medical Research Institute
48 Little France Crescent
Edinburgh, EH16 4TJ

11.35 – 12.00
COFFEE

Session II - Intestinal Failure

Chairs:

Dr Charlie Charlton - Consultant Paediatric Gastroenterologist
Queen's Medical Centre, Nottingham
And
Ms Jenny Livingstone - Senior GI Dietitian
Royal Hospital for Sick Children, Edinburgh

12.00 – 12.15

Medical and nutritional therapy – the evidence

Dr Andrew Barclay
Consultant Paediatric Gastroenterologist
Division of Child Health
University of Glasgow
Yorkhill Hospital
Dalnair Street
Glasgow, G3 8JS

12.15 – 12.45

Non-transplant surgery – the evidence

Professor Agostino Pierra
Nuffield Professor of Paediatric Surgery and Head of Department of Paediatric Surgery
Institute of Child Health
University College London Medical School.
30 Guilford Street
London, WC1N 1EH

12.45 – 13.00

The Scottish Home PN Managed Clinical Network

Dr Janet Baxter
Network Manager at Scottish Home HPN Managed Clinical Network
HPN and Complex Burn Injury
Kingscross Health and Community Care Centre
Cleppington Road
Dundee
DD3 8EA

13.00 – 14.00
LUNCH

Session III - Surgery and sedation

Chairs:

Dr Mark Beattie - Consultant Paediatric Gastroenterologist
Southampton General Hospital, Southampton
and
Dr Paraic McGrogan - Consultant Paediatric Gastroenterologist
Royal Hospital for Sick Children, Glasgow

14.00 – 14.30

Laparoscopic surgery update

Mr Gordon MacKinlay
Senior Lecturer in Paediatric Surgery
Royal Hospital for Sick Children
9 Sciennes Road
Edinburgh
EH9 1LF

14.30 – 14.50

Total intravenous anaesthesia

Dr Alistair Baxter
Consultant Anaesthetist
Royal Hospital for Sick Children
9 Sciennes Road
Edinburgh
EH9 1LF

Session IV – Abstract Session II

Chairs:

Dr Peter Sullivan - Consultant Paediatric Gastroenterologist
John Radcliffe Hospital, Oxford
and

Dr Annemarie Broderick - Consultant Paediatric Gastroenterologist
Our Lady's Hospital for Sick Children, Dublin

14.50 – 15.05

Oral Poster Session I

These will be judged and chosen on Thursday 27th January

14.50 – 14.55

14.55 – 15.00

15.00 – 15.05

15.05 – 15.35
AFTERNOON TEA

15.35 – 16.35 Plenary abstract session II:

15.35 – 15.45

Phenotypic variation and long term outcome of hepatobiliary and renal manifestations in children with congenital hepatic fibrosis

Rawat D¹, Kelly D A¹, Sharif K S¹, Lloyd C¹, Milford D², McKiernan P J¹

¹Department of Hepatology, ²Department of Nephrology, Birmingham Children's Hospital, Birmingham

15.45 – 15.55

Hepatic lumican expression and paediatric non-alcoholic fatty liver disease

Emer Fitzpatrick, Ragai Mitry, Alberto Quaglia and Anil Dhawan.

Paediatric Liver, GI and Nutrition Centre and Institute of Liver Studies, King's College Hospital, Denmark Hill, London

15.55 – 16.05

Treatment of chronic viral hepatitis C in children and adolescents: Experience of 3 UK national centres

Abdel-Hady M^a, Bansal S^b, Davison SM^c, Brown M^a, Tizzard SA^b, Mulla S^c, Davies P^d, Mieli-Vergani G^b, Kelly DA^a

^aLiver Unit, Birmingham Children's Hospital, Birmingham

^bPaediatric Liver Centre, King's College Hospital, London

^cLiver Unit, Leeds Teaching Hospitals, Leeds

^dInstitute of Child's Health, Birmingham Children's Hospital

16.05 – 16.15

Double-balloon Enteroscopy in Children – A Tertiary Care Experience

Urs A¹, Rao P¹, Arain Z², Thomson M¹

¹Centre for Paediatric Gastroenterology, Sheffield Children's NHS Trust, UK;

²Department of Paediatrics, Armed Forces Hospital, Riyadh, Saudi Arabia

16.15 – 16.25

Is Exclusive Enteral Nutrition (EEN) enough for Children with Crohn's Disease (CD)?

Gerasimidis K¹, McGrogan P², Buchanan E², Duncan A³, Talwar D³, O'Reilly DS³, Edwards CA¹

¹College of Medicine, Veterinary and Life Sciences, University of Glasgow, Glasgow

²Department of Paediatric Gastroenterology, Yorkhill Hospitals, Glasgow

³Trace Elements and Micronutrient Reference Laboratory, Glasgow Royal Infirmary, Glasgow

16.25 – 16.35

6 TGN levels- Is the target range different in children as compared to adults on Azathioprine for Inflammatory Bowel Disease (IBD)

Batra A, Protheroe S. Dept of Gastroenterology, Birmingham Children's Hospital

Session V – Endoscopy

Chairs:

Dr Mike Thomson - Consultant Paediatric Gastroenterologist
Sheffield Children's Hospital, Sheffield
and

Dr Mary-Anne Morris - Consultant Paediatrician
Norfolk and Norwich Hospitals, Norfolk

16.35 – 16.50

Endoscopy – training update

Dr Paraic McGrogan

Consultant Paediatric Gastroenterologist

Royal Hospital for Sick Children

Dalnair Street

Glasgow, G3 8JS

16.50 – 17.20

Procedural GI endoscopy – Looking forward

Dr Ian Penman

Consultant Gastroenterologist

Centre for Liver & Digestive Disorders

Royal Infirmary

48 Little France Crescent

Edinburgh, EH16 4TJ

17.20 Close

17.30 – 19.00 BSPGHAN Annual General Meeting

20.00

Gala Dinner - Dancing to Ceilidh with 'Heeliegoleerie' and June Underwood (caller), and dancing and listening with 'The Sunshine Delay'

Friday 28th January 2011

“MORE OF THE SAME”

Session VI - Nutrition

Chairs:

Dr David Mitchell - Consultant Paediatric Gastroenterologist
Royal Hospital for Sick Children, Edinburgh
and
Ms Kathleen Ross - Chief Paediatric Dietitian
Royal Aberdeen Children's Hospital, Aberdeen

08.30 – 08.50

Clinical Nutrition – Looking back

Professor Ian Booth
Consultant Paediatric Gastroenterologist
Dean's Office
College of Medical & Dental Sciences
University of Birmingham
Edgbaston
Birmingham B15 2TT

08.50 – 09.10

Home enteral tube feeding – emerging trends

Ms Catherine Paxton
Nutrition Nurse Specialist
Royal Hospital for Sick Children
9 Sciennes Road
Edinburgh, EH9 1LF

09.10 – 09.30

Stopping HETF

Professor Charlotte Wright
Professor of Community Child Health
Paediatric Epidemiology and Community Health (PEACH) Unit
8th Floor Tower Block
The Queen Mother's Hospital
Yorkhill, Glasgow, G3 8SJ

09.30 – 10.00

New trends and issues in paediatric obesity

Professor John Reilly
Professor of Paediatric Energy Metabolism
1st Floor Tower Block
The Queen Mother's Hospital
Yorkhill
Glasgow, G3 8SJ

10.00 – 10.30
COFFEE

Session VII – Gastroenterology

Chairs:

Dr Mike Bisset - Consultant Paediatric Gastroenterologist
Royal Aberdeen Children's Hospital, Aberdeen

And

Dr Michael Mahony - Consultant Paediatrician
Children's Ark, Limerick Regional Hospital, Limerick

10.30 – 11.00

Coeliac disease – old disease, new issues

Professor David van Heel
Professor of Gastrointestinal Genetics
Centre for Digestive Diseases
Blizard Institute of Cell and Molecular Science
Barts and The London School of Medicine and Dentistry,
The Blizard Building, 4 Newark Street
Whitechapel
London E1 2AT

11.00 – 11.30

Lessons from *H. pylori* for other GI conditions

Professor Emad El-Omar
Professor of Gastroenterology and Honorary Consultant Physician
Division of Applied Medicine
School of Medicine & Dentistry
University of Aberdeen
Institute of Medical Sciences, Foresterhill
Aberdeen AB25 2ZD

Session VIII – Plenary Abstract Session 3

Chairs:

Dr Diana Flynn - Consultant Paediatric Gastroenterologist
Royal Hospital for Sick Children, Glasgow

and

Dr Rafeeq Muhammed - Consultant Paediatric Gastroenterologist
Birmingham Children's Hospital, Birmingham

11.30 – 11.40

Variations in the gene encoding C-reactive protein suggest that CRP is a candidate susceptibility gene for inflammatory bowel disease in the Scottish paediatric population.

Henderson P^{1,2}, van Limbergen J³, Anderson NH⁴, Cameron F⁵, Cameron E², Nimmo E², Russell RK⁵, Satsangi J², Wilson DC¹

¹Department Child Life and Health, University of Edinburgh, Edinburgh

²Gastrointestinal Unit, University of Edinburgh, Edinburgh

³Department of Paediatric Gastroenterology, Hepatology and Nutrition, University of Toronto, Toronto, Ontario, Canada

⁴Centre for Population Health Sciences, University of Edinburgh, Edinburgh
Department of Gastroenterology, Royal Hospital for Sick Children, Glasgow

11.40 – 11.50

Biological therapy for paediatric IBD – effective but associated with financial and safety issues

Cameron, FL¹; Wilson, ML²; Basheer, N²; Jamieson, A³; Bisset, WM⁴; Russell, RK¹; Wilson, DC^{2,5}.

¹Paediatric Gastroenterology, Royal Hospital for Sick Children, Glasgow; ²Child Life and Health, University of Edinburgh, Edinburgh; ³University of Glasgow, Glasgow; ⁴Paediatric Gastroenterology, Royal Aberdeen Children's Hospital; ⁵Paediatric Gastroenterology and Nutrition, Royal Hospital for Sick Children, Edinburgh

11.50 – 12.00

Colonic Mucosal Bacterial Diversity of de-novo Extensive Paediatric Ulcerative Colitis by Next-Generation Sequencing

Hansen R^{1,2}, Reiff C³, Russell RK⁴, Bisset WM⁵, Berry SH¹, Mukhopadhyay I¹, Barclay AR⁴, Bishop J⁴, Flynn DM⁴, McGrogan P⁴, Loganathan S⁵, Mahdi G⁵, Thomson JM¹, Helms PJ², El-Omar EM¹, Hold GL¹

¹Gastrointestinal Research Laboratory, University of Aberdeen

²Child Health, School of Medicine, University of Aberdeen

³Medical Genetics, School of Medicine, University of Aberdeen

⁴Department of Paediatric Gastroenterology, Royal Hospital for Sick Children, Glasgow

⁵Department of Paediatric Gastroenterology, Royal Aberdeen Children's Hospital, Aberdeen

12.00 – 12.10

Duodenal bulb biopsies should be routinely obtained in suspected Coeliac Disease

Srinivasan R, Auth M, El-Matary W, Dalzell AM, Shukla R*

From the department of Gastroenterology and Histopathology*

Alder Hey NHS Foundation trust, Liverpool, UK.

12.10 – 12.20

Iron studies in children with coeliac disease compliant with gluten free diet

Hunt V¹, Whittle E², Auth M, El-Matary W, Dalzell AM, Newland P³, Srinivasan R.

From the Medical School, Liverpool¹, Departments of Gastroenterology, Dietetics², Biochemistry³, Alder Hey Children's NHS Foundation Trust, Liverpool

12.20 – 12.30

Randomised Controlled Trial Comparing Liquid Diet Therapy (LDT) with Corticosteroid Therapy (CST) for Episodes of Active Disease Over a 12 Month Period: Report of Clinical Outcomes

¹Murphy MS, ²Dalzell AM ³Mitton S, ⁴Spray C, ⁵Taylor C, ⁶Rodriguez A.

On behalf of participating centres: ¹Birmingham, ²Alder Hey (Liverpool), ³St George's (London),

⁴Royal Bristol, ⁵Sheffield, ⁶John Radcliffe (Oxford) Children's Hospitals NHS Foundation Trusts

12.30 – 13.20
LUNCH

13.20 – 13.35

GORD: the surgical approach

Mr Fraser Munro

Consultant Paediatric Surgeon

Royal Hospital for Sick Children

Sciennes Road

Edinburgh EH9 1LF

Session IX – Oral poster presentations 2

Chairs:

Dr Jon Bishop - Consultant Paediatric Gastroenterologist
Royal Hospital for Sick Children, Glasgow
and

Dr Assad Butt - Consultant Paediatric Gastroenterologist
Royal Alexandra Hospital, Brighton

13.35 – 13.50

These will be decided on Friday 28th January 2011

13.35 – 13.40

13.40 – 13.45

13.45 – 13.50

Session X – Inflammatory Bowel Disease

Chairs:

Dr David Wilson - Reader in Paediatric Gastroenterology
Royal Hospital for Sick Children, Edinburgh
and

Dr Iuean Davies - Consultant Paediatric Gastroenterologist
University Hospital of North Wales, Cardiff

13.50 – 14.00

National IBD audit 2010 – initial paediatric results

Dr Richard Russell
Consultant Paediatric Gastroenterologist
Yorkhill Hospital
Dalnair Street
Glasgow, G3 8SJ

14.00 – 14.30

IBD genetics and beyond

Professor Jack Satsangi
Professor of Gastroenterology
Molecular Medicine Centre
University of Edinburgh
Western General Hospital
Crewe Road
Edinburgh EH4 2XU

14.30 – 14.50

Autophagy: a key pathogenetic mechanism

Dr Craig Stevens
Scientist, GI Unit,
Molecular Medicine Centre
University of Edinburgh
Western General Hospital
Crewe Road, Edinburgh EH4 2XU

14.50 – 15.20

Paediatric ulcerative colitis comes of age

Dr Dan Turner
Consultant Paediatric Gastroenterologist
Shaare Zedek Medical Center
Jerusalem

15.20 – 15.55

Paediatric IBD – Looking forward

Professor Anne Griffiths
Division Head
Dept of Paediatrics, University of Toronto
Hospital for Sick Children
Division of Gastroenterology, Hepatology and Nutrition
555 University Avenue
Toronto, M5G 1XB

15.55 – 16.00

Prize presentation and closing remarks

Dr Mark Beattie
BSPGHAN President
Consultant Paediatric Gastroenterologist
Southampton General Hospital
Tremona Road
Southampton, SO16 6YD

16.00

Close

26th Annual Meeting

25th – 27th January 2012
Nottingham

Host: Dr Charlie Charlton

27th Annual Meeting

January 2013
Manchester
Host: Dr Adrian Thomas

ABSTRACTS FOR WEDNESDAY 26TH JANUARY 2011

Invited Speakers' and Selected Oral Plenary Session Abstracts

How to do research in a busy clinical service

Dr David C Wilson, Reader in Paediatric Gastroenterology and Nutrition, University of Edinburgh and Department of Paediatric Gastroenterology and Nutrition, Royal Hospital for Sick Children, Edinburgh

It can be daunting for anyone appointed to a permanent position to envisage how they will fit clinical research into a busy job, particularly if there is no well established academic infrastructure present. In this talk I will provide some ideas and tips of how to start performing clinical research, based on personal experience of arriving as a consultant in a new city in a new country to build up a PGHAN service in a region where there was none present before, and where there was no clinical infrastructure (eg no dedicated PGHAN trainees nor specialist nurses) in place.

Firstly, take stock of your own clinical and research interests, what is possible within the constraints of your desired work-life balance, what research strengths and potential collaborations are available, and what under-exploited 'resources' (clinical work load, enthusiastic others) are present. Unremitting clinical work rarely provides satisfaction over a whole career, and people doing so are much more likely to retire early – that is why your colleagues traditionally embrace other professional interests as well, be they research, education, management, committees and professional bodies, or private practice. However, don't take stock for ever – and remember that clinical research is fun, intrinsically satisfying, influences and empowers people, and allows you to give important clinical messages for many more patients than you could possibly see, even if doing a lifetime of non-stop clinics every week!

And what tips can I provide?

- Use a highly prevalent condition – gives you the numbers to complete single centre studies (logistically easier)
- Clinical audit does not need ethics approval – it is part of a high quality service
- Take advantage of nursing and other AHP staff interests and enthusiasm
- Take advantage of colleagues' established research interests
- Medical student study projects – students are always on tap, free, and the results can be very satisfying for all!
- Medical trainees will do projects – you must spend the time to ensure presentations and publications ensue
- Don't neglect that case report! And can you change the case report to a case series?
- The case series – a publication, but also part of pilot or feasibility work for a bigger clinical study
- Record carefully all your cases locally or regionally – a cohort study has higher impact than a case series
- Consider use of a low prevalence condition – if of interest (high tech, expensive or under-researched)
- Don't shy from publishing from a regional service just because most literature is from quaternary services – it's relevant information
- Don't be shy of 'hanging your dirty washing out' – it's important real world data!
- No time or opportunity to do research at work? – do secondary (data synthesis) not primary clinical research
- What clinical questions interest you? - formulate them as 'PICO'
- Use a librarian to teach you to search the literature

Performing Research as a nurse specialist**C E Paxton, Nutrition Nurse Specialist, Royal Hospital for Sick Children Edinburgh**

Research methods and more importantly the practicalities of how to actually do research and integrate it into practice have not traditionally been taught to nursing students. This makes it difficult for anyone to then become involved in research if they are pursuing a clinical career instead of an academic career pathway. As a relative novice, with an interest and enthusiasm for research, I share with you what can be achieved within the confines of a busy clinical job.

From a simple audit to a cohort study to a randomised controlled trial and onto a Joanna Briggs systematic review.

A trainee's first faltering steps**Dr Paul Henderson, Clinical Research Fellow and Paediatric Registrar, Edinburgh**

In the current climate of run-through training and competency based assessments it is becoming increasingly difficult to make any meaningful headway in the field of academics. In addition, the European Working Time Directive has put further limits on the time available for extra-curricular activities such as audit and research. These academic pursuits can not only lead to a more colourful CV but also provide the opportunity to develop new skills such as statistical analysis and study design, as well as the ability to present work both orally and in written form. This short talk will provide some ideas of how to get started in the world of academia, with tips on case reports, the sign of a worthwhile audit, getting yourself to an international conference and that all important publication

Academic Activities: An NHS consultant's contribution**Dr Mark Beattie, Consultant Paediatric Gastroenterologist
Southampton General Hospital, Southampton**

The consultant role is a combination of service delivery and activities to support that. The service delivery component is increasingly consultant delivered rather than consultant led although strong leadership remains crucial. There are many facets to this including continuing professional development, service development, education and training and research. The 'academic' component crosses all these domains. Academic activities are therefore an essential part of the consultant role. These can be achieved by engagement of the individual and motivation to impact on patient care in the wider sense supported by opportunity, appraisal and mentoring. This is facilitated through local, regional and national networking. Frontline clinicians can therefore impact on the wider NHS and patient care by recognition of the Academic component within their job plan and thereby enhance the quality of their role and the service they provide.

A dietitian's experience – from audit to PhD**Dr Laura Stewart, Team Lead, Paediatric Overweight Service Tayside
Perth Royal Infirmary, Perth**

Laura Stewart first started working as a basic grade dietitian in the early 1980s and as a mature student undertook a part time PhD from the Medical Faculty, University of Glasgow graduating in 2008. For Laura the journey from a clinical dietitian to a dietitian with a PhD is one filled with a lot of determination and just a little bit of hard work. While on the working group of the SIGN 2003 guidelines on childhood obesity Laura undertook an audit on the outcomes of obesity treatment at the Royal Hospital for Sick Children, Edinburgh. Both of these pieces of work lead her to undertake research on the dietetic treatment of childhood obesity and to register as a PhD student in 2003. During this presentation Laura will discuss the importance to her of support and mentoring as well as the invaluable need for team work in both audit and research. Learning new skills, in particular statistics and computing programmes only became standard with practice and frequent use. Laura will discuss how research has offered her opportunities to travel and collaborate as well as help with her career choices. Please note that no ages will be disclosed

Doing a higher degree in PGHAN

**Dr Richard Hansen, Clinical Lecturer in Child Health
Royal Aberdeen Children's Hospital, Aberdeen**

With increasingly streamlined training, what are the advantages and disadvantages of stepping "off the conveyor belt" to undertake a higher degree? The obvious advantages are: the opening up of academic career options, strengthening appointability for NHS teaching hospital positions if no longer wishing to be a clinical academic in a University position, the ability to gain true expertise in an area, discovering science and the scientific lifestyle, a breadth of experience that can be added to one's CV and of course, the opportunity to publish original peer-reviewed papers. Disadvantages might include: a longer training period compared to peers (and watching them all take Consultant posts!), stepping away from clinical duties, financial constraints and perhaps the amount of commitment and work involved. This frank and honest talk by a PGHAN trainee in the last year of his PhD will build on talks earlier in the day to provide the facts that trainees will need when assessing their options in pursuing a higher degree (MD or PhD).

Running an MSc programme

**Dr Nick Croft, Consultant Paediatric Gastroenterologist
Barts and the London NHS Trust, London**

The MSc in Gastroenterology at Barts and the London School of Medicine has been established now for 17 years and has successfully recruited students throughout that time. Suitable for both adult and paediatric gastroenterologists it has this year established a distance learning course (Postgraduate Diploma in Gastroenterology) making this more accessible to trainees in the UK and Europe. This talk will give some experiences and insights into the reasons for, the setting up and running of a successful MSc programme and most importantly how to keep the University hierarchy happy

"A clinician in the lab?...How precious!"

**Professor Billy Bourke, Consultant Paediatric Gastroenterologist
Our Lady's Hospital, Dublin**

There is little doubt that the undertaking of research, and especially laboratory-based research, acts a proxy for creative endeavor. Immersion, enthusiasm, dedication and the foregoing of the basic indulgences of our vocation (patient esteem, Mammon and golf) form the backdrop to what can become the most fulfilling aspect of a career. There are some simple rules of thumb to help make it happen but remember; don't expect recognition from fellow clinicians or respect from scientific colleagues and if you haven't done your Noble work before you're married - modify your goals!

Performing nationwide Audit

**Dr Richard Russell, Consultant Paediatric Gastroenterologist
Yorkhill Hospital, Glasgow**

Local audits of clinical care are useful for reviewing practices within a hospital, region or local network and have been shown to change clinical practice.(1) However, for conditions which are uncommon locally, to get a wider clinical perspective or in order to detect rarer outcomes national audits are beneficial. National audits performed recently that have helped to illustrate this point are eg the BSPGHAN adalimumab audit where a total of 19 UK paediatric centres contributed data on 72 cases looking at adalimumab use and complications in children across the UK. (2)

Organising national audit is best done when supported by appropriate funding and manpower. A successful audit (national or otherwise) needs an individual or steering group to drive forward the audit to ensure timely data collection and audit completion. The UK IBD audit is a great example of a well organised professional audit. The last IBD audit in 2008 collected data from around 90% of tertiary paediatric centres in the UK and collected data on more than 500 paediatric IBD patients.(3) The initial organisational data from the 2010 audit will be presented on 28/1/11.

Participation within a national audit can be a both rewarding but also on occasions timely experience. The good news is currently there is an opportunity for most BSPGHAN members to take part in, or even organise their own national audit.

Intended Learning Outcomes for the session are:

1. The advantages of national vs. local audit
2. Organising a national audit
3. A practical approach to your next involvement in national audit

- (1) Garrick V, Atwal P, Barclay AR et al. Successful implementation of a nurse-led teaching programme to independently administer Methotrexate in the community setting to children with Crohn's disease. *Alimentary Pharmacology and Therapeutics* 2009;29(1):90-6.
- (2) Russell RK, & BSPGHAN Adalimumab study group. (manuscript submitted)
- (3) UK Inflammatory Bowel Disease Audit Steering Group. UK IBD Audit 2008 (Executive Summary). 2009. Royal College of Physicians of London.

Paediatric surgical research opportunities

**Professor Agostino Pierro, Nuffield Professor of Paediatric Surgery and Head of Dept of Paediatric Surgery
University College, London Medical School, London**

Severe early-onset colitis due to a mutations in Interleukin-10

I. Yeop¹, E. Glocker², B. Grimbacher², M. Elawad¹, K. Lindley¹, N. Thapar¹, N. Shah¹,
¹Paediatric Gastroenterology, Great Ormond Street Hospital, University College London,
²Immunology and Molecular Pathology, Royal Free Hospital & University College London

Background:

IL-10 is secreted by many cells. It limits the secretion of pro-inflammatory cytokines such as TNF- α . Loss of IL-10 function cannot be compensated and results in an imbalance of the immune system, leading to excessive inflammation and an IBD-like phenotype. These children present from as early as the neonatal period with intractable and untreatable mucosal inflammation and severe perianal fistulae with haemorrhage.

Aim:

To identify mutations in the IL-10 pathway in all cases of infant early-onset colitis and to understand the natural progression of this condition in children treated and untreated with Bone Marrow Transplantation (BMT).

Methods:

Gene Search: All children under 1 year of age with IBD were screened for mutations in the IL-10 receptor chains, alpha and beta (IL10RA and IL10RB). If none were found, the coding regions of the IL-10 gene was sequenced. If none were found, linkage analysis was performed with direct mutation screening of potential candidate genes.

Functional analysis: The impact of detected mutations on function was assessed by using Polymorphism Phenotyping (Polyphen; <http://genetics.bwh.harvard.edu/pph/>) and the affect on the protein tertiary structure was assessed by using Swiss PDB viewer (<http://spdbv.vital-it.ch/>).

Results:

Out of 20 children screened with early IBD, we identified 6 patients (3 boys, currently aged 1-22 years, median 6 years) with IL-10 pathway defects.

IL-10 mutation: 2 children from Northern Pakistan with as yet unknown homozygous non-synonymous single nucleotide polymorphism at codon 113, resulting in an amino acid exchange from glycine to arginine. Both have undergone BMT and are well.

IL-10 receptor mutation: 2 children, 1 Arab and 1 Indian, with IL-10RB mutation. Both have NOT been transplanted. One, aged 14 years, has had a colectomy and has associated deafness. The other, aged 22 years, previously had a large pelvic EBV-driven lymphoma and several intestinal symptoms including fistulae despite colectomy.

IL-10 ligand: 2 Romany brothers, with origins of distant consanguinity, had linkage analysis and direct sequencing. Unique mutations were identified in IL-10 ligand, causing a stop codon and leading to early protein truncation. Both had BMT and are well 6 and 9 years post-BMT. The elder brother had developed EBV-driven Non-Hodgkins lymphoma prior to BMT.

Conclusion: IL-10 receptor and ligand mutations are present in 30% of children with early-onset IBD. Untreated children develop EBV-driven Non-Hodgkins Lymphoma. In those treated, BMT is curative.

The Role of Microaerophilic Colonic Mucosal Bacteria in de-novo Paediatric Inflammatory Bowel Disease

Hansen R^{1,2}, Mukhopadhyay I¹, Russell RK³, Bisset WM⁴, Berry SH¹, Barclay AR³, Bishop J³, Flynn DM³, McGrogan P³, Loganathan S⁴, Mahdi G⁴, Thomson JM¹, Helms PJ², El-Omar EM¹, Hold GL¹

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2. Child Health, School of Medicine, University of Aberdeen
3. Department of Paediatric Gastroenterology, Royal Hospital for Sick Children, Glasgow
4. Department of Paediatric Gastroenterology, Royal Aberdeen Children's Hospital, Aberdeen

Introduction/Background:

There is animal evidence that *Helicobacter* species can initiate a colitis similar to human ulcerative colitis (UC) and recent work has linked *Campylobacter concisus* to paediatric Crohn's disease (CD). Microaerophilic organisms such as *Helicobacter* and *Campylobacter* may therefore potentially be involved in the initiation of paediatric IBD.

Aim:

To establish the prevalence of *Helicobacter* and *Campylobacter* organisms in treatment naïve, de-novo paediatric IBD compared to controls.

Subjects and Methods:

Paediatric patients undergoing colonoscopy were recruited to two groups: those with a new diagnosis of IBD at their first presentation and controls with a macroscopically normal colon and no evidence of IBD on biopsy. All subjects were free from systemic antibiotics, steroids and immunosuppression for at least 3 months prior to colonoscopy. 24 IBD patients and 26 heterogeneous controls were analysed. The IBD cohort comprised 12 (50%) CD patients, 8 (33.3%) UC patients and 4 (16.7%) inflammatory bowel disease unspecified (IBD-U) patients. 15 (62.5%) were male with a median age of 12.4 years. The control group had a median age of 11.0 years, 20 (77.8%) were male.

5-6 colonic mucosal biopsies were taken: samples in controls were predominantly taken from the sigmoid/rectum and IBD patient biopsies from the most distal inflamed site. 3 biopsies were stored at -80°C before DNA extraction and subsequent PCR studies. 1-2 biopsies were used for bacterial culture. 5 selective media plates were used alongside blood agar. All cultures were incubated in microaerophilic conditions (Anoxomat) at 37°C. Culture plates were reviewed twice weekly for up to one month. Isolates deemed Gram-negative and microaerophilic were subjected to DNA extraction and PCR of the 16S rRNA gene for phylogenetic identification.

Results:

No *Helicobacter* organisms were cultured. 3 *Campylobacter* species were cultured: *C. concisus* from a subject with Crohn's disease, *Campylobacter curvus* and *Campylobacter showae* from controls. *Sutterella wadsworthensis* was isolated from 13 subjects: 8 controls and 5 IBD (1 Crohn's, 3 UC and 1 IBD-U). All biopsies were positive for bacterial DNA with universal eubacterial primers. Nested PCR analysis for *Helicobacter* genus was positive in 5 (10%) subjects, comprising 3 (12.5%) IBD and 2 (7.7%) controls. PCR analysis for *Campylobacter* genus was positive in 38 (76%) subjects, comprising 19 (79.2%) IBD and 19 (73.1%) controls. Nested PCR for *C. concisus* was positive in 25 (50%) subjects, comprising 14 (58.3%) IBD (8/12 CD, 3/8 UC and 3/4 IBD-U) and 11 (42.3%) controls. In response to frequent isolation of the organism, PCR analysis for *S. wadsworthensis* was positive in 48 (96%) subjects, comprising 23 (95.8%) IBD and 25 (96.2%) controls.

Summary and Conclusion:

Campylobacter spp. and *Sutterella wadsworthensis* are commonly identified in the paediatric colon. In keeping with previous observations, *C. concisus* appears more prevalent in CD although this was not significant. *Helicobacter* spp. appear relatively uncommon. PCR and culture methodology have revealed no significant distinction between the microaerophilic microbiota of paediatric IBD when compared with controls. It is unlikely that these organisms have a role in the initiation of paediatric IBD.

What about the parents? Parental anxiety and depression is associated with lower quality of life of teenagers with IBD

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Background and aims:

There have been few studies which have examined the predictive influence of factors such as psychological functioning, parental psychological functioning, gender and overprotection on health-related quality of life outcomes in adolescents with IBD. We aimed to ascertain factors associated with variance in health related quality of life (HRQoL) outcomes in teenagers with IBD.

Methods:

Teenagers (aged 13-17 years) with a diagnosis of IBD and their parents attending the SE Scotland regional PIBD clinic in RHSC, Edinburgh between September 2008 and May 2009 were invited to take part in a pilot project implementing a cross-sectional design on psychological functioning and HRQoL in adolescents with IBD. Teenagers were asked to fill in questionnaires on HRQoL (PedsQL), depression (Beck Depression Inventory - BDI) and anxiety (Spence Children's Anxiety Scale -SCAS), self-esteem (Rosenberg Self Esteem Scale - RSES), and parental over-protection (Parental Bonding Instrument - PBI), plus complete a visual analogue scale (0-100 mm) of wellness in the previous week. Parents filled in questionnaires on their teenagers HRQoL (PedsQL), and parental depression (BDI) and anxiety (Beck Anxiety Inventory - BAI).

Correlational design was used to investigate the relationship between psycho-social functioning (i.e. anxiety, depression and self esteem) and parental overprotection on HRQoL in adolescents with IBD. Correlational design was also implemented to assess level of agreement between proxy and self report on HRQoL. Regression analysis was used to investigate whether psycho-social factors predicted HRQoL outcomes. Ethical approval was obtained

Results:

57 teenagers (36 male) of mean (SD) age 14.7 (1.2) years (43 CD, 11 UC, 3 IBDU) and their parents took part in the research from 67 prospectively approached; 6 declined and 4 did not return their questionnaires. The mean (SD) 'wellness' score for all participants was 72.9 (27.1). Means (SD) for scaled scores across all domains of the PedsQL were 78 (17) and 71 (18) for teenagers and parents respectively. Key results shown were: (i) Higher anxiety & depression in teenagers with IBD related to lower QoL (ii) Low self-esteem associated with lower QoL (iii) Higher parental anxiety & depression associated with lower QoL (iv) Teenage girls reported poorer QoL than boys (v) Parent and teenager responses on QoL were found to be closely related.

Summary and Conclusions:

Psychological factors (particularly depression), parental anxiety and depression and gender predicted HRQoL outcomes for a sample of Scottish adolescents with IBD. This study highlights that psychological functioning in adolescents with IBD and their parents has an influence on HRQoL outcomes.

Osteoporosis in paediatric Crohn's disease: Influence of immune cells on proliferation of the osteoblast like cell line Saos2

Dr G Penman, Clinical Fellow, Academic Unit of Child Health, Sheffield University; Dr D Campbell, Consultant Paediatric Gastroenterologist, Sheffield Children's Hospital; Professor A.G. Pockley, Department of Oncology, University of Sheffield.

Background:

Crohn's disease is associated with reductions in bone mineral density and an increased risk of fracture. Measurement of bone turnover markers suggest that in children this is due to reduced bone formation. This study determined the potential impact of inflammatory events on osteoblast function in paediatric Crohn's disease by investigating the influence of resting and activated leukocytes and their secreted products on the growth of osteoblast-like Saos2 cells in vitro.

Methods:

Osteoblast-like Saos2 cells were cultured with resting or polyclonally activated populations of peripheral blood mononuclear cells (PBMCs) or isolated CD4+ T cells for 4 days. Cells were activated using anti-CD3/anti-CD28 monoclonal antibody-coated beads. The use of transwell inserts, which physically separate the different cell populations, determined the comparative influence of cell-cell contact and secreted factors on the observed effects.

Results:

The culture of Saos2 cells with resting PBMCs and CD4+ T cells increased their proliferation, whereas activated cells inhibited the proliferation of Saos2 cells. These effects were still present with the use of transwell inserts. Although differences were not of statistical significance, there was a clear dose-response effect. Supernatants from activated CD4+ T cells (50% v/v) significantly reduced the number of Saos2 cells at day 5 (492349 vs 224325; $p=0.01$). The effect of the PBMC supernatant at day 5 was only marginally greater than that of the CD4+ T cells (263824 vs 224325; not significant). All data are derived from three independent experiments.

Conclusions:

These results are consistent with a hypothesis that activated immune cells and/or their products are at least partially responsible for the reduced osteoblast activity that is seen in paediatric Crohn's disease. Furthermore, CD4+ T cells are mediators of inflammation in inflammatory bowel disease and these experiments demonstrate that these cells are primarily responsible for the effects seen. Ongoing studies are investigating the influence of resting and activated CD4+ T cells on alkaline phosphatase activity of the Saos2 and their ability to form mineralized nodules. Translational studies are evaluating relationships between immune cell populations isolated from gut and blood, markers of bone turnover and bone mineral density in paediatric patients with Crohn's disease.

This research was funded by the Children's Hospital Charity, Sheffield.

A fat lot of good: An 8 year longitudinal study of the balance and trends in fat intakes in children with cystic fibrosis.

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¹Department of Nutrition and Dietetics, Royal Alexandra Children's Hospital; ²Department of Computing, Mathematics and Information Sciences, University of Brighton; ³Respiratory Medicine, Royal Alexandra Children's Hospital; ⁴Brighton and Sussex Medical School. Brighton.

Background:

Dietetic management is seen as an integral part of cystic fibrosis (CF) both from a medical and patient perspective with good nutrition associated with better lung function and survival. Emphasis on nutrition, especially during infancy, has heightened recently. Nutritional treatment includes recommending 35-40% of total calories obtained from fat(1). However, this approach, although well established, causes concern to families of children with CF in relation to the potential for longer term health issues. This was highlighted in a national CF Trust survey published earlier this year(2).

Aim:

To describe changes in macronutrient intake and balance of fat sources in children with CF.

Method:

We conducted a prospective longitudinal study from 2002 to 2009 at a single paediatric CF clinic. Inclusion criteria were: 1) positive sweat test and/or identification of two CF genetic mutations; 2) over 1 year of age 3) seen annually for dietary review at the Royal Alexandra Children Hospital. Three-day estimated food diaries (as recommended for quantitative assessment of energy or nutrient intake) (1) were completed annually over an eight-year period. Nutrient composition was analysed (Compeat, Nutrition Systems, UK). Influence of year on % energy by type (fat, carbohydrate, protein) and by fat component [saturated (SFA); monounsaturated (MUFA) and polyunsaturated (PUFA)] was examined.

Results:

A total of 134 of 202 (66 %) food diaries were completed over an 8 year period from 28 patients (10 male) aged between 1 and 18 years (median 7 years) Three patients were pancreatic sufficient. % energy from fat decreased and that from protein increased but these trends were not significant (protein $p=0.06$, Fat $p=0.07$). % energy derived from SFA, MUFA and PUFA also remained statistically unchanged (SFA $p=0.10$, MUFA $p=0.20$, PUFA $p=0.15$). SFA consistently contributed >120% of reference nutrient intake (mean 153%) and PUFA < 100%.

Summary:

In the context of increasing survival in CF there is a need to consider the consequences of interventions introduced earlier in life. The longer term effects of high levels of fats were previously thought not to be associated with detrimental effects such as raised lipid profiles in children or adults with pancreatic insufficiency. However, more recent work has suggested that isolated hypertriglyceridemia is common in CF. While it remains uncertain if this is associated with increased risk of cardiovascular disease, complications such as premature ageing of large vessels have recently been reported in CF. Increased ratios of saturated fats to polyunsaturated fats could contribute to cardiovascular risk.

Conclusion:

Macronutrient intakes are not changing significantly in our population of children with CF but there is a clear imbalance of fat-sources with over-dependency on saturated fats.

References:

- 1) Borowitz D, Baker RD, Stallings V. Consensus report on nutrition for pediatric patients with cystic fibrosis. *J Pediatr Gastroenterol Nutr* 2002; 35:246-259
- 2) Food for Thought. Parents' and Carers Views on dietetics care in Cystic Fibrosis. January 2010. CF Trust UK.

The value of faecal calprotectin in the investigation of suspected early-onset inflammatory bowel diseaseCasey A¹, Henderson P^{1,2}, Rogers P¹, Gillett P¹, Wilson DC^{1,2}¹Department of Paediatric Gastroenterology, Hepatology and Nutrition, Royal Hospital for Sick Children, Edinburgh. ²Child Life and Health, University of Edinburgh, Edinburgh.**Background:**

The measurement of faecal calprotectin (FC) in patients with suspected bowel inflammation has become more routine in recent years. Although FC levels have been shown to correspond with radio-nucleotide labelled neutrophil scans and endoscopic appearances in inflammatory bowel disease (IBD), it is still unclear as to the value of FC to inform IBD diagnosis especially with regard to endoscopic investigation.

Methods:

Patients who were referred to the Department of Paediatric Gastroenterology in Edinburgh between 1.1.05 and 31.5.09 aged 1-17yrs with a FC performed during initial workup were identified. FC and other clinical parameters were recorded using the local laboratory results system and additional information compiled from case note review. Only FC values taken at referral/initial investigation (not repeat samples) in those without any previous gastroenterological diagnosis were included. Patients who provided insufficient samples (<2g) and those less than 1 year of age were excluded.

Results:

A total of 226 patient samples met the inclusion criteria. Of these, 96 (42%) patients had sufficient clinical concerns about a possible diagnosis of IBD to proceed to endoscopic assessment, and 71 (74%) had confirmed IBD. 86 (38%) patients had a raised FC (>50ug/g) of which only 68 had endoscopy performed - 18 of these patients had no clinical indication for endoscopy. In addition, 10 (4%) patients had endoscopic assessment due to clinical concerns despite a normal FC, 3 of whom subsequently were given a diagnosis of IBD. Of the 98 undergoing endoscopy, 68/71 patients with IBD had a raised FC (mean 854ug/g) at referral whilst 23/25 patients had a raised FC (mean 193ug/g) but no subsequent IBD diagnosed. Those who had no clinical indication for endoscopy had a mean FC of 50ug/g. With regards to other inflammatory markers in those with confirmed IBD, ESR was raised in 86%, platelets elevated in 66% and CRP in 64% compared to 96% demonstrating a raised FC.

Conclusions:

It can be seen that FC is a useful tool in determining those who require endoscopy for suspected bowel inflammation. Those with subsequent IBD have significantly higher FC levels at referral and high values should prompt further GI investigation. Compared to other inflammatory markers FC is most likely to be raised in IBD patients at diagnosis and is the key member of the inflammatory panel in this paediatric population.

Expert Groups – how to start and succeed**Dr Dan Turner, Consultant Paediatric Gastroenterologist
Shaare Zedek Medical Centre, Jerusalem**

Expert groups can be a powerful research tool if used appropriately. It ensures generalizability and face validity. Involving leading experts in the field in the research process increases its acceptability. However, rigorous methodology should be employed in constructing and organizing the group in order to avoid biased results. At times, it may not be as easy as it might seem. The structure of the group should carefully balance various opinions, geographical regions, political groups and disciplines. A clear description of the research aim should be provided and the initial contact should be made by a well reputed figure.

One of four major methodologies may be applied for expert groups: 1) Interacting groups: free discussion within a group for obtaining views; 2) Focus groups: structured way of obtaining views within a group; 3) Nominal groups: structured way of reaching consensus within a group that meets; 4) Delphi groups: structured way of reaching consensus within a group that never meets. The latter is an extremely useful and feasible iterative method in the email era and has the advantage of eliminating dominant participants since the participants are usually anonymous. An organizing panel sends predefined gradable questions to the group, formulates the replies and resends to the group until the group reaches consensus or a point of diminishing response. The process should be kept short and simple to avoid fatigue and reduced compliance. An important disadvantage of expert groups is the regression to the mean phenomena in which extreme views are likely to be diluted, even in justified cases. When used in the appropriate setting, expert groups may generate important data for guidelines, common practice and beliefs.

Qualitative research: techniques and tools

Rachel Taylor, Research Associate
University College London & London South Bank University

Qualitative research originated in the social sciences and while there are many philosophical paradigms (e.g. ethnography, phenomenology), the principal aim of qualitative research is to gain an in-depth understanding of human behaviour. Qualitative methods focus on the 'why' and 'how' rather than the 'what', 'when' and 'where'.

The aim of this presentation is to debunk the myths surrounding qualitative research and to argue why they are necessary for health care research in the National Health Service, especially in children with chronic illness. An overview of sampling issues, methods of data collection and analysis techniques will be presented. Where possible this will draw on personal examples and those in the literature related to paediatric gastroenterology, hepatology and nutrition.

Mentoring and promoting clinical research

Professor Anne M Griffiths, Division Head
Hospital for Sick Children, University of Toronto

Mentoring is usually understood to define the process by which an experienced person provides guidance, support and encouragement to a less experienced person. All of us learn from our experiences, and especially from our mistakes! This hindsight can be passed on to become someone's foresight.

There are many models of mentoring, which can be considered. In the context of promoting clinical research, it is important to wisely advise more junior colleagues in both the acquisition of necessary research skills and in the selection of appropriate and feasible projects; to encourage them constructively; to facilitate for them opportunities for collaboration and for recognition in their chosen field.

Mentoring relationships are undertaken to benefit the mentee, but the mentor also derives tremendous personal satisfaction from observing the career development of others.

ABSTRACTS FOR THURSDAY 27TH JANUARY 2011

Invited Speakers' and Selected Oral Plenary Session Abstracts

Paediatric Hepatology – Looking back

**Professor Deirdre Kelly, Consultant Paediatric Hepatologist
Birmingham Children's Hospital, Birmingham**

Paediatric liver disease is a significant cause of morbidity and mortality worldwide and 21 years ago was usually fatal. Advances in our understanding of the pathophysiology, diagnosis and treatment, particularly the success of liver transplantation have transformed outcomes for children with liver disease, of whom 80% will now survive into adult life.

Much of our new understanding of liver disease has been based on the development of sophisticated molecular genetic techniques that have not only identified new genes and categorised rare diseases but has given us an insight into pathophysiology and potential therapy.

The recognition of the importance of the liver as a metabolic organ essential for growth and nutrition has changed our concepts of management and introduced nutritional supplementation as vital therapy for many forms of chronic liver disease.

National and international collaboration through clinical databases have helped us refine our diagnosis and treatment of diseases such as biliary atresia and acute liver failure, providing important data on long term outcome.

The recognition of the incidence of liver disease, the implications of new therapies and the necessity for multidisciplinary working has led to the development of strong networks and referral pathways involving many practitioners in the care of children with liver disease.

This success brings its own challenges as the increasing survival young people with liver disease into adult life means that it is essential for adult practitioners to be cognisant of paediatric liver disease.

Finally, research and development into better ways of diagnosis and treatment continue to challenge the profession and improve outcomes for children.

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Griggs RC, Batshaw M, Dunkle M et al. Clinical research for rare disease: opportunities, challenges, and solutions. *Mol Genet Metab*. 2009 Jan;96(1):20-6

Alpha-1 Anti-Trypsin Deficiency**Dr Dino Hadzic, Consultant Paediatric Hepatologist
King's College Hospital, London**

Alpha-1-antitrypsin (A1AT) is a proteolytic enzyme from SERPIN (serine protease inhibitor) family with a physiologic role to interrupt activation of neutrophil protease during systemic inflammatory response. Its deficiency is the commonest genetic cause of chronic liver and lung disease. The symptomatic liver and lung disease occur in an indeterminate, but probably small proportion of the individuals carrying abnormal PiZ allele, secondary to a single amino-acid substitution (lysine for glutamate) at residue 342 in A1AT gene on chromosome 14q32.1. Furthermore, there is a significant intrafamilial variation in the clinical manifestations and effect of environmental factors such as cigarette smoking and alcohol abuse is regarded considerable, although a number of other yet unrecognised factors undoubtedly play a role. The lung disease is caused by a lack of activity of the A1AT (loss-of-function effect), leading to interalveolar wall damage and early-onset emphysema, while the liver disease is secondary to retention of the abnormal protein in the endoplasmic reticulum (ER) of the hepatocytes (gain-of-toxic function) and its incompletely understood secondary effects on the intracellular physiology.

The subtle modification in the structure of PiZ A1AT leads to polymerisation of the polypeptide in the hepatocytes ("loop-sheet" polymers), which represents a hallmark of A1AT deficiency, but not of A1AT deficiency-related liver disease. The entrapped polymers escape cellular degradation processes, which include ER autophagic degradation (ERAD) and proteasomal degradation. In PiZ A1AT deficiency upregulation of autophagy has been demonstrated in the fibroblasts and hepatocytes. Recently, aberrant cellular mechanisms leading to progressive liver damage have been proposed, including intracellular activation of nuclear factor- κ B, leading to activation of caspases, mitochondrial damage and ultimately, cell death. Interestingly, activation of unfolded protein response (UPR), common in many of conditions associated with intracellular retention (conformational diseases), is not seen in PiZ A1AT deficiency. Potential therapeutic strategies in the A1AT deficiency-associated liver disease include: a) prevention of polymerisation by small molecules, b) extracellular chaperoning and export of the retained polymers, and c) augmentation of intracellular disposal processes such as autophagy. While progress in the first two approaches was limited to in vitro studies, Hidvegi and colleagues have recently demonstrated in a transgenic mouse model of PiZ A1AT deficiency that carbamazepine given at pharmacological doses could enhance autophagy and improve histological features of the liver damage. If this observation is confirmed in the clinical setting it could herald a long-awaited medical means of preventing liver damage in a minority of PiZ individuals destined to develop end stage liver disease. In addition, this could also offer a potential therapeutic avenue for other presently untreatable conformational diseases.

Stem Cell therapy for liver disease**Professor Stuart Forbes
Professor of Transplantation and Regenerative Medicine, University of Edinburgh**

Liver transplantation is a successful therapy for advanced adult and paediatric liver disease but still required lifelong immunosuppression and adequate donor organ supply. Alternative "stem cell therapies" are potentially attractive. Broadly, this could occur in two distinct ways: (1) Generation of hepatocyte-like cells for liver support or (2) cell therapy to remodel liver cirrhosis. For disorders of hepatocyte metabolism transplantation of hepatocyte-like cells derived from embryonic and induced pluripotent stem cells have promise -although long term safety of such cells would need to be established.

By contrast, end stage liver cirrhosis is characteristic disturbed vasculature, excessive fibrosis and reduced number of compromised hepatocytes. This is not an environment conducive to hepatocyte transplantation and clinical studies using this approach have been unsuccessful. This suggests that for the treatment of liver cirrhosis, transplantation of stem cell derived hepatocyte like cells may also be unsuccessful. Remodelling the cirrhotic liver to degrade excess scar tissue and promote endogenous regeneration may be a more realistic approach.

Bone marrow (BM) derived cells influence hepatic scarring, scar resolution and liver regeneration. Autologous BM cell therapy for liver disease has shown promise in preliminary clinical studies however these studies have been non-randomised and the mechanisms of action are unclear. Further mechanistic studies are required as are randomised clinical trials to progress "regenerative medicine" for liver disease. We have been developing cell therapy strategies to enhance liver regeneration. We have found that in rodent models intra-portal infused BM derived naïve macrophages can promote liver regeneration and aid scar resolution. This resulted in early chemokine upregulation with hepatic recruitment of endogenous macrophages and neutrophils. These cells delivered matrix metalloproteinases 13 and -9 into the hepatic scar, reduced hepatic myofibroblasts numbers and reduced fibrosis. Liver regeneration occurred through expansion of endogenous Hepatic Progenitor Cells and serum albumin increased. We hope that the use of a single cell type that promotes scar degradation and regeneration will aid the clinical development of cell therapy for liver cirrhosis.

Is cirrhosis actually reversible?**Professor John Iredale, Professor of Medicine
University of Edinburgh, Edinburgh**

Liver fibrosis represents the end stage of the wound healing response of the liver and results from the excessive secretion of matrix proteins by activated Myofibroblast-like hepatic stellate cells (HSC) and myofibroblasts recruited from mesenchymal stem cells. Additionally hepatic, particularly periportal, myofibroblasts may contribute to the wound healing response in the liver. In this activated phenotype HSC proliferate and are the major source of collagens I and III that characterise fibrosis. In addition, activated HSC express both matrix degrading metalloproteinases (MMPs) and their inhibitors the tissue inhibitors of metalloproteinases (TIMPs) - leading to the hypothesis that progressive fibrosis is in part the result of a failure of matrix degradation. Whilst previously viewed as irreversible, we have used models of biliary and parenchymal liver injury, to demonstrate that established fibrosis is reversible and have studied these models to determine the critical roles of individual cell lineages and the changes in cell behaviour and matrix turnover that mediate resolution of fibrotic change.

Recovery from fibrosis induced by both CCl₄ and bile duct ligation will occur over 4-6 weeks following withdrawal of the insult (cessation of dosing with CCl₄ and biliojejunal reanastomosis respectively). Recovery is associated with histological resolution and a return of the normal architecture and histological and biochemical evidence of matrix degradation. Resolution is accompanied by apoptosis of the activated HSC. In association with HSC apoptosis the hepatic levels of TIMPs 1 and 2 decrease to levels comparable with normal untreated liver and collagenase activity within liver homogenates increases in parallel, coinciding with evidence of matrix remodelling. Therefore, HSC apoptosis appears to serve the dual function of removing the cells responsible for both producing the neomatrix and ensuring its protection from collagenase digestion through expression of the TIMPs. Apoptosis may represent a default pathway for stellate cells; this pathway is forestalled during progressive injury because HSC are provided with survival signals. Increasing evidence indicates that contact with a collagen-I rich fibrotic matrix may promote survival of activated HSC. In addition, TIMPs 1 and 2 act as autocrine survival signals for HSC by reducing MMP mediated matrix turnover. Additionally MMP activity may be critical to the cleavage and inactivation of survival factors such as N-cadherin and Pro-NGF. The development of a more advanced cirrhosis is, however not entirely reversible. Remodelling of this lesion results in the conversion of a micronodular to attenuated macronodular cirrhosis. The features of the irreversible components of fibrosis include a relative paucicellularity of the persistent scar and the cross-linking of matrix within the scar. Most recently, by showing that macrophage depletion retards resolution of fibrosis, we have demonstrated a key role for these cells in liver remodelling. These observations will be discussed in greater depth during the presentation. Our increasing understanding of the process of spontaneous recovery from liver fibrosis is likely to be invaluable to the design of future therapeutic strategies targeted at this and other fibrotic disorders. Therapeutic approaches to enhance matrix degradation, myofibroblast apoptosis and the potential for macrophage and stem cell based therapies will be discussed in the presentation.

Our increasing understanding of the process of spontaneous recovery from liver fibrosis is likely to be invaluable to the design of future therapeutic strategies targeted at this and other fibrotic disorders. Therapeutic approaches to enhance matrix degradation, myofibroblast apoptosis and the potential for macrophage and stem cell based therapies will be discussed in the presentation.

Medical and nutritional therapy – the evidence**Dr Andrew Barclay, Consultant Paediatric Gastroenterologist
Yorkhill Hospital, Glasgow**

Intestinal failure (IF) affects a growing number of children due to increasing numbers of preterm infants surviving intestinal resection for necrotising enterocolitis (NEC) and improving surgical techniques for congenital gut anomalies. Parenteral nutrition (PN) is the mainstay of therapy; enteral nutrition (EN) may have trophic effects on the gut. We recently aimed to systematically review evidence for the effectiveness of medical and nutritional interventions in the treatment of IF in children (1). We retrieved data from studies of patients aged <18yrs and receiving >28 days PN. Outcome measures included improvement in intestinal function; intestinal adaptation; growth; prevention and treatment of IF-associated liver disease; mortality. Cochrane Database (November 2009), Medline (1950-November 2009) and CINAHL (1982-November 2009) electronic database searches were made using keyword and subject headings (MeSH); IF; Short Bowel Syndrome (SBS); PN and Child. The level of the evidence (EL) was assessed using Scottish Intercollegiate Guidelines Network (SIGN) methodology (www.sign.ac.uk). From 1607620 hits, 720 abstracts were reviewed. 33 original papers were included. No studies were of high methodological quality. Studies of higher evidence level included the use of bile analogues, oral antibiotics, hydrolysed milk formulae and novel parenteral lipid. No published data on Tauralock (Taurapharm GmbH, Waldebrunnen, Germany), or cycled enteral antibiotics exist for this population (1). Further, no new RCTs or high quality cohort studies of relevant interventions have been published since the systematic search was performed.

Much interest has focussed on the use of novel lipids for the amelioration of IFALD, however despite several recent published studies there are no well designed randomised controlled trials, and the evidence base is limited to Omegaven (Fresenius Kabi AG, Bad Homburg, Germany) which is in contrast to current UK practice for the majority of IF centres (2), where SMOF (Fresenius Kabi AG, Bad Homburg, Germany) tends to be preferentially used.

The evidence base for medical and nutritional interventions in paediatric IF is limited and of poor quality. RCTs of novel lipids are underway in North America. In the absence of RCTs, this evidence base can improve through case control and cohort research, and with better multi-agency communication the study of inter-centre differences is possible. Out-with the remit of our review, outcomes relating to specialist multidisciplinary management of IF, non-transplant surgery, isolated liver transplant and combined small bowel liver transplant, all merit further investigation. Achievable short-term goals would include the study of; optimal ursodeoxycholic usage; novel intralipid formulations; cycled enteral antibiotics; enteral probiotics and new enteral feeding strategies.

1. Barclay AR, Beattie LM, Weaver LT, Wilson DC. Systematic review: medical and nutritional interventions for the management of intestinal failure and its resultant complications in children. *Aliment Pharmacol Ther* 2011;33:175-84
2. Flynn DM, Gowen H. Paediatric parenteral nutrition and lipid usage in the UK - A pick N' mix situation? *Clin.Nutr.* 2010; 29: 275-276.

The Scottish Home PN Managed Clinical Network

Dr Janet Baxter, Network Manager Scottish Home PN Managed Clinical Network, Kings Cross Health and Community Health Centre, Dundee

The Scottish Home Parenteral Nutrition Managed Clinical Network was launched in November 2000. The MCN aims to improve the quality of care provided to adults and children who need long term parenteral nutrition as treatment for chronic intestinal failure.

As with all national MCNs that have been in existence for 5 years or more, the network has been subject to strategic review to ensure that it continues to fulfil its designated aims and meets the criteria of Scottish Government Health Department Letter (2007) 21.

- To ensure patients are managed according to evidence-based, nationally agreed procedures and protocols
- To enable provision of HPN in as cost effective manner as possible
- To develop and maintain a register of patients and families
- To allow audit of practice and outcomes and hence provide a basis for improving the quality of care
- To promote equity of access and service delivery at the most appropriate point of contact (supported by agreed clinical standards and transparent service model)
- Provide a full list of clinicians/sites with expertise

The paediatric group of the MCN has worked hard to maintain a register of patients and have developed audit to provide prevalence and outcome data. The challenges facing the network are to improve service user participation – in particular, learning from patient/family experiences; using identified clinical indicators to continue to inform audit using a new national IT solution; and also, working with NHS Education Scotland to develop an education strategy to support the learning of all health professionals involved in the management of this patient group.

Laparoscopic Surgery Update

**Mr Gordon Mackinlay, Senior Lecturer in Paediatric Surgery
Royal Hospital for Sick Children, Edinburgh**

The old maxim 'a big surgeon makes a big incision' is no longer tenable. Operative scars are there for life and in paediatric practice they upset not only the parents, who sign consent forms to agree to such surgery, but as the child grows they may have a particularly damaging effect on the individual's body image.

In addition pain and stress following a surgical operation are often related to the surgical scar. Laparoscopic and thoracoscopic surgery have the advantage that the scars are minimised, usually 2, 3 or 5mm. If a wider incision is required to remove tissue mobilised through laparoscopic surgery then this can be placed in a more cosmetically acceptable site to avoid significant alteration to the body image.

The greatest change in surgical practice, which came about towards the end of the last century, is laparoscopy. Laparoscopic techniques have been used for some time by gynaecologists. Paediatric surgeons adopted laparoscopy in the 1970s, but this was largely confined to carrying out inspections for intra-abdominal testes and this has been the norm since the 1970s. Laparoscopic cholecystectomy in adults has only been popularised over the last two decades or so, since the first description of a cholecystectomy was published in 1985. The procedure has become increasingly popular in adult surgical practice over recent years and it is now unusual for the gall bladder to be removed through an open operation.

Apart from 'spot the ball' investigations for undescended testes, paediatric surgeons have been very slow to develop laparoscopic and thoracoscopic techniques for use in children for various reasons. The initial adult equipment was relatively large and the child's body cavity, being relatively small, led to some difficulties. Many paediatric surgeons pride themselves in operating through small incisions, which usually heal neatly without undue scarring. The scars, however, grow with the child.

Modern fine instruments and miniature video cameras have gradually enabled laparoscopic techniques to be applicable to children leaving tiny scars that are less apparent than freckles.

The techniques can be used even in tiny premature babies these days to correct complex problems that normally need a wide incision for access. It is also now the favoured approach for more common conditions such as appendicitis. A few years ago the first integrated operating theatre in Europe was installed at The Royal Hospital for Sick Children in Edinburgh. Plasma screens are suspended from the ceiling and can be swung down over the patient to facilitate endoscopic surgery. The theatre images can be linked to other centres in the world through teleconferencing facilities so that operative procedures can be demonstrated to surgeons elsewhere.

Many paediatric surgeons still have a limited repertoire of endosurgical procedures. In Edinburgh over the past 17 years we have acquired the expertise and confidence to use these techniques for most abdominal and thoracic surgical procedures and this presentation will illustrate the possibilities in GI surgery from the oesophagus to the anus.

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Senior Lecturer in Paediatric Surgery,
University of Edinburgh
Consultant Paediatric Surgeon,
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Total intravenous anaesthesia

Dr Alistair Baxter, Consultant Anaesthetist
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Phenotypic variation and long term outcome of hepatobiliary and renal manifestations in children with congenital hepatic fibrosis.

Rawat D¹, Kelly D A¹, Sharif K S¹, Lloyd C¹, Milford D², McKiernan P J¹

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Introduction:

Congenital hepatic fibrosis (CHF) is a developmental disorder of the hepatobiliary system due to defective remodelling of the ductal plate (ductal plate malformation) and is characterised by portal hypertension. When combined with nonobstructive dilatation of intrahepatic bile ducts it is called Caroli's syndrome. CHF is usually associated with renal diseases as part of spectrum of hepatorenal fibrocystic disease. The lack of studies about the natural history of CHF and the variability in progression makes prognostication difficult.

Aim:

We aim to describe the clinical characteristics and long term outcome of patients with congenital hepatic fibrosis seen at a single centre.

Subjects & Methods:

We conducted a retrospective analysis of children who were diagnosed with CHF at our institution between Jan 1990 and Nov 2009 based on clinical, ultrasonographic, endoscopic and histopathological features. Hepatobiliary complications (varices, GI bleeding, hypersplenism, cholangitis) and renal complications (hypertension, chronic renal insufficiency, end-stage renal disease) were recorded at baseline, 2 year, 5 year and 10 yr follow-up where available. Patients were categorised depending on whether transplant indicated (Group 1) or not necessary (Group 2). Presence of oesophageal varices grade 2 and above was considered as moderate to severe portal hypertension.

Results:

There were 40 children with 21 males, median age at diagnosis of CHF was 5 yrs (range 7 months-16 yrs). 20 children had CHF and 20 had Caroli's syndrome. Four children had affected siblings. Portal hypertension was present in all children based on endoscopic findings or ultrasonographic evidence. CHF was associated with autosomal recessive polycystic kidney disease (n=30), miscellaneous renal diseases (n=7) while 3 patients had isolated CHF. Group 1 included 20 children of whom 80% presented in neonatal period or early infancy with renal insufficiency. The main indication for transplant was end stage renal disease with portal hypertension or cholangitis and combined liver/kidney transplant was performed in 18 children at a median age of 7 yrs. One child had isolated liver transplant for significant portal hypertension. One child has developed end stage renal disease and has been recommended for combined liver/kidney transplant. Moderate to severe portal hypertension was noted in 8/20 with variceal bleeding in 5 children while cholangitis occurred in 7/20 in this group. Group 2 included 20 children who presented with hepatosplenomegaly at a median age of 5 yrs. Moderate to severe portal hypertension was noted in 8/20 with variceal bleeding in 5 and cholangitis occurred in 2/20. Portal hypertension progressed during follow-up in 11/20 (55%) and chronic renal insufficiency developed in 6/20 (30%) in group 2. Median age at last follow up was 11 yrs.

Summary:

The children who were transplanted had early presentation with predominant renal manifestations. There was no difference in the severity of portal hypertension between the transplanted and nontransplanted children while cholangitis was more common in the transplanted children prior to their transplant. Portal hypertension and renal insufficiency progressed independently in nontransplanted children.

Conclusions:

Patients with CHF presenting beyond infancy exhibit a milder renal phenotype and demonstrate progression of portal hypertension which is independent of the progression of renal disease. End stage renal disease develops in all patients presenting in the neonatal period or early infancy and combined liver-kidney transplant is the favoured approach.

Hepatic lumican expression and paediatric non-alcoholic fatty liver disease

Emer Fitzpatrick, Ragai Mitry, Alberto Quaglia and Anil Dhawan.

Paediatric Liver, GI and Nutrition Centre and Institute of Liver Studies, King's College Hospital.

Aim:

Lumican is a glycoprotein involved in collagen cross-linking and modulation of the innate immune system. Overexpression of lumican was recently described in a group of adults with histologically progressive NASH but has not yet been evaluated in paediatric NAFLD. The aim of this study was to determine the degree of lumican expression in the liver of children with varying stages of NAFLD.

Methods:

24 children (17 boys), median age 13.1 years, with liver biopsy-proven NAFLD and 6 children with chronic liver disease other than NAFLD (4 with autoimmune hepatitis and 2 with Wilson disease) were included in the study. Paraffin-embedded biopsy sections were scored according to the NAFLD Activity Score (NAS). Sections were immunostained for lumican using HRP-DAB. Quantitative analysis was performed using imageJ (NIH, USA); staining was expressed as percentage of the total area. Relative quantification real-time PCR for lumican was undertaken on frozen biopsies.

Results:

Median BMI z-score of those with NAFLD was 2.2 and median HOMA-IR; 4.4. 58% had splenomegaly. Thirteen children scored ≥ 5 (NASH), 6 scored 3 - 4 (borderline) and 5 scored ≤ 2 (simple steatosis). Fibrosis was minimal in 10 (F<2) and significant in 14 (F ≥ 2). The pattern of lumican staining followed the sinusoidal contour, and marked the portal vascular endothelium and the luminal border of bile ducts. There was no clear staining of hepatocytes. Lumican was overexpressed in those with significant fibrosis (F ≥ 2) versus those with minimal fibrosis (F<2); (168%, p=0.01). Lumican was also overexpressed in NASH versus simple steatosis (215%, p=0.012). At gene level, lumican was upregulated (compared to normal control liver) in those with F ≥ 2 (15.8-fold) and in those with F<2 (10.9-fold). Lumican expression was not related to age, BMI z-score, HOMA-IR, splenomegaly or transaminase levels. There was variable expression of lumican in the biopsies of those with chronic liver disease other than NAFLD. Percentage area stained did not correlate with degree of fibrosis in these patients.

Conclusions:

Lumican is expressed with increasing severity of paediatric NAFLD. Upregulation at gene level in those with both minimal and histologically more severe disease is also evident. The role of lumican in progression of disease has not yet been elucidated and should be the focus of further investigation.

Treatment of chronic viral hepatitis C in children and adolescents: Experience of 3 UK national centres.Abdel-Hady M^a, Bansal S^b, Davison SM^c, Brown M^a, Tizzard SA^b, Mulla S^c, Davies P^d, Mieli-Vergani G^b, Kelly DA^a^aLiver Unit, Birmingham Children's Hospital, Birmingham^bPaediatric Liver Centre, King's College Hospital, London^cLiver Unit, Leeds Teaching Hospitals, Leeds^dInstitute of Child's Health, Birmingham Children's Hospital**Background:**

Chronic hepatitis C infection (HCV) is endemic in most parts of the world with a prevalence of 0.4% in the United Kingdom (UK). Children with HCV in the UK are managed in 3 national paediatric specialist liver centres funded by the Department of Health (Birmingham Children's Hospital, King's College Hospital & Leeds Teaching Hospital). The combination therapy of pegylated interferon alfa 2a/2b (PEG-IFN α 2a/2b) and ribavirin is the regimen used in the 3centres.

Aim:

The aim of this study was to review efficacy, tolerability and quality of life (QoL) in children with chronic hepatitis C (HCV) treated with the combination therapy in 3 national referral centers in the UK.

Methods:

Demographic, laboratory and clinical outcome data on children up to 18 years of age treated for HCV with pegylated interferon alfa and ribavirin were reviewed. Information gathered from QoL questionnaires -CHQ-PF28 completed by parents during their children's treatment was also available for one of the centers. Sustained viral response (SVR) was defined as undetectable HCV RNA at 24 weeks following end of treatment.

Results:

The study sample comprised 75 children of whom 38 were males. The median age at the start of the treatment was 10 years (3.0-17.2 years). The most common mode of infection (83%) was via maternal transmission. Thirty-four patients were Genotype 1; 39 Genotype 2&3; 2 Genotype 4. SVR was achieved in 75%; 53% Genotype 1; 89% Genotype 2&3; 100% Genotype 4. There was no significant difference between baseline ALT and/or AST levels in those who achieved SVR compared to the non responder group. However the first group had at least 30% lower ALT and /or AST levels at 24 weeks post treatment compared to the latter group p=0.003 and p=0.001 respectively. Younger children had higher SVR compared to older age groups, however this was not statistically significant p=0.5. Low viral load at the start of the treatment (<500,000iu/mL) did not have significant effect on viral response p=0.5. Early viral response (EVR) at 12 weeks of treatment was achieved in 46 and sustained in 40/46 (87%). Data on rapid viral response (RVR) at 4 weeks of treatment were available in 25; 17/25(68%) achieved (RVR) which was sustained in 16(94%). There was no significant change in the z scores for weight and height from start of treatment compared to 24 weeks post treatment follow-up (p 0.2 and 0.5 respectively). Data on QoL were available for 31/75 children and their families. At 12 weeks of treatment the child's general health was perceived to be poorer with limitation of physical activity and higher frequency of pain compared to other stages of treatment with values returning to baseline at the end of treatment and at follow up. There were no serious side effects reported and none discontinued treatment due to side effects.

Conclusion:

HCV treatment with pegylated interferon and ribavirin is well tolerated by children with minimal negative impact on the quality of life of a cohort of the studied children and no significant effect on growth. EVR and RVR are good predictors of treatment response.

Double-balloon Enteroscopy in Children – A Tertiary Care Experience

Urs A¹, Rao P¹, Arain Z², Thomson M¹

¹Centre for Paediatric Gastroenterology, Sheffield Children’s NHS Trust, UK; ²Department of Paediatrics, Armed Forces Hospital, Riyadh, Saudi Arabia

Background:

Double-balloon enteroscopy (DBE) has become a preferred method for management of small bowel disorders in adult population. Experience in paediatric population remains limited with regards to utility, therapeutics and safety profile of DBE. We present our experience with the use of DBE in our paediatric population.

Methods:

Thirty-four procedures were performed on thirty-three patients (22 M;11F) from January 2004 to October 2010, with median age of 12.9 years (range 2-18) and median weight of 39.8 kg (range 15.5-95); nine for Peutz-Jeghers syndrome (PJ syndrome), seven for obscure gastrointestinal (GI) bleeding, five with angiomatous malformations (3 blue rubber bleb nevus syndrome) having persistent GI bleeding, five with Crohn’s disease, three for chronic abdominal pain, and two with Cowden’s syndrome with multiple polyps , one for lymphangiectasia, pseudo-obstruction and jejunal stenosis. Thirty-one procedures were performed under general anaesthesia and three with deep sedation.

Results:

The entire small bowel was examined in 11 patients and a length between 150 cm and 400 cm distal to pylorus in the remaining 23. Twenty-one patients had both antegrade (trans-oral) and retrograde (trans-anal and via ileostomy in 2 cases) examinations. Two patients underwent DBE with planned laparoscopic assistance. The remaining 11 had trans-oral examination only. The median examination time was 118 min (range 50-320). No complications were encountered. Polyps were detected and successfully removed in all nine patients with PJ syndrome, in a patient with tubulo-villous adenoma of the distal duodenum, in three patients with significant anaemia and occult bleeding, and in two patients with Cowden’s syndrome. The source of bleeding was identified in a further patient with oesophageal varices. Diagnosis of Crohn’s disease was confirmed in two suspected patients. Three patients, known for Crohn’s underwent DBE, to examine the extent of disease. One patient with feed intolerance found to have severe dysmotility. A diagnosis was made in a patient with multiple angiomata not amenable to endotherapy, and in three, with a discrete angioma which were treated with argon plasma coagulation. One patient with protein-losing enteropathy was diagnosed to have isolated intestinal lymphangiectasia and underwent laparoscopic assisted surgical resection with transmural transillumination by enteroscope. One patient with GI bleed had large ulcer at ileocolonic anastomosis site. DBE was normal or revealed minor mucosal friability in the remaining six patients. Hence a diagnostic yield of 28/34(82%) with therapeutic success in 17/34 (50%) was achieved.

Conclusion:

DBE appears to be a safe diagnostic and therapeutic tool with suspected small bowel disorders. Further larger studies are required to establish widespread application.

Is Exclusive Enteral Nutrition (EEN) enough for Children with Crohn’s Disease (CD)?

Gerasimidis K¹, McGrogan P², Buchanan E², Duncan A³, Talwar D³, O’Reilly DS³, Edwards CA¹

1. College of Medicine, Veterinary and Life Sciences, University of Glasgow, Glasgow
2. Department of Paediatric Gastroenterology, Yorkhill Hospitals, Glasgow
3. Trace Elements and Micronutrient Reference Laboratory, Glasgow Royal Infirmary, Glasgow

Introduction: Nutritional therapy is the primary treatment for active paediatric CD improving disease activity and anthropometry but data on micronutrient status changes during EEN are lacking.

Methods: Seventeen children (8 boys; median age:12.7) with active CD were treated exclusively for 8 weeks on a polymeric feed (Modulen IBD®; Nestle). Body impedance was measured at baseline, 4 and 8 weeks and converted to z-scores of fat and lean mass (Wright et al 2008). Blood samples for nutrient analysis (Table) were collected for 13 children at baseline, end of EEN and post-treatment on normal diet (median: 59; IQR: 48 days after EEN).

Results: At baseline several children presented with suboptimal levels of carotenoids, trace elements, vitamin C, B6 and folate in plasma (Table). Treatment with EEN improved the levels for many nutrients, but the plasma levels of antioxidant carotenoids further deteriorated with more than 90% of the patients having depleted levels below the detection limit of the assay. The latter improved on normal diet but those micronutrients that had improved returned towards previous levels. Lean but not fat mass z-score significantly improved at the end of EEN [EEN Initiation vs End of EEN; Fat mass (z-score): -0.5 vs -0.3; p=141; Lean mass (z-score): -2.1 vs -0.8; p<0.0001].

Micronutrient	EEN Initiation		End of EEN		On Normal Diet	
	Median	% children with low levels [§]	Median	% children with low levels [§]	Median	% children with low levels [§]
Vit A (µmol/l)	1.2	8	1.7	0	1.2 ^b	0
Vit E / Chol* (µmol/mmol)	7.9	0	6.5	0	6.9	0
Lutein (µg/l)	63	83	29.5 ^a	93	113 ^b	30
Lycopene (µg/l)	65	67	12 ^a	100	139 ^b	30
α-carotenoid (µg/l)	10	75	10	100	13 ^b	50
β-carotenoid (µg/l)	46	75	41 ^a	92	97 ^b	40
Vit D (nmol/l)	56	0	93	0	59 ^b	0
Vit C (µmol/l)	29	25	49 ^a	0	46	9
Vit B1 (blood) ng/g Hb	559	0	669 ^a	0	573	0
Vit B2 (erythrocytes) (nmol/g Hb)	2.5	0	2.5	0	2.1	0
Vit B2 (blood) (nmol/l)	461	8	447	0	435	0
Vit B6 (nmol/l)	36	27	63 ^a	0	21	44
Vit B6 (erythrocytes) (pmol/g Hb)	662	0	721	0	438	0
Vit B12 pg/ml	662	0	843	0	505 ^b	0
Folate ng/ml	2.8	40	10.5 ^a	0	7.7	13
Zinc (µmol/l)	8.5	90	11.3	70	10	100
Zinc (erythrocytes; nmol/ g Hb)	597	0	531 ^a	0	547	0
Copper (µmol/l)	21.2	10	24.3	20	24.5	11
Copper (erythrocytes; nmol/ g Hb)	47.3	0	55.3 ^a	0	46.4 ^b	0
Selenium (µmol/l)	0.5	80	1 ^a	10	0.7 ^b	56
Selenium (erythrocytes; nmol/ g Hb)	4.2	15	4.5	8	4.5	18
Magnesium (mmol/l)	0.8	0	0.9	0	0.8	0
Magnesium (erythrocytes; nmol/ g Hb)	8.8	0	8.4 ^a	0	7.9	0
CRP (mg/l)	14.5	-	7	-	11	-
Albumin (g/l)	29.9	-	36	-	32	-
Ferritin (ng/ml)	28.6	40	6.4 ^a	70	14.8	22

^a: p < 0.05 from ‘EEN Initiation’; ^b: p < 0.05 from ‘End of EEN’ for Wilcoxon signed rank test; [§]: with reference to normal range

Conclusion: Lean but not fat mass was suboptimal and significantly improved at the end of EEN. Children with CD present suboptimal levels for many micronutrients in plasma some of which improved on EEN. Modulen IBD® lacks carotenoids and the results of this study may have implications for clinical practice and producers of enteral feeds. As plasma levels for many micronutrients can be affected by the acute phase response measurements of micronutrients in erythrocytes may be a better marker of actual body stores.

References: Wright et al (2008) Eur J Clin Nutr;62(2):210-7

Endoscopy – training update

Dr Paraic McGrogan, Consultant Paediatric Gastroenterologist
Royal Hospital for Sick Children, Glasgow

Procedural GI endoscopy – Looking forward

Dr Ian Penman, Consultant Paediatric Gastroenterologist
Centre for Liver and Digestive Disorders, Royal Infirmary, Edinburgh

Adult endoscopy has taken strides forward and these developments, both technical and organisational, have occurred across the spectrum of diagnostic and therapeutic upper and lower GI procedures. Much has stemmed from advances in digital electronic technology coupled with a greater focus on improving cancer outcomes through screening, diagnosis and detection of precursor lesions as well as methods of treating these. Diagnostic imaging has improved with the introduction of high resolution CCDs, magnification facilities (up to x150) and enhanced imaging including narrow band imaging (NBI, FICE, iSCAN), confocal laser endomicroscopy (CLE) and autofluorescence. These often allow detection and characterisation of otherwise undetectable lesions but the ability to provide 'optical biopsies' in e.g. Barrett's oesophagus or inflammatory bowel disease has not yet materialised. NBI and CLE appear deceptively simple but harnessing their power requires patience and detailed knowledge of the microscopic anatomy of crypt and vessel patterns. Detection of early lesions is only half the story: effective and safe methods of treating them are essential. While endoscopic mucosal resection (EMR) has become widely adopted, endoscopic submucosal dissection (ESD) remains restricted to a few enthusiastic centres in Europe. In contrast radiofrequency ablation (RFA) for dysplastic Barrett's oesophagus is an accepted and effective therapy; time will tell if it can offer durable ablation of non-dysplastic Barrett's. Endoscopic therapies for GORD have largely disappeared in adults due to lack of efficacy or safety concerns but are much needed as are endoscopic alternatives to surgery such as transoral gastroplasty or insertion of removable gastrojejunal bypass sleeves. Dealing with complications of bariatric operations will also be an increasing part of endoscopists' workload. Interest in natural orifice transluminal endoscopic surgery (NOTES) continues to grow but is largely experimental at present and is likely to remain within the realm of surgeons, at least in the UK. Advanced techniques such as EUS and ERCP will always have a niche role in children despite their increasingly important interventional role in adults.

All of this growth in endoscopy, coupled with the rollout of bowel cancer screening services has focussed many questions on those who provide endoscopy services: who should undertake them, how do we train and accredit endoscopists and where should complex or low-volume procedures be performed? How do we quality assure individuals and units undertaking endoscopy and the training provided to them? Success requires more than safe technical completion of a procedure: aspects such as appropriateness, timeliness, safety, decontamination processes and patient satisfaction are equally important. These are examined in adult units through the Global Rating scale (GRS), the Joint Advisory Group (JAG) accreditation process and the quality assurance of training, also overseen by JAG. Valuable lessons have been learned and thus it seems the time is right to foster ever closer working links between paediatric and adult services at this exciting juncture for gastrointestinal endoscopy.

ABSTRACTS FOR FRIDAY 28TH JANUARY 2011

Invited speakers' abstracts

Clinical Nutrition – Looking back

Professor Ian Booth

**Leonard Parsons Professor of Paediatrics and Child Health, University of Birmingham
and Consultant Gastroenterologist, Birmingham Children's Hospital**

The availability of parenteral nutrition has changed fundamentally the practice of paediatric gastroenterology in my professional life time. From the 1970s onwards, it became increasingly clear, that intestinal failure, once a death sentence, became eminently treatable, at least in the short to medium term. John Harries' 1971 publication provided a very practical approach to the provision of parenteral nutrition and this was followed up by Vic Larcher's publication with Dorothy Francis and John Harries, which established the principles of concurrent enteral nutrition which are still in use today.

Problems immediately became apparent: venous access, catheter sepsis and liver disease. The need to provide multi-disciplinary care for the children also became clear and one of the first benefits of this approach was dramatic reductions in catheter sepsis.

By the mid-1990s, paediatric hepatology, and liver transplantation in particular, had become firmly established in the UK, and collaboration with the paediatric gastroenterology and nutrition team led to the provision of small bowel transplantation in Birmingham. It rapidly became clear that pre-transplant outcomes were not uniform across the country and in particular, care by a nutritional care team appeared to have a major impact on the duration for which parenteral nutrition could be sustained before consideration of a transplant. Just as the provision of multidisciplinary nutritional care was far from uniform, so did partnership with paediatric surgeons vary enormously between centres.

By this time we were aware that we had little information about the number of patients with intestinal failure, let alone those who might need transplantation and coupled with this, little understanding of the natural history, particularly of short bowel syndrome. The British Intestinal Failure Survey was designed not only to address these unknowns but also to engage with paediatric surgeons and to involve them and BAPS in the process. The effort has been only partially successful despite heroic efforts by members of this Society and its administrators.

Beginning in the 1990s, substantial increases took place in the numbers of patients with short bowel syndrome, related to an unexplained increase in patients with gastroschisis, and in far greater numbers of preterm infants surviving necrotising enterocolitis. The opportunity to mount an irrefutable need for more resource based on data that the Survey would have provided, has been lost forever.

Despite these regrets, the treatment of infants with short bowel syndrome has almost certainly improved across the UK. Patients are being referred earlier for pre-transplant assessments, in better condition, and probably in smaller numbers as a result of more patients being successfully weaned off parenteral nutrition.

The lack of agreed care standards for patients with intestinal failure and the continuing, long-standing inability of paediatric surgeons to agree a set of criteria for submitting patients to intestinal lengthening (against which outcomes could be assessed) remained challenging.

Home enteral tube feeding – emerging trends**Catherine E Paxton, Nutrition Nurse Specialist, Royal Hospital for Sick Children Edinburgh**

Children must receive adequate nutrition to achieve their growth potential and avoid adverse consequences of undernutrition. Even in children who are acutely ill or have chronic conditions this may be achieved orally, provided they are safe to do so, but for most nutrition support needs to be provided by enteral tube feeding (ETF). ETF is predominantly established in hospital; during this time, family and carers are trained to provide the care required to administer home ETF (HETF). The British Artificial Nutrition Survey (BANS) aims to capture 100% of those children and adults receiving home artificial nutrition, however this is not achieved due to problems with incomplete registration. Worsening over recent years, the 2010 annual report indicates that BANS are only capturing 9% of estimated paediatric cases. This provides major problems for epidemiological study and guidance for appropriate service design.

Within our tertiary paediatric centre we have maintained an HETF database since the establishment of the regional paediatric nutrition support team (NST) in 1997. All children (under 18 years of age), resident within south east Scotland (static childhood population of 280,000) requiring HETF are entered onto our database. Unlike BANS, we have complete ascertainment of data, with 1014 children receiving HETF since 01/08/97. Emerging trends from the 13 years of collated data include:

- Confirmation of effect of initial service design - A rise in point prevalence of HETF from 1997-2001 which can be attributed to the establishment of the NST, with a predominance of neurodisabled children, all previously well documented.
- Effect of changing clinical practice - Following a plateau of numbers of children receiving HETF, there has been a rise in prevalence again from 2006. We believe this is associated with greater recognition of the benefits of paediatric nutrition support, more aggressive interventions for acute and chronic disease, and the increased survival of severely ill infants and children due to improved technology.
- Wider usage of HETF in non-neurodisabled children – Overall, 33% of these children had an underlying neurodisability, less than both BANS estimates of approximately 50% and data usually quoted in the nutrition support literature.
- Utility of initial nasogastric (NG) feeding – Despite our and others rapid recourse to gastrostomy tube, the majority of children still commence HETF via a NG feeding tube. This is an easily established and non-permanent route of HETF, allowing a period of time to determine whether longer term nutrition support is needed or will be successful.
- Workload due to severe GI dysmotility - Jejunal tube feeding is increasingly used by nutrition NSTs, particularly for those children with severe or worsening GI dysmotility. Only 2.5% of the children were jejunally fed, but they are a challenging group whom we estimate currently constitute 25% of our workload, and this trend is increasing.

Withdrawing enteral tube feeding**Charlotte Wright, Professor of Community Child Health, Glasgow University**

Enteral feeding provides vital support in severely ill or developmentally delayed children, but once a child is medically stable or more developmentally advanced the aim would be to progress back to oral diet. However this transition may be difficult, particularly where enteral feeding started in early infancy. This may reflect a lack of feeding skills and/or oro-facial hypersensitivity, but most commonly the major impediment is a lack of hunger, due to the high volume of tube feeds. A multidisciplinary approach to 'hard to wean' children is ideal, with medical assessment of growth and body composition, dietetic input to optimise feed delivery, speech and language input to aid desensitisation and assess oro-motor skills and clinical psychology input to support anxious parents and advise on feeding behaviour management. In practice most hard to wean children are adequately, or over nourished, although this may not be apparent without formal assessment of body composition, using skinfolds. Successful management thus requires a steady reduction in feeds to stimulate hunger, and the multidisciplinary team can help anxious parents persist in the face of short term weight loss.

In our clinical series in Glasgow, if withdrawal started before age 5 years, 50% ceased feeds within 6 months, but withdrawal still took over two years in 20%. In older children withdrawal usually took much longer, but was still achieved in the majority eventually. Failure to withdraw feeds, or restarting of feeds was associated in a few cases with complex oro-motor difficulties, but more commonly with non-compliance. Where there has been prior overfeeding, weight loss and decline in BMI may be substantial, but this is not associated with slow growth.

Progressive withdrawal of feeds is usually required before a child can be expected to eat more normally. Some weight loss is common and should not interrupt withdrawal, as long as the child was initially at least sufficiently nourished.

Wright CM, Smith K, Morrison J. 2010. Withdrawing feeds from children on long term enteral feeding: factors associated with success and failure. Arch-Dis-Child <http://adc.bmj.com/content/early/2010/07/22/adc.2009.179861.full.pdf>.

New Trends and Issues in Paediatric Obesity

**Professor John Reilly, Professor of Paediatric Energy Metabolism
The Queen Mother's Hospital, Edinburgh**

The rate of increase in childhood obesity in the UK may be slowing, though there is some controversy over this issue, and there is evidence that prevalence continues to increase in more socio-economically deprived groups, and prevalence is much higher in some high risk sub-groups. Prevalence in the general population remains high though, with around 10% of UK children obese (defined conservatively as BMI at or above the 95th centile relative to UK 1990 reference data) by age of primary school entry, and around 20-25% obese by age of secondary school entry. Systematic reviews have shown that childhood and adolescent obesity have a number of adverse short and long-term health consequences, and the presentation will summarise these. Recent evidence based guidance (e.g. SIGN 2010), has established the BMI for age as the most appropriate simple means of defining or diagnosing childhood obesity, and it performs better diagnostically than the alternatives, including the use of informal methods, and the use of waist circumference or waist circumference centiles. There is good evidence from systematic reviews that parents, children, and health professionals tend to grossly under-recognise and under-diagnose child and adolescent obesity, and it has been described as 'practically invisible', despite recent media interest in the topic. Failure to recognise the problem probably constitutes a major barrier to preventive and treatment interventions. Recent evidence-based guidance (SIGN, NICE, Cochrane reviews, American Academy of Pediatrics) has been positive about the prospects for interventions to prevent and treat child and adolescent obesity. While no simple 'off the shelf' interventions for prevention and treatment exist, following this guidance should produce modest benefits for families participating both in prevention and treatment interventions. The presentation will summarise the current evidence based 'best bets' in obesity treatment and prevention interventions. Children and adolescents who are obese tend to remain in excessive positive energy balance even with treatment, and are on extreme trajectories for body composition development- this limits the success of treatment for many patients. One major barrier to undertaking obesity prevention or treatment interventions is the possibility of adverse effects- these are unlikely though, and the presentation will also summarise the evidence on possible adverse effects of treatment and prevention. The most recent evidence on the long-term follow up of children and adolescents treated for obesity is generally encouraging, and suggests that modest benefits of treatment might extend well beyond the period of treatment. Finally, the presentation will consider some topical questions in obesity treatment including how to establish a treatment service, whether or not measuring body composition is practical and helpful, and child protection issues.

Coeliac disease – old disease, new issues

**Professor David van Heel, Professor of Gastrointestinal Genetics
Barts and the London School of Dentistry and Medicine, London**

David van Heel trained in the Oxford Region as an adult gastroenterologist, obtaining a PhD in inflammatory bowel disease genetics in Derek Jewell's lab in 2002. He moved to Imperial College with a Wellcome Trust Clinician Scientist Fellowship, and subsequently to Barts and The London in 2006, where he was appointed to a Chair and as Honorary Consultant Gastroenterologist. His research has included function of the NOD2 gene in Crohn's disease patients (Lancet 2005), new genetic risk factors for coeliac disease (Nature Genetics 2007, 2009, 2010), overlapping genetic risk for coeliac and type 1 diabetes (NEJM 2008), and coeliac disease T cell immunology (Immunity 2007, Science Translational Medicine 2009).

The talk will be a mix of clinical nuggets and basic science research, with a theme of interlinked genetics and immunology. Coeliac disease is much the best understood human 'autoimmune disease' with much known about the role of the HLA, T cells and toxic cereal peptides. Clinical topics will include current presentations of coeliac disease, the use of HLA genetic tests in clinical diagnosis, spontaneous "cure" of coeliac disease, breastfeeding and coeliac disease, and new treatments entering clinical trials. Research topics will include genome wide association studies identifying immune system genes and their function, and improved understanding of the key toxic peptides in cereals.

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Lessons from *Helicobacter pylori* for other GI conditions

**Professor Emad M El- Omar, Professor of Gastroenterology and Honorary Consultant Physician
University of Aberdeen, Aberdeen**

Helicobacter pylori is the commonest chronic bacterial infection in the world and is causally associated with peptic ulcer disease and gastric cancer. The elucidation of the pathogenesis of *Helicobacter pylori* infection has shed light on many basic pathophysiological processes in the human body, most notably the role of microbially-induced inflammation in carcinogenesis. The better understanding of host-bacterial interactions in this relatively simple model has provided transferrable knowledge to several other GI, and indeed non GI, conditions. This is most evident in inflammatory bowel disease where there has been tremendous progress in appreciating the contribution of the gut microbiota to pathogenesis of this chronic relapsing condition. The legacy of *Helicobacter pylori* extends to several other chronic disorders such as gallbladder disease and liver cancer. With the advent of impressive new technologies including the various *omics*, it is only a matter of time before the aetiologies of many of the fascinating conditions that afflict adults and children are uncovered. Perhaps the best lesson we can learn from the *Helicobacter pylori* story is to keep an open mind, a philosophy that will always deliver the truth in the end.

Variations in the gene encoding C-reactive protein suggest that CRP is a candidate susceptibility gene for inflammatory bowel disease in the Scottish paediatric population.

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Introduction:

C-reactive protein (CRP) is an acute phase reactant which may possibly link innate and adaptive immunity by binding proteins such as complement factor H. IBD patients with an elevated serum CRP have demonstrated a superior response to biological therapies suggesting that CRP may also play a role in IBD pathogenesis. In addition, a proportion of IBD patients do not have a raised CRP even in the presence of severe inflammatory disease. We aimed to assess the gene-wide association signal of the CRP gene to IBD and Crohn's disease (CD) susceptibility by means of a detailed haplotype-tagging investigation.

Methods:

1215 subjects consisting of 465 robustly phenotyped patients diagnosed with inflammatory bowel disease (IBD) <17yrs within Scotland (311 CD, 111 UC and 43 IBD-U) and 797 parents (284 complete trios) were genotyped for 7 single nucleotide polymorphisms (SNPs). 5 CRP-tagging SNPs were selected using HapMap data (using solid spine of LD, MAF > 0.1): rs1417938, rs1205, rs1130864, rs1935193 and rs11265263. Two additional SNPs, previously shown to influence serum CRP levels (rs3091244 and rs1800947) were also genotyped. Detailed phenotypic characteristics of this cohort were previously described. Detailed single marker and haplotype analysis by transmission disequilibrium testing (ParentTDT) was carried out using Haploview (with permutation analysis, n=100,000).

Results:

After stringent permutation analysis the rs1417938 A allele, located in the first 5' intron of the CRP gene, showed significant over transmission to affected IBD patients (p=0.0446). The 7-marker haplotype ACACATC also showed significant distortion of transmission (p=0.0068) This same 7-marker haplotype was also significantly associated with Crohn's disease (p=0.0165). Using a sliding-haplotype analysis to assess the extent of the IBD and CD-associated signal from the 5' end to the 3'UTR of the CRP coding sequence demonstrated that the strongest signal (p=0.0013 for IBD, p=0.0050 for CD) was achieved with a haplotype spanning the entire CRP gene. It should be noted that the rs1205 SNP also showed significant replication in the Wellcome Trust Case Control Consortium analysis for CD (p=0.028).

Conclusion:

We have demonstrated that in a well defined population, using analysis that eliminates the need for population stratification, that inherited variation of the haplotype containing CRP is associated with IBD and CD susceptibility. Our analysis indicates that it is now warranted to submit the CRP gene to further deep sequencing and to re-evaluate the contribution of CRP to IBD pathogenesis beyond its usefulness as an inflammatory marker.

Biological therapy for paediatric IBD – effective but associated with financial and safety issues

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Background and aims:

Biological agents are increasingly used as treatment for paediatric inflammatory bowel disease (IBD) in the UK, yet the evidence base is very limited and safety concerns are rising. We aimed to evaluate pattern of usage, effectiveness and safety in the clinical setting using a Scottish national framework.

Methods – Usage of the biological agents infliximab (IFX), adalimumab (ADA) and natalizumab (NAT) for treatment of paediatric IBD (aged <18 years of age at start of biological therapy) from 1/1/00 to 30/04/10 was collated in a retrospective audit. Treatment was administered by members of the Scottish Society of Paediatric Gastroenterology, Hepatology and Nutrition (all regional academic paediatric centres and interested DGHs in Scotland).

Results:

112 children had 1 or more biological agent administered from a median (range) age of 14.3 (6.6-17.9) years; 50 (45%) were female and 102 (91%) had Crohn's disease (CD), 8 (7%) had ulcerative colitis (UC) and 2 (2%) had indeterminate colitis (IC). Twenty-two (20%) had trials of 2 biological agents. 104 children (98 CD) had IFX, with a median (range) of 4 (1-25) infusions and almost all with moderate-severe IBD. 38 entered remission, 34 responded, and 32 had no response. 11 of the 46 (24%) proceeding to maintenance IFX required escalation of therapy. 14 (13%) had infusion events with 3 having anaphylaxis, and 7 reactions led to discontinuation. 1 child developed a lupus-like reaction requiring prolonged hospitalisation and 1 had severe infection, with no deaths. 19 (18%) proceeded to ADA. 23 children (all CD) had ADA therapy (including 19 after IFX, 2 as first biological and 2 with inflammatory arthritis in whom CD developed whilst on etanercept), with a median of 20 doses and nearly all with moderate-severe IBD. 11 entered remission, 6 responded, and 6 had no response. All proceeded to maintenance and 11 (50%) required escalation of therapy. 13 had pain at injection site and none had reactions leading to discontinuation. 1 child developed leucopaenia and 1 had a severe viral infection, with no deaths. 2 children with CD had NAT, both in a trial, and both proceeded to IFX after the agent was withdrawn.

Conclusions:

Our nationwide 'real-life' experience shows that biological agents are effective in moderate-severe paediatric IBD in the clinical setting, but there are significant financial issues (need for dose escalation or multiple biological usage), as well as safety issues.

Colonic Mucosal Bacterial Diversity of de-novo Extensive Paediatric Ulcerative Colitis by Next-Generation Sequencing

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Introduction/Background:

Dysbiosis which denotes as an imbalance between "healthy" and "harmful" bacteria with resultant inflammation may contribute to inflammatory bowel disease (IBD) pathogenesis along with a reduced bacterial diversity. Limited bacterial diversity studies have been performed at the onset of disease in adults but rarely in children. High-throughput, parallel sequencing technology (next-generation sequencing) provides the means of assessing microbial diversity in samples from diverse ecosystems such as the colonic mucosa.

Aim:

To examine bacterial diversity in mucosal biopsies of treatment naïve, de-novo paediatric ulcerative colitis (UC) compared to controls.

Subjects and Methods:

Paediatric patients undergoing colonoscopy were recruited to two groups: those with a new diagnosis of IBD at their first presentation and controls with a macroscopically normal colon and no evidence of IBD on biopsy. All subjects were free from systemic antibiotics, steroids and immunosuppression for at least 3 months prior to colonoscopy. 5 UC patients deemed extensive (E3) by Montreal criteria and 5 controls with macroscopically and microscopically normal colons were selected for bacterial diversity assessment. The UC group had a median age of 11.5 years whilst the control group had a median age of 10.7 years. All patients were male. Colonic mucosal biopsies were taken from the rectum/sigmoid.

DNA extraction was performed by a modified Qiagen QiAMP mini-kit method. The presence of bacteria was confirmed by universal eubacterial primers before next-generation PCR utilising V3 Forward/V6 Reverse primers. Bacterial diversity was assessed by 454 Titanium sequencing (Newgene, Newcastle). Sequencing data was filtered and chimera-checked before rarefaction to 13,000 reads per sample. Statistical comparisons were made by Mann Whitney U tests using PASW Statistics version 18.

Results: All biopsies were positive for bacterial DNA with universal Eubacterial primers. The most commonly identified bacterial classes (comprising 92.6% of sequence reads) were Bacteroidetes (45.2%), Clostridia (36.2%), Gammaproteobacteria (8.0%) and Erysipelotrichi (3.4%). Bacteroidetes were significantly more common in the control colon than in UC (7724.6 mean reads versus 4020.2, $p=0.028$) whereas Clostridia were significantly more common in the UC colon than in controls (5869.6 mean reads versus 3530.2, $p=0.028$). The differences between Gammaproteobacteria and Erysipelotrichi were not significant. Bacterial diversity assessed by the Shannon index was similar in both groups (Means of 9.80 in UC and 10.51 in controls, $p=0.251$).

Summary and Conclusion:

Colonic mucosal bacteria differ between paediatric patients with extensive UC at diagnosis and controls. UC microbiota was typified by a reduction in Bacteroidetes and an increase in Clostridia. Surprisingly, a reduction in bacterial diversity is not present in extensive UC at diagnosis. This is contrary to findings from previous studies in established disease and warrants further investigation.

Duodenal bulb biopsies should be routinely obtained in suspected Coeliac Disease

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Background:

It is conventional to obtain multiple duodenal biopsies beyond the ampulla of Vater (D2-3 biopsies) to histologically determine if a subject has Coeliac Disease (CD). There is increasing evidence that duodenal bulb biopsies (D1 biopsies) may complement diagnosis and increase diagnostic yield.

Aim:

To examine the diagnostic yield of D1 biopsies in the diagnosis of CD.

Methods:

Children (< 16 yrs of age) referred to our centre for diagnostic confirmation of CD following positive serological testing had a solitary biopsy obtained from the duodenal bulb in addition to four biopsies obtained from the distal duodenum (D2 and beyond) at upper gastrointestinal endoscopy. Biopsies were interpreted as part of the clinical service using the modified marsh criteria.

Results:

Thirty five patients (20 F: 15 M; median decimal age of 7.06 yrs) underwent diagnostic upper gastrointestinal endoscopy for suspected CD following positive serological testing. Histological confirmation was obtained in 31/ 35 cases. In 6 of the 31 patients (19.3%) a diagnosis of CD was made solely on basis of findings on the D1 biopsies. In 3/31 cases D1 biopsies were normal whilst clear changes of CD were seen on D2-3 biopsies. In 22/31 cases D1 biopsy findings were similar to D2-3 biopsy findings. Diagnostic yield from D1 biopsies (28/31) was comparable to D2-3 biopsies (25/31); p = 0.47.

Discussion:

In this series up to 20 % of patients with CD may have been misdiagnosed if D1 biopsies had not been obtained. These results are based on a solitary D1 biopsy compared to multiple D2-3 biopsies. Multiple D1 biopsies if taken might increase the yield further. We acknowledge the small number of patients studied.

Conclusions:

D1 biopsies complement D2-3 biopsies and increase positive yield in the confirmation of a diagnosis of CD. D1 biopsies should be routinely obtained when patients are subjected to endoscopy for the confirmation of CD.

Iron studies in children with coeliac disease compliant with gluten free diet

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Background:

Patients with untreated coeliac disease (CD) often have nutrient deficiencies at presentation such as iron deficiency anaemia. While a lot is known about this, iron status in CD patients compliant with a gluten free diet (GFD) is not widely studied, and guidelines on the long term follow up of these patients are inconsistent.

Aim:

The aim of this audit was to investigate the prevalence of iron deficiency in well-controlled CD patients compliant with a gluten free diet and to provide recommendations for future practice.

Subjects and Methods:

We run a dietician led coeliac clinic four times a year at our centre and routinely assess CD patients at their annual review for dietary compliance, growth, CD control (tTg measurement) and obtain blood tests to check their biochemical and haematological indices. Patients with elevated tTg levels (suggestive of poor control) and those with IgA deficiency and those already on treatment with iron were excluded from this analysis.

Results:

A cohort of 40 children with previous diagnosis of CD, who were compliant with gluten free diet were studied (median age 2.8 years, median duration of follow up 3.8 yrs). Iron studies from 226 well children from the Mersey region (age 1-5 yrs; 118 male, 93 female) served as the control group¹. Results are shown in the following table.

Iron Status	Current study (n=40)	Control Population ¹ (n= 226)	Chi Square results (with Yates correction) P values
Normal (Ferritin > 16 mcg/L, Trans sat > 15 %)	22/40 (55%)	59/ 226 (26%)	0.0005
Borderline Iron deficiency (Ferritin > 16 mcg/L, Trans sat < 15 %)	7/40 (17.5%)	65/226 (28.6%)	0.1990
Iron deficiency Ferritin < 16 mcg/L , Normal HB, MCV, MCH	11/40 (27.5%)	84/226 (37%)	0.3186
Iron deficiency Anemia Ferritin < 16 mcg/L , Low HB, MCV, MCH	None (0%)	19/226 (8.4%)	^{0.11}

References:

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Randomised Controlled Trial Comparing Liquid Diet Therapy (LDT) with Corticosteroid Therapy (CST) for Episodes of Active Disease Over a 12 Month Period: Report of Clinical Outcomes

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On behalf of participating centres: ¹Birmingham, ²Alder Hey (Liverpool), ³St George's (London), ⁴Royal Bristol, ⁵Sheffield, ⁶John Radcliffe (Oxford) Children's Hospitals NHS Foundation Trusts

Background:

Previous trials and systematic reviews comparing LDT with CST in Crohn's disease (CD) focussed on short term outcomes – primarily remission rate. It has been reported that CST is somewhat more effective in that respect, but many still favour LDT based on the potential advantages of steroid avoidance – including better growth and bone mineral density (BMD). We undertook a RCT of LDT v CST for use in all episodes of active disease occurring during a 1-year period of follow-up in order to compare longer-term clinical outcomes and in particular to examine the effects on bone metabolism and BMD.

Aim:

To present the clinical outcomes from that RCT.

Methods:

Multi-centre RCT of LDT v CST, the allocated treatment at entry being the treatment for relapses during the follow-up year. Alicalm (SHS International Ltd) was used as the liquid nutrition formula. Eligibility required a PCDAI > 20, and no previous use of LDT, CST or major immunosuppressive or biologic agents. Azathioprine was commenced in either arm of the study, if the allocated treatment failed to induce remission or if there were > 2 episode of active CD in 6 months. Remission, time to remission and subsequent outcomes, including adherence to allocation, relapse rate, quality of life (IMPACT III) and growth velocity were compared. All analyses were based on 'intention to treat'

Results:

In total 83 children (mean 13y, range 7.3-16.6) were recruited, 40 being allocated to LDT 43 to CST. The groups were comparable in age and disease activity at entry.

	LDT n=40	CST n=43	
Subjects at entry			
Age median (range)	13.2 (7.3-16.6)	12.8 (7.6-15.9)	p=0.58
PCDAI at entry, mean (SD)	40.1 (10.5)	39.9 (10.9)	p=0.95
Response to initial therapy			
Remission at 6wk (PCDAI ≤ 10)	20/37	27/40	p=0.25
Fall in PCDAI at 6wk, mean (SD)	24.6 (13.3)	28.5 (12.6)	p=0.19
Time (wks) to response, median (IQ range)	2 (2-3)	2 (2-4)	P=0.44
Adhered to allocation for 1 st treatment	29/40	37/43	p=0.17
Follow-up outcomes			
Number experiencing relapse within 1yr	23/40	23/43	p=0.83
Number having 2 relapses within 1yr	5/40	43	p=0.73
Adhered to allocation on relapse	15/28	19/27	p=0.27
Growth velocity cm/yr, mean (SD)	3.8 (2.8)	3.9 (2.6)	p=0.86
QoL score at 0wk, mean (SD)	59.5 (17.7)	57.7 (19.4)	P=0.66
QoL score at 6wk, mean (SD)	38 (15.2)	36 (23.4)	p=0.66
QoL score averaged at 6+12mo, mean (SD)	28.6 (17.2)	28.4 (17.8)	p=0.72

There was no significance between LDT and CST in relation to induction of remission. Neither was there any difference in rate of relapse or adherence to allocated treatment for relapses. There was no significant difference in growth velocity over one year. In both treatment groups there was a significant improvement in the QoL IMPACT III score following initial treatment and this was sustained over a 12 months follow-up (ANOVA p<0.001). There was no significant difference between the IMPACT scores at 6 wk, 6 months and 12 months in either treatment group. There was no significant difference in the QoL scores of the two groups.

Conclusions:

No clinical differences were identified between LDT and CST. The effects of these treatments on bone metabolism and BMD will be important in determining whether LDT has an important role for the treatment of active CD.

National IBD audit 2001 – Initial paediatric results

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Dr Sally Mitton, Consultant Paediatric Gastroenterologist, St Georges Hospital, London.
Calvin Down, RCP, London

The UK IBD audit is now in its 3rd round (2nd round for paediatrics) which is generating a large amount of useful local and national data simultaneously. The audit is a unique IBD collaboration between paediatric (BSPGHAN) and adult gastroenterologists (BSG), nursing (RCN), dietetics (BDA), surgeons (Association of Coloproctology of Great Britain and Ireland), GP's (primary care society) and patient organisations (Crohn's and Colitis UK). Funding support for the audit comes from Healthcare Quality Improvement Partnership (HQIP) and NHS Quality improvement Scotland (QIS). The audit is co-ordinated by the clinical effectiveness and evaluation unit of the royal college of physicians (London).

For the Organisational Data collection in the 2010 audit tertiary paediatric units in the UK were asked to supply data on their IBD service in September 2010. The participation rate for paediatric units was excellent and therefore the data presented represents a true perspective of paediatric IBD services in the UK in 2010. The data generated will be used to adapt the paediatric IBD service in the UK and highlight areas of good practice and areas for improvement. All units who participated will get their own local report as well as a written national report which will be available to all.

The collection of clinical cases started prospectively in September 2010 and will continue until 20 cases each of UC and CD are collected or 1 year after collection was started. As well as collecting clinical data for the first time a patient and GP questionnaire will accompany each clinical case. The clinical data which the audit will generate is a rich and unrivalled source of paediatric IBD data (outside of that generated by clinical trials) which can be used by all BSPGHAN members to the benefit of their IBD patients.

For this reason your previous and ongoing participation in the audit is vital.

Please note: The data shown in the presentation is censored and cannot be reproduced or quoted until the publication of the written organisational report. A copy of the talk will therefore not be made available to BSPGHAN members after the meeting.

GORD: The surgical approach

**Mr Fraser Munro, Consultant Paediatric Surgeon,
Royal Hospital for Sick Children, Sciennes Road, Edinburgh.**

Fundoplication is the most commonly performed major elective abdominal operation in paediatric surgical practice. In most centres this is now routinely performed as a laparoscopic procedure, with reduced post-operative analgesic requirements, fewer ICU admissions and shorter stay.

In the UK most funduplications are performed in children with co-existing neurological impairment. This is a group in whom the leading symptom suggesting a diagnosis of GORD is usually vomiting. It is not always clear whether this is simple reflux or part of a more complex upper gut dysfunction. Consequently the outcomes of surgery in this group are less good with post-operative retching and eventually recurrent vomiting being common. Management of these patients is difficult. Manipulation of feeds or drugs may be helpful in some. Re-do fundoplication for recurrent vomiting has a very high failure rate and has led to the development of other surgical procedures such as gastro-oesophageal disconnection. Our preference is to try gastro-jejunal feeding initially, and if this is well tolerated to move to a permanent surgical jejunostomy.

In the small number of normal children with severe GORD the most common problem post-operatively is dysphagia. There is little information in children but adult series suggest rates of 10-15% post laparoscopic fundoplication. Large adult studies have not found any of the suggested technical operative factors to be significant. Treatment is again problematic. Some will resolve with time and some will improve after dilatation of the wrap. A number will however continue with disabling problems and may require take down of the fundoplication.

In summary fundoplication is widely performed successfully for GORD in children. There are, however significant numbers of patients who have a poor result from surgery and this is not always easily predicted. Families need to be aware of these possibilities.

Inflammatory Bowel Disease – Gene Discovery And Beyond

**Professor Jack Satsangi, Professor of Gastroenterology
Molecular Medicine Centre, University of Edinburgh, Edinburgh**

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Over the last decade, over 100 genetic determinants of disease susceptibility in Crohn's disease and ulcerative colitis have been identified. The success of genome wide association studies in both Crohn's disease and ulcerative colitis is remarkable, and the data thus far strongly support the model that Crohn's disease and ulcerative colitis are related polygenic disorders sharing some, but not all susceptibility genes.

The challenge for the next decade is to capitalise on the success of gene-discovery programmes, and to build programmes of translational research which in turn will have real impact on clinical care and improve disease prognosis. The optimists and enthusiasts in the field hope for a seamless progression from the discovery of genetic determinants, through to full characterisation of the disease associated variants; a full understanding of the functional importance of the inherited genetic variation; and in turn translations to clinical practice – both in terms of early diagnosis, patient stratification, and response to therapy.

The success will depend critically on the integration of ever expanding scientific knowledge, with the detailed understanding of the clinical characteristics of Crohn's disease and ulcerative colitis.

Progress to date will be reviewed in this lecture, together with a review of the hopes and challenges over the next decade.

Autophagy: a key pathogenetic mechanism**Dr Craig Stevens, Scientist, Gastroenterology Unit, Molecular Medicine Centre, University of Edinburgh, Edinburgh**

The inflammatory bowel disease Crohn's disease (CD) has been intensively studied in recent years. The disease is complex resulting from a combination of genetic and environmental factors. The first insight into the molecular pathways associated with CD came from the identification of mutations in the CARD15/NOD2 gene. NOD2 protein is an intracellular receptor for the bacterial cell wall component muramyl dipeptide (MDP), and upon sensing of MDP, NOD2 activates the NF- κ B and MAPK inflammatory signaling pathways. It is now widely believed that CD comprises an aberrant immune response to intestinal bacteria. Due to recent advances in the field of genetics a significant number of genes have now been associated with CD. Of particular interest two genes, ATG16L1 and IRGM function in the autophagy pathway. Autophagy is a cellular degradation pathway that has been implicated in a growing number of clinical scenarios. During autophagy cellular components are sequestered into a structure called the autophagosome, which can fuse with a lysosome where cargo are degraded. Autophagy can degrade proteins, whole organelles as well as invading viruses and bacteria and participates in the delivery of their degradation products to major histocompatibility complex (MHC) molecules for activation of the adaptive immune response. Several recent studies have demonstrated that NOD2 and ATG16L1 function together to stimulate autophagy in response to bacterial infection. A basic overview of the autophagy pathway, how autophagy may contribute to CD and the therapeutic potential of manipulating autophagy in the treatment of CD will be discussed.

Paediatric Ulcerative Colitis comes of age**Dr Dan Turner, Consultant Paediatric Gastroenterologist
Shaare Zedek Medical Centre, Jerusalem**

Despite the fact that 17 of 20 epidemiological studies reported an increase or no-change in the incidence of pediatric UC, the management of pediatric ulcerative colitis (UC) has been heralded until recently by extreme paucity of clinical studies, even compared with pediatric Crohn's disease. The evidence for formulating management protocols have been extrapolated from adult literature. Over the last five years, however, numerous pediatric studies have been published in UC, which shed some light on this somewhat forgotten disease. There are several aspects in which pediatric onset UC is distinct from adults. In regards to infantile colitis, genetic linkage analysis of consanguineous families found the association of mutations in the IL-10R and IL-10 genes with infantile colitis. A pediatric GWAS study revealed three susceptibility loci, unique to children in pediatric UC. The management of young patients demands consideration of age-related concerns about body image, growth, toxicity of medications, and outcomes following colectomy. In the aim of developing a pediatric-friendly, non-invasive disease activity outcome measure, the Pediatric UC activity index (PUCAI) was formulated and evaluated in several independent studies. This simple 6-item index has been proven to be highly correlated with endoscopic appearance even in the absence of blood tests.

In comparison to adult-onset disease, UC occurring in childhood is much more often extensive and, as such, is associated with higher likelihood for acute severe exacerbations (28% over 2-3 years compared with 25%, at most, over 10-11 years) and slightly higher failure rate of corticosteroids (28% vs. 34% in two meta-analyses). Among the different predictors of steroid failure in acute severe colitis, the PUCAI has proven to perform best in a retrospective single center study and in a large multicenter prospective cohort study, even in comparison with several biomarkers including fecal calprotectin, M2-pyruvate kinase, lactoferrin and S100A12, and serum IL-6. In the "Get set, Go!" criteria, a PUCAI score greater than 45 points on the third hospital day should dictate preparation for second line therapy and a PUCAI > 65 on the fifth day should dictate execution of the planned therapy. Intermediate patients may be treated for additional 2-5 days until decision is reached. This treatment paradigm has been found to have high positive and negative predictive value at days 3 and 5, respectively. General predictors of response to both steroids and infliximab salvage therapy all relate to disease activity; the more severe disease at admission, the less likely the child will respond. A recent meta-analysis of cohort studies, mainly retrospective, shows that the effectiveness of infliximab, cyclosporine and tacrolimus in pediatric acute severe UC is similar to adults with a short term response rate of 76-79%. More recently, an international group of experts in pediatric IBD formulated guidelines for managing acute severe UC in children. The guidelines, consisted of 28 formal recommendations and 34 practice points, have been endorsed and supported by the European Crohn's and Colitis Organization (ECCO) and the pediatric IBD Porto group of ESPGHAN.

Paediatric IBD – Looking forward**Professor Anne Griffiths, Division Head
Hospital for Sick Children, Toronto**

The past decade has been one of major advances in paediatric IBD, most notably the elucidation of genes influencing its complex development, and the emergence of anti-TNF antibodies as therapies targeting intestinal healing. The coming decade promises intense exploration of the role of the enteric microbiome in search of IBD triggering and perpetuating factors, which might be modifiable in affected or genetically at-risk hosts.

As the heterogeneity of paediatric “Crohn diseases” and “colitides” are increasingly appreciated, efforts to understand the genetic and environmental influences on phenotypic variation will continue. Genotyping of known IBD susceptibility genes and studies of gene expression in tissues can be expected to play an increasing role in elucidation of pathways involved in disease, with the goal ultimately of optimizing therapy for individual patients.

As basic researchers struggle to understand the complex pathogenesis of paediatric IBD, clinician/researchers must organize to standardize and prospectively evaluate and refine treatment protocols, recognizing and aiming to understand the heterogeneity of disease and diversity of clinical course.

POSTER ABSTRACTS

A Case Report of Distal Colonic Cotton Bezoar Obstruction in a child with PICA, Severe Iron Deficiency Anaemia and previous Short Gut Syndrome (SGS) related Surgery.

Abul-eis H, Hallows R, Butt A.M.

Royal Alexandra Children's Hospital, Brighton & Sussex University Hospitals

Background and Aim:

Colonic bezoar is very rare in children (total of only 4 reported cases in the literature of colonic lithobezoar). To our knowledge this is the first reported case of cotton colonic bezoar and any type of bezoar in a child with previous SGS related surgery. We report a unique case of an unusual complication to illustrate recognition of this problem and describe its management in a patient with previous intestinal surgery.

Subject and Methods:

The male subject was antenately diagnosed with Gastroschisis, managed by silo reduction shortly after birth but complicated on day (D) 29 by volvulus and bowel infarction. Following surgery he was left with 50 cm of small bowel and absent ileocaecal valve. He required Parenteral nutrition (PN) for 6 months and suffered from intestinal failure-associated liver disease (IFALD). At two and half years of age he presented acutely with intermittent brief self-limiting screaming episodes associated with drawing up of his legs, abdominal distension but no vomiting and failure to open his bowels for one week. In the preceding 6 months he had developed 'constipation' and despite regular maintenance Polyethylene Glycol (PEG) electrolyte solution, he was hospitalised on 2 occasions to administer enemas for faecal disimpaction. Furthermore, his mother recognised new unusual behaviour of chewing on linen and clothing over a few months but was not overtly concerned attributing this to part of his normal behavioural problems relating to his age and 'fussy' eating. On admission, marked abdominal distension, prominent superficial veins overlying the neck and abdomen and a large palpable pelvic presumed faecal mass were noted.

Results:

Plain Abdominal X-ray showed gross 'constipation' including appearance of ball-like faecal shadows and prominent distal colonic distension. Abdominal ultrasound confirmed bowel distension but absence of free fluid and normal portal venous flow. Neck ultrasound showed only previously known finding of right internal jugular vein occlusion and associated collateral vessels. He was managed initially with intensification of both rectal (including Phosphate, olive oil enemas and saline washouts) and oral PEG electrolyte solution treatment with minimal response. On D2, nurses documented the appearance of pieces of cloth per rectum and later that day, a rectal suction tube removed a large 5x 8 cm piece of cotton material with marked clinical improvement in abdominal distension. The characteristics of the piece, later identified it as having originated from a cotton T-shirt belonging to the child. On D4, Klean-prep infusion via NG tube was commenced and smaller pieces of cotton material were retrieved. A contrast study with follow through on D11 revealed no evidence of obstruction but persistence of a degree of bowel distension. Subsequently over a 2 week period treatment was transitioned to a combination of oral PEG electrolyte solution and twice weekly rectal washout prior to discharge. Screening blood investigations showed severe iron deficiency anaemia (Hb =6.7g/dl MCV=58.9, ferritin = 4.3); coeliac serology, folate and vitamin B12, LFT's, clotting were normal.

Summary and Conclusion:

Our case highlights the very rare complication of Colonic bezoar in a patient with SGS-related surgery and its successful conservative management. In retrospect, the pattern of 'constipation' in the preceding months, unusual in SGS patients (tendency for fast transit) could be considered as a potential 'warning' feature. PICCA secondary to iron deficiency is likely caused by a combination factors including poor dietary intake and malabsorption; bacterial overgrowth would typically cause diarrhoea. Bezoars usually collect in the stomach or in the small intestine (latter, often requiring surgical intervention). In our case we speculate that the short intestinal length and absence of ileo-caecal valve has facilitated the passage of material to the colon causing progressive impaction which mimicked 'constipation' and eventually caused obstruction.

Reference:

Numanoglu KV, Tatli D. A rare cause of partial intestinal obstruction in a child: colonic lithobezoar. *Emergency Medicine Journal* 2008;25:312-3.

An Audit to assess patient outcome and time saving benefits of referral to the Specialist nurse led constipation clinic

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Background:

Constipation is one of the most common childhood ailments, accounting for around 25% of paediatric gastroenterology referrals in one year. The University Hospital of North Staffordshire has run a specialist nurse led constipation clinic since April 2008 in an attempt to provide more support to children and families with constipation and to relieve the time pressures on consultants. Attendance at the clinic includes supporting the child and family, providing education, and promotes parental involvement in the titration of maintenance medications.

Aim:

The Aim of this Audit is to assess the outcome and treatment satisfaction of the families and children attending the specialist nurse led clinic, and whether this could indicate a positive shift towards the handling of more common conditions by specialist nurses

Subjects and Methods:

A retrospective review of children (2-18 years) who attended the nurse led clinic between April and December 2008 was conducted. Children with organic disorders underlying the diagnosis of constipation were excluded. Data was collected from clinical notes, letters, computer records and clinic attendance sheets. A concomitant questionnaire was also sent to parents to assess their satisfaction with the outcome and process of attending the clinic.

Results:

Twenty children were included in the audit. Of these, (9) 45% had soiling behaviour at initial assessment. Following attendance at the clinic, none were soiling (6 months follow up). (15) 75% children were treated with a stimulant laxative before attendance at the clinic. Following attendance, all children were maintained on mavicol only. Prior to referral to the clinic, all twenty children used a total of 78 appointments with consultant paediatricians regarding their constipation. During attendance at the clinic, the twenty children used 82 appointments with the nurse specialist. In the 6 months following discharge from the nurse led clinic, only one consultant appointment was required for a child with medication compliance issues. Following attendance at the nurse led clinic, (16) 80% of children have returned to the care of their GP's, (3)15% continue to be under follow up. One child was diagnosed with celiac disease whilst attending the nurse led clinic and is now under consultant care.

The parental questionnaire results indicated that 94% of those attending were happy to see the nurse. The same number also reported that they felt their questions were answered readily and children were treated with privacy and dignity. All were satisfied or very satisfied with the service they received.

Summary and Conclusion:

Chronic constipation is a common causes of morbidity in childhood. Other studies have demonstrated greater patient satisfaction and better response to treatment when children are managed in a nurse led clinic. The audit results echo these findings, with an overwhelmingly positive response to treatment and attitude towards the clinic. No children were soiling up to 6 months post-discharge and use of stimulant laxatives reduced. There was also a significant reduction in the number of consultant appointments needed for the children.

The nurse led clinic is successful, potentially financially beneficial and reduces pressures on specialist consultants. In the time of this newly reforming and re-structuring NHS, perhaps nurse led clinics can take the clinical lead in more conditions.

Auto-immune Sclerosing Cholangitis (ASC) in children with inflammatory bowel disease (IBD)

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Introduction/ Background:

Primary sclerosing cholangitis (PSC) is a chronic progressive disorder characterised by chronic inflammation and stricture formation of the biliary tree. It occurs in 2-5% of adult patients. Response to immunosuppressive treatment is poor and the long term risks for colorectal cancer, cholangio-carcinoma and risk of liver transplantation are increased significantly. In contrast, paediatric patients often have auto-immune features at presentation and respond well to immunosuppression. It is important to confirm the diagnosis by liver biopsy before starting immunosuppressive treatment for colitis, as optimal management of PSC requires additional therapy. Maintenance drug treatment and follow up schedules differ for patients with IBD complicated by ASC.

Aim and Subjects/Methods:

A retrospective review of nine patients with a histological diagnosis of auto-immune sclerosing cholangitis (ASC) or auto-immune hepatitis (AIH)/ASC overlap syndrome at Addenbrookes NHS Trust between 2002 and 2010.

Nine (5.4%) out of 147 children with IBD were diagnosed with ASC or AIH/ASC overlap syndrome over the 8 year period. Eight of the nine children presented with colitic symptoms while in one child the diarrhoea had settled but liver function tests (LFT's) remained abnormal. The Gamma glutamyl transpeptidase (GGT) was the most sensitive liver function test with all nine children having abnormal values ranging from more than 3 x to 8 x normal. Further blood tests showed auto-immune features including an elevated total IgG and positive auto-antibodies in all children.

All 9 children underwent upper and lower endoscopy and percutaneous liver biopsy under one general anaesthetic (Table 1).

All 9 patients in our series receive maintenance treatment for their PSC with ursodeoxycholic acid and prednisolone 5mg/day and are in remission 6 to 93 months from diagnosis.

Patient	1	2	3	4	5	6	7	8	9
Liver Histology	ASC	ASC	ASC	AIH/ASC	AIH/ASC	ASC	ASC	AIH/ASC	AIH/ASC
Fibrosis	mild	mild	severe	severe	mild	mild	mild	severe	mild
MRCP	N	AB	N	AB	AB	AB	AB	AB	AB
IBD diagnosis	UC	UC	UC	UC	UC	UC	UC	UC	UC

Conclusion:

We recommend that all children with colitic symptoms, who undergo endoscopy for suspected IBD, require liver function tests including GGT at presentation. If there is elevation in either transaminases or GGT, the patient should ideally undergo a liver biopsy at the time of endoscopy to confirm the diagnosis of suspected ASC. Blood test investigations most strongly associated with ASC were an elevated GGT and a positive auto-antibody screen (ANA, anti-smooth muscle, anti-LKM or p-ANCA). Once the histological diagnosis of cholangiopathy is confirmed, MRCP can distinguish between large and small duct ASC.

Biochemical markers in paediatric inflammatory bowel disease

Soman S, Gautam S, Charlton C. Department of Paediatric Gastroenterology, Queen's Medical Centre, Nottingham.

Introduction:

Routine blood investigations are regularly performed in secondary and tertiary care to aid in predicting the presence or absence of intestinal inflammation. There is a need for laboratory time and costs to be taken into account when planning these investigations.

Aim:

To determine the most effective routine blood investigation as a marker of inflammation in paediatric inflammatory bowel disease (IBD).

Methods:

A retrospective case note review of patients attending the paediatric gastroenterology department, Queen's Medical Centre, Nottingham with a confirmed histological diagnosis of Crohn's disease (CD) or ulcerative colitis (UC) was performed. Values for haemoglobin (Hb), neutrophils (neut), lymphocytes (lymp), platelet count (plt), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), albumin (alb) and alpha-1-acid glycoprotein (AGP) were noted at the time of diagnosis and again when the patient was completely asymptomatic. Receiver operating characteristic (ROC) curves were analysed.

Results:

A total of 62 patients (CD n=36; UC n=26) were included. ROC curve analysis for presence or absence of disease activity (n=124 events) is shown in Table 1. The area under curve (AUC) for a test parameter approaching a value of 1.0 gives almost 100% reliability that the test is able to distinguish between disease activity or inactivity. The AUC for a test parameter approaching a value of 0.5 implies the test is not likely to differentiate between disease states. AGP is a clinically significant discriminator compared to CRP (p<0.001) and ESR (p<0.05). The criterion values suggested by the analysis for each parameter to differentiate between disease activity and quiescence were similar to the actual laboratory reference ranges.

Table 1

Parameter	AUC	Sensitivity %	Specificity %
AGP	0.902	80.6	90.3
Alb	0.853	69.4	93.5
ESR	0.833	67.7	90.3
Hb	0.816	59.7	88.7
Plt	0.804	82.3	71.0
CRP	0.754	61.3	91.9
Neut	0.732	71.0	69.4
Lymp	0.585	32.3	83.9

Table 2

Parameter	AUC CD	AUC UC
Alb	0.944	0.726
AGP	0.931	0.885
Hb	0.861	0.757
ESR	0.856	0.801
CRP	0.850	0.634
Plt	0.837	0.742

Table 2 demonstrates that AGP functions as a good test parameter in both CD and UC, but that CRP and albumin are better discriminators of disease activity in patients with CD than UC (p<0.05). In patients with UC, ESR was a superior discriminator over CRP (p<0.05). A cost analysis for the test parameters is presented.

Conclusion:

Of the routine blood investigations commonly performed in monitoring paediatric patients with IBD, AGP gives the best likelihood of defining disease activity or quiescence. This could be extrapolated to screening for presence of IBD. Albumin is a good discriminator of disease activity in CD but not UC. CRP is not a useful marker in UC

Bone health in paediatric intestinal failure patients receiving long-term home parenteral nutrition.

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Introduction:

Paediatric patients receiving long-term home parenteral nutrition (PN) may present with low bone mineral density (BMD). It is uncertain whether this reflects small body size or suboptimal bone mineralization.

Aim:

To assess bone health in paediatric patients receiving long-term home PN due to severe intestinal failure.

Methods:

Bone mass was measured using Dual X-ray Absorptiometry (DXA; GE Lunar Prodigy) at the lumbar spine (LS; L2-4) in 46 patients (24 boys) aged median 5 years (range: 3.2- 12.3 yr). PN duration was median 5 years (range: 3.1- 12.2 yr).

Results:

Mean weight, height, and BMI Standard Deviation Scores (SDS) were -0.8 (SD 1.01), -1.80 (1.46), and 0.48 (0.89). Mean age-matched LS BMD SDS were -1.3 (SD 1), -2 (1.7), and -1.6 (1.9) for patients with short gut (n=12), enteropathy (n=20), and pseudo-obstruction (n=14). To assess the effect of body size, Bone Mineral Apparent Density (BMAD) SDS were calculated. Mean BMAD SDS was -1 (SD 1.3), -1.7 (1.2), and -1.8 (1.9), for the three groups respectively. Overall, 18 patients (40%) had low BMD (SDS < 2.0) and 15 (32%) had low BMAD. Ten patients (of 24 with bone age data) had delayed bone age > 2SD. Patients with gut inflammation (n=20) were significantly shorter than those without (mean height SDS -2.6 vs. -1.1, p 0.06).

Conclusions:

Despite close nutritional status monitoring, paediatric patients on long-term PN, especially those with underlying enteropathy, were shorter than the UK reference and had low bone mass. Small skeletal size contributes to low bone mass but there was evidence of reduced mineralization at the LS after adjusting for size.

Catch up growth after use of monoclonal antibodies to tumor necrosis factor alpha (TNF) in children with Inflammatory Bowel Disease (IBD)

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Introduction/Background:

Infliximab, a chimeric monoclonal antibody to tumor necrosis factor alpha (TNF α) is effective in inducing and maintaining remission in children with Inflammatory Bowel Disease (IBD). It can achieve significant catch up growth in children with IBD who respond to it. More recently Adalimumab, a humanised monoclonal antibody to TNF α is also used in treating IBD.

Aim:

To describe the experience in our hospital with the use of monoclonal antibodies to (TNF) in children with IBD.

Subjects and Methods:

Data was collected from case notes retrospectively over a 10 year period from 1999-2009.

Results:

- A total of 30 children received infliximab during the 10 year period; 26 had Crohn's Disease (CD) inflammatory in 14, fistulating in 7 & structuring in 5; 2 had Ulcerative colitis (UC) and 2 In determinate colitis (IBDU). The ages ranged from 6 to 17 years at the time of diagnosis with 73% in the range 10 -15 years. Common symptoms included abdominal pain, weight loss and diarrhoea in 80%, perianal disease in 36% and 50% had extraintestinal manifestations. 70% of patients with CD had granulomas in endoscopic biopsies. All were treated with other immunomodulators prior to commencing infliximab. The indications for induction with infliximab were severe Crohn's disease (19), fistulating CD (7), and 30 (all cases of IBD) were, or had become, unresponsive to other immunosuppressants. Time from diagnosis to starting infliximab was median (range) 18 months (10 days - 85 months). Age at which infliximab started was median (range) 14 yrs (7-18yrs).
- 24 of 30 patients (80%) responded to the induction course (3 doses) of infliximab. Of those unresponsive (6); 2 came to colectomy, one had laparotomy without corrective surgery, 1 child was lost to follow up, 1 had a severe hypersensitivity reaction after the 1st dose and 2 had a second induction course at varying intervals after the 1st. 1 had anaphylaxis during the 1st dose of the 2nd course so infliximab was discontinued. The other had a 2nd induction course after a 2 year and responded well. This patient could not receive maintenance as their PCT refused funding. Of the 24 who responded, 22 received maintenance therapy (1 dose x 6-8wky) for a median duration of 4 years (range 1 -10 yrs). 3 patients relapsed during maintenance. 4 children relapsed after stopping maintenance. 3/4 restarted infliximab. 2 responded and were in remission. 1/3 lost response and therefore started on Adalimumab.
- 10 children who were growth faltering on other immunosuppressants had catch up growth crossing 2 centiles after commencing and maintaining on infliximab.
- Side-effects noted in 20% (1 anaphylaxis, 1 hypersensitivity, 4 mild)

Summary:

Indication for starting infliximab complied with NICE guidance

80% responded to induction course after 3 doses of Infliximab

73% had maintenance of remission at 1 year with duration of remission: median (range) 4yrs (1-9yrs).

There was significant improvement in growth in 45% of those on maintenance (crossed at least 2 centiles upwards in height)

Episodic treatment was given in 2 due to funding problems from PCT

Conclusion:

Infliximab has helped to achieve and maintain remission in children with IBD refractory to conventional immunomodulators and also to achieve significant catch up growth.

CMV PCR is indicated in symptomatic children whereas routine EBV PCR screening is necessary in effective management of post-intestinal transplant patients

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Background:

EBV related PTLD and CMV viraemia is seen in donor to recipient mismatch (D-R-M) population in solid organ transplantation. CMV status of donor is routinely tested but no current regulations exist regarding EBV testing. Historically higher incidence of PTLD is seen in intestinal transplant (ITx) due to higher intensity of immunosuppression (iMs).

Aims:

To audit if children undergoing ITx had pre-transplant serology testing, to identify incidence and if CMV and EBV infection occurs irrespective of D-R-M and identify factors (apart from iMs) that increases risk.

Method: Retrospective analysis was performed in children undergoing ITx from January 2005-February 2010. EBV, CMV serology & PCR levels were obtained from microbiology records.

Subjects: 42 children were identified: 10 had an isolated ITx, 26 had a liver and ITx and 6 had a modified multivisceral transplant. Median age at time of transplant was 1.91 years (range 0.64-16.18).

Results: Donor status of CMV and EBV was recorded in 42/42(100%) and 21/42 (50%) respectively.

Table 1: Incidence of CMV, EBV viraemia and infection depending on D-R-M

N=42	CMV viraemia	CMV infection	EBV viraemia	PTLD
Total number of children	10 (24%)	1	21 (50%)	6 (14%)
Donor recipient mismatch	5	1	4	2
No Donor-recipient mismatch	5	0	12	3
Unknown serology	0	0	1	1

Table 2: Detection of children with CMV,EBV viraemia and infection by screening or symptoms

N=42	CMV viraemia	CMV infection	EBV viraemia	PTLD
Detection by screening	3	0	17	1
Detection by symptoms	7	1	4	5
Median time from ITx to viraemia/ infection(days)	100	1501	41	102.5

17 (81%) children were picked up through screening and 4 (19%) children had their EBV status checked directly because of symptoms. Not all recipients or donors had pre-transplant EBV serology(including some in the no D-R-M), it is therefore difficult to analyse the significance of donor mismatching to future development of viraemia/ PTLD. 5 children developed EBV driven PTLD; whereas 1 child had EBV negative PTLD. Of the 10 children with CMV viraemia, 3 (30%) were identified through screening and 7 (70%) were tested directly because of symptoms. 1 child developed CMV enteritis, 2 children had concurrent PTLD.

Median age (in years) at transplant was 1.76 for the PTLD group and 3.39 for the non-PTLD group, p=0.0004. 1 child died as a consequence of brain PTLD.

Conclusion:

Donor screening for EBV should be made mandatory by the regulatory authorities. CMV screening should be done routinely if there is a donor mismatch otherwise testing when symptomatic should be sufficient. All paediatric ITx particularly the younger children acquiring donors from older children or adults should have routine EBV PCR screening as there is a potential for development of PTLD.

Comparison of cost effectiveness of Transoral Incisionless Fundoplication (TIF®, EsophyX®) with conventional laparoscopic and open fundoplication.

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Introduction:

TIF® is a novel, completely incisionless approach in the treatment of gastro-oesophageal reflux disease (GORD) using EsophyX® device from EndoGastric Solutions. The objective of this study was to compare hospital costs of children undergoing EsophyX® fundoplication to open and laparoscopic surgical fundoplication for chronic GORD.

Methods:

The hospital costs of children undergoing EsophyX® fundoplication (n=10), laparoscopic nissen fundoplication (LNF, n=10), and open nissen fundoplication (ONF, n=7) were retrospectively analysed and were provided by the administration of Sheffield Children's Hospital NHS Trust. All the procedures were performed between December 2008 to September 2010 at the same hospital and team. Operative time, hospital stay, hospital charges excluding high dependency/Intensive care/neonatal surgical unit and total costs was recorded. Ten children in EsophyX® fundoplication group were part of the feasibility study with median age 12 (range 9-16) years, ten children in LNF were randomly selected with median age 11 (range 0.5-16) years and seven of ten children's data was available in ONF group with median age 2.5 (range 2-16) years were recorded.

Results:

Medians of operation times in EsophyX®, LNF and ONF were 54.5, 92.5 and 106 minutes respectively. Hospital stay is significantly shorter in EsophyX® fundoplication group when compared to ONF and comparable to LNF. The hospital charges including total costs were significantly lower in EsophyX® when compared to both LNF (P<0.05) and ONF (p<0.001).

Table: Median (Range) and 95% Confidence Interval for difference between the means.

	EsophyX® (n=10)	LNF(n=10)	ONF(n=7)
Operative time (mins)	54.5(35-128) 45.04-89.56	92.50(43-195) 72.51-128.89	106.00(71-130) 78.83-122.88
Hospital stay (days)	2(1-4) 1.709-3.91	5.5(2-7) 3.267-6.133	10(7-30) 5.836-20.164
Hospital costs excluding HDU/ITU/NSU (pounds)	2616.0(2443-3679) 2419.7 – 3020.7	4662.5(2616-9012) 3141.4 -5733.8	4667.0(3081-12242) 2801.5-8543.9
Total costs (pounds)	2616.0(2443-3679) 2419.7 – 3020.7	4666.8(2616-10169) 4025.7-7989.1	10892(4666-20002) 6918.5-16130

Conclusion: EsophyX® TIF® has reduced stay in hospital and is cost effective when compared with LNF and ONF.

Confocal Endomicroscopic Features of Gastrointestinal Graft-Versus-Host Disease in Children

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Background and aims:

Confocal laser endomicroscopy (CLE) is a recent development which enables surface and subsurface imaging of living cells in vivo at x1000 magnification. The aim of the present study were to define confocal features of Gastrointestinal Graft-Versus-Host Disease (GI GVHD) in children developing GVHD following bone marrow transplantation (BMT) in comparison to histology.

Patients and methods:

5 patients (1 female) with a median age 7.83 years (range 0.66 – 14.41 years) and a median weight of 29.34 kg (range 7.4-37.7 kg) suspected with GVHD following BMT underwent colonoscopy or proctoscopy using the confocal laser endomicroscope (EC3870CILK; Pentax, Tokyo, Japan). confocal images were compared with same site histological sections by 2 experienced paediatric histopathologists and endoscopists.

Results:

The median procedure time was 22.4 minutes (range 12 -30 minutes). During CLE a total of 608 confocal images were captured and 22 same site biopsies were taken. The confocal images and biopsies were subsequently compared and the following confocal features of GI GVHD were defined.

1. Distortion of crypt architecture or even complete loss of crypt architecture.
2. Oedema of epithelial cells with loss of definition of cell membranes
3. Increased vascularity of lamina propria
4. Variable degrees of crypt destruction

Conclusion:

This is the first report of the use of CLE in GI GVHD in children and provides the description of confocal features of GI GVHD in children. This pilot study shows that it is now possible to make an in-vivo diagnosis of GI GVHD during endoscopy using CLE. In addition, CLE enables targeting biopsies to abnormal mucosa thus aiding a definitive histological diagnosis and also reducing the number of biopsies needed in GvHD patients.

Cycled enteral antibiotics to reduce catheter related systemic bacterial infection in paediatric intestinal failure: A case control study

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Background:

Long-term Parenteral Nutrition (PN) has transformed the prognosis for children suffering from Intestinal Failure (IF). However, PN is associated with considerable morbidity and mortality including catheter related systemic bacterial infections (CRBSI). Bacterial overgrowth and abnormal intestinal permeability leading to bacterial translocation is implicated in the pathogenesis of CRBSI, with a strategy of cycled enteral antibiotics (CEA) proposed to reduce CRBSI. However there are no published data on CEA in paediatric IF (1).

Aims:

This study examines a strategy of CEA in reducing the incidence of sepsis in paediatric IF patients on long-term PN.

Methods:

Retrospective database analysis of the incidence of sepsis rates of patients on long-term PN at a tertiary paediatric hospital. Baseline demographics; diagnosis; surgery; intestinal length: ileocaecal valve; PN duration; weaning were noted. CEA were started at clinicians discretion as metronidazole 7.5mg/kg tds for 2wk, followed by a combination of colistin 100 000u qds with tobramycin 25mg qds daily for 2wk. This was followed by 2wk of no antibiotic therapy before recommencing the cycle. Patients were retrospectively assigned into those that received CEA or a control group. A CRBSI from case-note search was defined as clinical evidence of sepsis (fever, systemically unwell) resulting in active antibiotic therapy being prescribed by the medical team, with a positive growth from peripheral or central line culture. A recurrent growth of bacteria was only considered a 'new' CRBSI episode if the patient had been well for 5 days after cessation of antibiotics (2). Adverse outcomes recorded included antibiotic reaction or positive blood culture with organisms resistant to CEA in the treatment group. Central venous catheter (CVC) removal rates for CRBSI were gathered. Infection rate was expressed as number of infections per 100 PN patient days. CRBSI rates before and after starting CEA were compared for each patient using Wilcoxon signed rank test.

Results:

Fifteen patients received 9512 PN days with a total of 131 sepsis episodes at 1.38CRBSI/100days. 8 patients received CEA with 7 controls; baseline demographics were comparable at start of study. The 8 patients received CEA for 47% of the study period. All of the CEA patients demonstrated a decrease in the number of episodes of sepsis following the introduction of CEA viz there was a significant reduction in the CRBSI rate during treatment with CEA (2.14/100days vs. 1.06/100days (median effect size -1.04, CI 95% -1.93,-0.22 p=0.014)). 2/7 of the control group demonstrated a reduction in CRBSI in the comparable part of the study when the intervention group received CEA with the remaining 5/7 showed an increase in CRBSI rates The control group did not show a significant change in their CRBSI rate during the latter part of the study (1.91/100 days vs. 2.38/100days (median effect size 0.92, CI 95% -1.96, 4.17, p=0.53)). There were no CEA related adverse outcomes. Although over all CRBSI rate fell after the introduction of CEA the proportion of gm -ve organisms remained constant in the treatment group. CVC removal did not change significantly in the treatment or control group throughout the study.

Conclusions:

This study demonstrates that the eight patients evaluated, who received a total of 5457 days of PN, had a significant reduction in CRBSI once CEA were introduced. A control IF population who did not receive CEA during an equivalent phase of treatment did not demonstrate a significant change in CRBSI. As far as we can ascertain, this is the first study to review the effectiveness of CEA in any IF population. CEA may be beneficial to IF patients and larger prospective multicentre studies are required to ascertain this fully.

References

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Diagnostic Yield of Upper GI Investigations in Children Presenting With Symptoms of GOR

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Introduction:

Gastroesophageal reflux (GOR) represents the most common gastroenterological symptom that leads to a referral to pediatric gastroenterologists during infancy. As many as 60-70% of infants at least experience regurgitation during one feeding per 24-hour period by the age of 3-4 months. The distinction between primary GOR and secondary GOR (due to food allergy) in infancy and childhood is not always easy and may warrant specific investigations to determine the underlying cause.

Aim of the study:

To assess the diagnostic yield of different diagnostic modalities for children presenting with different GOR symptoms.

Patient and methods:

We prospectively studied 73 patients (M:F 2:1, mean age 5yrs, range 1yr to 10yrs) over a 6 months period referred to our tertiary GI center with regurgitation, abdominal pain and recurrent chest infections. All patients underwent upper GI endoscopy, 24 h pH study and upper GI contrast study. Patients were divided into two groups according to their presentation; the first group was with regurgitation and abdominal pain and the second was with regurgitation and recurrent chest infections.

Results:

Out of the 73 cases studied, 48 cases (66%) had primary GOR. 24 h pH study was significantly positive in 38/48 cases (79 %). Evidence of oesophagitis was demonstrated on macroscopy and histology in 28/48 case (58%). Upper GI contrast studies showed normal anatomy in all patients but reflux was seen in 19/48 cases (40 %). 30/48 (62.5%) had regurgitation as the main presenting symptom, of whom 21/30 (70%) had both positive 24h pH study and oesophagitis. 25/48(52%) presented with recurrent chest infections, of whom 22/25 (88%) had a positive 24 h pH study and 14/25 (56%) had oesophagitis. 22 (30%) of the 73 cases had secondary GOR on the background of food allergy. All of them presented to us with abdominal pain (100%) and 17/22 (77%) had regurgitation. Gastritis and eosophagitis were documented in 20/22 (91%), whilst 24 h pH study and upper GI contrast were only positive in 7/22 (33%) for each of them.

Conclusion:

GOR symptoms continue to present a common GI problem in children. Our data suggest that GOR represents a heterogeneous group of patients, with primary and secondary causes. Our study suggests that regurgitation is a common presentation in both groups. Recurrent chest infections tend to be more primary than secondary GOR, whilst abdominal pain tends to reflect a secondary cause with food allergy, particularly in the form of inflammatory and eosinophilic gastritis and oesophagitis. We found that upper GI endoscopy with abnormal macroscopical and histological findings, was of great value in diagnosing secondary GOR, while 24 h pH studies were more helpful in diagnosing primary GOR without evidence of gut inflammation.

Although one quarter of patients had coincidental findings of reflux on upper GI contrast studies, we suggest that this is of little value in diagnosing both primary or secondary reflux and its role should be limited to assess anatomical abnormalities, such as malrotation or hiatus hernia.

Patients who are labeled as primary GOR may well still reflect a secondary phenomenon such as reduced gastric compliance or oesophageal dysmotility and other specific tests such as Electrogastrography, gastric emptying studies or oesophageal manometry might be of help in such conditions. A larger study is needed to address this issue.

Efficacy of single intravenous Iron Dextran infusion in children with IBD who are resistant to oral iron therapy.

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Background:

Anaemia is a frequent finding in children with Inflammatory Bowel Disease (IBD). Iron deficiency is at least in part responsible for this and hence iron supplementation is an important part of the management of patients with IBD. Oral iron is safe and inexpensive and is usually the preferred treatment for iron deficiency anaemia. However, it has been shown to be less effective in active IBD, when intravenous iron therapy can lead to rapid replenishment of iron stores in otherwise resistant cases of iron deficiency anaemia. Parenteral iron therapy is less often used because of the potential side effects. There is only limited evidence in children with IBD on the use of parenteral iron therapy.

Aim:

To retrospectively review efficacy and safety of single dose intravenous iron dextran infusions in children with IBD.

Materials & Methods:

A complete list of children with IBD aged 13y (range 5-17y) who received intravenous iron dextran infusion was obtained from the department of Pharmacy and departmental diary. Electronic medical records and hospital electronic results reviewing system (e-MR/ Web -OCS) were used to gather diagnostic and haematological information pre-infusion (median 4m (2-10m), at time of infusion and post-infusion (median 3m (1-12m). Staff administering the infusions were interviewed and electronic discharge letters reviewed to identify any side-effects. All children had either failed to respond to oral Fe supplementation for a median of 8 weeks (1-12 weeks), or been intolerant to oral iron supplements. Results were then charted and analysed.

Results: 11 patients (4 females), total number of infusions = 11

	Pre-infusion	At infusion	Post infusion	Δ pre-infusion v. Δ post-infusion (p value)
Hb	10.5 (8.4-12.1)	10.2 (8.2-12.4)	12.2 (11-13.7)	0.56
MCV	70.7 (67-77.3)	70.75 (64-83.5)	81.2 (72.2-82.6)	0.25
Serum Iron	3.3 (1.6-5.2)	3.2 (2.3-5.1)	7.5 (2.9-12.4)	0.11
Ferritin	9.85 (4.1-73)	7.2 (<1 – 32.5)	80.5 (30.7-116.9)	<0.0001
% iron saturation	5.5 (3-36)	5 (3-11)	18 (9-23)	0.002

All results show median (range)

Discussion:

Iron deficiency anaemia is a common problem in children with IBD. There is only limited experience in the use of systemic iron supplementation in children with IBD. This small retrospective review of patients shows that a single IV iron dextran infusion can be safe and efficacious for children with IBD who fail to respond to oral Fe supplementation.

Evaluation of non-invasive markers of fibrosis in paediatric liver disease.

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Background:

Outcome of liver disease in children is mainly determined by severity and progression of liver fibrosis. Liver biopsy is the accepted standard for evaluating fibrosis but is limited by the need for sedation in children, sampling error and risks including bleeding. The aim of this study was to compare tools for noninvasive assessment of liver fibrosis in a paediatric cohort.

Methods:

Children were recruited at the time of liver biopsy and underwent transient elastography and serum collection on that day. Liver biopsies were scored by a hepato-histopathologist from F0 (no fibrosis) to F4 (cirrhosis). Serum samples underwent analysis for the Enhanced Liver Fibrosis (ELF) test; comprising hyaluronic acid, P3NP and TIMP1 (iQur, UK). CK18-M30 levels (caspase cleavage fragments) were measured using ELISA. Biomarkers were compared to biopsy score.

Results:

During the study period 79 children (51 boys) were enrolled. Median age: 13.8 (range 6–18 years). Diagnosis was autoimmune liver disease in 25; NAFLD in 25; 13 children were post-transplant; 8 children had Hepatitis B/C; 3 had Wilson disease and the remainder miscellaneous. FibroScan was not possible in 5 patients because of body habitus. FibroScan was a good discriminator of fibrosis \geq F2 ($p < 0.001$), \geq F3 ($p < 0.001$) and F4 ($p = 0.003$) with area under the ROC curve of 0.78, 0.81 and 0.91 respectively. ELF performed better with increasing stages of fibrosis. Area under the curve for cirrhosis was 0.74. CK18-M30 levels was accurate in distinguishing significant fibrosis (\geq F2) ($p = 0.015$) with an area under the ROC curve of 0.69.

Conclusion:

FibroScan was a reliable tool in distinguishing different stages of liver fibrosis in paediatric patients. Serum biomarkers may be of use in combination with FibroScan especially in the stratification of more severe disease. Routine use of these techniques may serve as a useful adjunct to liver biopsy for diagnostic purposes and provide a reliable method of non-invasively monitoring liver disease progression in children.

Evidence for impaired expression of extracellular matrix proteins and adhesion molecules in biliary atresia

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Background: The cause of biliary atresia is still controversially discussed. Gene arrays and structural assays suggest a predisposing role of impaired morphogenesis of the biliary tract. We analysed the expression of the extracellular matrix (ECM) and of corresponding adhesion molecules in children with biliary atresia (BA), with cholestatic liver disease of other origin (CLD), in comparison to normal control children to elucidate possible defects.

Subjects and Methods: A major accomplishment of this study was to obtain normal tissue from controls from infants for representative comparison (n=8) to infants with BA (n=13), or with CLD (n=6) for immunohistochemical staining. ECM proteins included basement membrane components Collagen type IV, Laminin subtypes, Perlecan, and Entactin. Adhesion molecules comprised of Integrin-alpha and -beta subunits. Statistical analysis was performed using chi-squared and Mann-Whitney tests. Results were defined as statistically significant if $p < 0.05$ in both tests.

Results:

Children with BA demonstrated statistically significant altered expression of ECM proteins considered key markers for epithelial migration, differentiation and regeneration: Laminin-beta1 was reduced in children with BA (23%) versus controls (80%). Its expression has been reported in foetal and neonatal liver and regeneration. Notably, adhesion molecule Integrin-beta1 was reduced on bile ducts of BA (61.5%) versus controls (100%). It has been attributed to morphogenesis and Laminin binding. Accordingly, Entactin was reduced around the biliary epithelium in BA (7.6%) versus controls (75%). On the contrary, Perlecan was increased in BA (84.6%) versus controls (23%). Perlecan has been reported enhanced during liver damage. Integrin-alpha3 was increased in the basal membrane of children with BA (76.9%) versus controls (12.5%). It has been associated with the development of immature, primitive bile ducts.

Conclusion:

This study demonstrates that the composition of the ECM in children with BA is impaired. The reduction of Laminin, Entactin and Integrin-Beta1 may exert an important impact on migration, matrix-epithelial binding, and differentiation. On the other side, over-expression of Perlecan and Integrin-alpha-3 could suggest ineffective proliferation of immature bile ducts. Our findings add further evidence to the hypothesis that morphogenetic defects of the biliary epithelium and surrounding extracellular matrix play a major role in the pathogenesis of biliary atresia.

EWTD: Incompatible with subspecialty training?

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Background:

Historically, the RCPCH College Specialty Advisory Committee (CSAC) recommends that a trainee in Paediatric Gastroenterology, Hepatology and Nutrition (PGHAN) spends at least 70% of working hours in that subspecialty. Since changes due to the European Working Time Directive (EWTD), there has been an increasing perception from both trainees and trainers that there is insufficient time spent within their subspecialty.

Aim:

To quantify the proportion of PGHAN trainees fulfilling RCPCH recommendations for training in terms of time spent in subspecialty and to assess the impact of the EWTD on this.

Subjects and Methods: A survey of current trainees at the British Society of Paediatric Gastroenterology, Hepatology and Nutrition (BSPGHAN) annual meeting in January 2010. This was then followed up with the survey being emailed to trainees to increase the response rate. The 13 trainees working on the national grid between January and June 2010 were surveyed.

Results:

10/13 trainees responded to questionnaire (77%). 2 were still working on rotas with more than 48 hours per week. Only 3 trainees replied that they were spending >70% of their contracted hours on subspecialty training, and 1 replied "40-49%". However, 8 respondents stated that they were spending >70% of hours at work between 9am-5pm. On being asked about attendance at endoscopy lists in the unit, 1 trainee replied ">70%", whereas 3 replied "<40%". When asked whether they felt it necessary to work out of contracted hours for training, there were only 8 responses. Of these, 1 was "never", 4 "occasionally" and 3 "often".

Summary:

The majority of trainees are no longer receiving the subspecialty training hours that is recommended by RCPCH. Given that most PGHAN trainees seem to be working >70% during 9am-5pm, it seems that many trainees are working outside of their subspecialty even within normal working hours. The majority of respondents are training outside of contracted hours, presumably on restricted access training opportunities such as endoscopy.

These results are subject to significant bias but demonstrate a challenge in training paediatric gastroenterologists. Inadequacy of subspecialty training may jeopardise both a centre's status as an accredited training unit and a trainee's ability to obtain certification of completion of training. While this is a survey of PGHAN trainees, these challenges face all paediatric subspecialties.

Gastroenterological Problems in Congenital Myotonic Dystrophy

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Background and Aims:

Congenital myotonic dystrophy (CMD) is an autosomal dominant condition with variable phenotype. Literature on gastrointestinal manifestations of CMD at birth and infancy is extremely limited. We report the gastrointestinal manifestations on four patients presenting in the neonatal period with CMD.

Subjects and Methods:

We identified 4 patients with CMD who presented with gastrointestinal manifestations during the neonatal period. The clinical presentation, investigations and management of nutritional and gastroenterological problems in these patients was documented till the age of one year.

Results:

Gestational age ranged from 33 weeks to 40 weeks at birth and all 4 patients were females. There was polyhydramnios in three pregnancies. Delivery was by emergency caesarean section in three of the patients due to reduced fetal movements. All 4 patients required ventilatory support ranging from 3-15 weeks of age due to poor respiratory effort. Enteral feeding was started between day 2-4 of life and all of them had abdominal distension, large bilious aspirates or bilious vomiting. Two of the patients had a trial of prokinetic medications and hydrolysed feeds without any improvement in enteral food tolerance. Three patients had a barium follow through study and enema and two of them showed slow small bowel motility, one of them showed thickened pylorus, ileal atresia and microcolon and one showed subtotal small bowel obstruction and microcolon. One patient had an ileostomy and a feeding jejunostomy and one had an ileostomy and gastrostomy after which there was improved tolerance to enteral feeds. The third patient gradually had improved tolerance to nasogastric feeding. The fourth patient died from overwhelming sepsis at 15 weeks of age. Three patients were on parenteral nutrition (PN) from week one of life and full enteral feeding was established between 22 and 39 weeks of age. The fourth patient was on PN till 15 weeks of age when she died. Meconium was passed between day 2-3 of age in all 4 patients and all patients required glycerine suppositories to open bowels every 4-5 days. Rectal biopsy in all 4 patients was normal. PN related cholestasis was noted in all 4 patients by 3-6 weeks of age. In 2 patients the PN related cholestasis completely resolved after PN was stopped however one patient continued to have significant but stable liver disease at one year of age. Oral feeding has not been possible due to unsafe swallow in the 3 surviving patients at one year of age. All 4 patients had multiple culture positive septic episodes especially urinary tract infections.

Summary and Conclusion:

The gastrointestinal symptoms were initially attributed to the well reported abnormal motility of the gastro-intestinal tract in CMD. However further investigations showed additional causes for these symptoms like a thickened pylorus, microcolon and ileal atresia. All our patients required nutritional support with parenteral nutrition but developed parenteral nutrition related cholestasis early in life. It is unclear whether this is peculiar to CMD or secondary to recurrent episodes of infections. With optimal management and early establishment of enteral feeding this would resolve in time.

These 4 cases provide the first detailed reports of gastrointestinal manifestations of CMD in neonates. Clinicians should look for upper and lower gastrointestinal symptoms in all patients with CMD.

Growth in Children with Crohn’s Disease Receiving Contemporary Therapy In The UK

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Introduction:

It is unclear whether recent advances in therapeutic regimens have had a beneficial impact on growth in children with Crohn’s Disease (CD).

Aim:

To study growth and its relationship to therapy at diagnosis (T0), after 1 year (T1), after 2 years (T2), after 3 years (T3) and at maximum follow-up (MF) in children with CD.

Subjects & Methods:

The anthropometric and treatment details of 116 children (68 M, 48 F) with onset of CD before the age of 17yr were reviewed. Median age at diagnosis was 11years(4.9, 15.5). Median age at MF was 16.1yr (9.4, 19.3).

Results:

At diagnosis mid parental height SDS was 0.2(-1.2, 0.9) compared to HtSDS -0.4(-2.0, 0.9) in patients (p=0.05). Median Height Velocity (HV) SDS increased from -1.9(-7.4, 7.5) to -0.7(-7.5, 6.1) (p=0.003) between T1 and T2, and from -0.7(-7.5, 6.1) and -0.5 (-6.8, 7.7) (p=0.007) between T2 and T3 (table below). HVSDS at T2 and T3 showed an association with the average ALP over the previous one year (r, 0.34, p=0.004) and (r, 0.36, p=0.016), respectively. Although HVSDS improved during follow up Ht SDS did not change from T0 to MF. In 22 children with puberty data, median HV SDS changed from -1.7(-4.0,1.7) to -1.6(-4.3,3.0) (p=0.48) between T1 and T2, and from -1.1(-4.0,4.2) and 0.0(-3.7,4.5) (p=0.29) between T3 and MF. No single drug or marker of disease activity showed a significant association with growth parameters.

	At diagnosis (n, 116)	T1 (n,115)	T2 (n,98)	T3 (n, 78)	MF (n, 78)
HtSDS	-0.4 (-2.9,0.9)	-0.6 (-2.1,0.6)	-0.7 (-2.2,0.7)	-0.7 (-2.0,0.6)	-0.5 (-1.8,0.5)
% HtSDS<-2	10%	10%	12%	10%	8%
% HtSDS-2 to -1	23%	18%	24%	23%	27%
% HtSDS<-1 to 0	31%	36%	33%	38%	29%
HVSDS		-1.9 (-4.1,1.8)	-0.7 (-4.4,4.0)	-0.5 (-3.4,4.3)	0.0 (-3.6,5.4)
% HVSDS <-2		48%	39%	24%	20%
% HVSDS -2 to -1		17%	9%	22%	20%
%HVSDS<-1 to 0		13.3%	7%	9.5%	8.5%
% BMISDS -2 to -1	25%	12.1%	23.5%	16.6%	11.5%
Pubertal status (I, II-III, IV-V) n,22		(18,4,0)	(14,5,3)	(10,8,4)	(6,6,10)

Conclusion:

Short stature and slow growth continue to be encountered in children with CD despite improvement in clinical management of the disease.

Gut inflammation in children with Juvenile Idiopathic Arthritis

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Aim:

The relation between inflammatory bowel disease (IBD) and joint complaints is well established. Gut inflammation has been described in adult patients with spondyloarthropathy (1). The type of gut pathology in paediatric juvenile idiopathic arthritis (JIA) is not well described. Our study is to evaluate the histopathological features in the gut mucosa of children with JIA who had gastrointestinal symptoms.

Methods:

All cases of JIA who underwent oesophageal gastroduodenoscopy and ileocolonoscopy were identified from a single paediatric specialist centre (2002-9). The mucosa histopathology features, types of JIA, gastrointestinal symptoms, treatment and presence of autoantibodies at the time of endoscopy were reviewed.

Results:

30 children (9 Female) with JIA had endoscopy: 7 oligoarthritis, 9 polyarthritis, 5 systemic-related-arthritis, 8 entheisis-related-arthritis and 1 psoriatic arthritis. All had one or more gastrointestinal symptoms including abdominal pain (n=15), abnormal bowels (n=8), vomiting (n=2), rectal bleeding (n=7) or faltering growth (n=7). 23/30 (77%) had abnormal histology (mean age 9.13 + 4.22) whilst 7/30 (23%) were normal (mean age 9.64 + 2.47).

10/23 (43%) patients had chronic/autoimmune inflammation of the gut, 7/23 (30%) had predominant eosinophilic gastrointestinal disease whilst 6/23 (26%) had active colitis/IBD. All but one had involvement of the colon, 10/23 (43%) the duodenum, 5/23 (22%) the terminal ileum and 3/23 (13%) the stomach and oesophagus.

61% (14/23) of patients with gut inflammation was on immunosuppression and 17% (4/23) on non-steroidals. 12% (3/23) were not on treatment. In the normal group, 5 were on immunosuppression whilst the other 2 were on non-steroidals.

43% had positive autoantibodies (abnormal group) whilst 3/7 in normal group had positive autoantibodies. No gut autoantibodies were performed.

Conclusion:

This is the largest paediatric series describing the mucosal histopathological features in the gut of children with JIA. 96% of the children had colitis while the small bowel was affected in more than half the cases. This matched the clinical presentation of abdominal pain and altered bowel habits as the predominant symptoms (76%). The type of gut inflammation was mainly chronic inflammation with a quarter having active IBD. The presence of eosinophilic GI disease in 30% of our study group is an important novel finding and may be used to guide therapy such as dietary exclusion, particularly in those with ongoing inflammation despite being on immunosuppressive therapy. Our data did not confirm a direct correlation between autoantibodies and specific mucosal disease; however a larger study might be needed to address this with particular emphasis on gut autoantibodies.

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Impact of specialised systematic ultrasound examination on the investigation of infants with neonatal cholestasis

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Introduction:

No single investigation can confirm the diagnosis of biliary atresia (BA). However between 2002 and 2005 our department investigated the use of detailed systematic abdominal ultrasound scans (USS) with a high frequency transducer to differentiate infants with BA from those with other causes of neonatal cholestasis. The overall accuracy was 98% and this method has become routine practice in our unit. The aim of our study was to assess how the incorporation of this technique has affected the need for invasive investigations.

Methods:

Case notes were reviewed retrospectively from 2 groups of 50 consecutive infants referred for investigation of neonatal cholestasis before (Gp 1) and after (Gp 2) the USS study. Patient characteristics, stool colour, laboratory tests, radiological and histological reports and final diagnoses were recorded. The range of investigations needed to exclude a diagnosis of BA was noted.

Results:

Notes were available for 48 infants in Gp 1 (24 male, median age 5 weeks (range 1 -19 weeks)) presenting between April 2000 and February 2002, and 49 infants in Gp 2 (29 male, median age 6 weeks (range 1 - 20 weeks)) presenting between November 2005 and July 2007. 10 infants in Gp 1 and 7 infants in Gp 2 had a final diagnosis of BA. All infants had the standard first line laboratory investigations for neonatal cholestasis and an USS; standard USS in Gp1 specialised USS in Gp 2. 4 infants in Gp1 and 5 infants in Gp 2 needed no further investigations for diagnosis. The number of other investigations required to achieve or refute a diagnosis of BA in the remainder is tabulated below.

	Gp 1 (n=48)	Gp 2 (n=49)	p value
Radioisotope scan	37 (77%)	41 (84%)	NS
Liver biopsy	22 (46%)	4 (8%)	<0.05
Operative cholangiogram	4 (8%)	1 (2%)	NS

Conclusion.

The introduction of specialised USS into our routine investigation of infants referred with neonatal cholestasis has been associated with a significant decrease in the number of liver biopsies performed to diagnose BA.

Indications and frequency of surgical interventions in children with Inflammatory Bowel Disease

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Aims:

The aim was to document, in children with Inflammatory Bowel Disease (IBD), the complications requiring surgical interventions and looking at factors influencing need for surgery in this group.

Methodology: A prospective database of children less than 16 years of age newly diagnosed with IBD has been kept at regional unit covering population of 5.2 million. Cases diagnosed between 1993-2003 were included (n=241). Those cases that, after 16 years of age, were followed by adult gastroenterologist locally were included. This group comprised of 24% of total (58/241). Case notes were analysed recording initial data at diagnosis and information about treatment used, surgical procedure performed and outcome.

Results:

The average follow up duration was 8.6 yrs (range 5-15yrs). Mean age at diagnosis was 12.74 yrs. 50%(29) had Crohn's disease (CD), 40%(23) Ulcerative colitis (UC), and 3% (2) Indeterminate colitis (IC). 45% (26) of the cases were treated at initial presentation with steroids, 36% (21) with enteral feeds and 19 % (11) with 5 Aminosalicylates. Average number of relapses was 0.4/year with no significant difference in time to first relapse between groups treated with steroid or enteral feeds (p=0.6). 23 % (6/26) were steroid dependent and 7.5% (2/26) were resistant. 18 out of 58 patients (31%) underwent surgery during the follow up period. 12 (36%) patients with CD needed surgery with total number of surgical procedures being 17. 26% of patients with UC needed surgery, which was colectomy in all cases. Of the 6 patients who had colectomy only 1 was an emergency colectomy for acute severe colitis, with rest all being planned procedures for poor disease control. None of the cases suffering from UC had surgery at the time of initial presentation. Among children with CD five developed stricturing disease of which 2 had strictures in terminal ileum, 1 in right colon, 1 in transverse colon and 1 had anorectal stricture needing diversion. 2 Cases had features of small bowel obstruction secondary to a mass in the illeocaecal region. 3 cases with CD developed perianal fistulae requiring fistulectomy(n=2) or seton suture(n=1). Time to relapse after initial surgery in cases with CD was 21.3months (range 4- 36months) and median being 9months. The mean duration of illness before surgery was 4.76years (Range 1-10) with mean for CD and UC being 3.8years (1-7years, mode 2) and 6.14 years (2-10, mode 10) respectively. There was a reduction in proportion of children needing surgery in those diagnosed between second five years (1998- 2003) in comparison to those diagnosed between 1993-1998 from 35% to 28%. This was mainly attributed to reduction in surgery for children with UC from 37.5% to 31%. The average duration of illness before needing surgery was increased from 4.9to 5.12years, with time to surgery in UC going up from 4.28 to 5.12 years between these 2 groups. The risk of need for surgery was increased by nearly two times in cases that had family history of IBD (RR= 1.77 95% CI 0.49- 5.5). Cases, which ended up needing surgery, had a higher average rate of relapse needing treatment with steroids per year as compared to those who did not (p value 0.015). Surgical rates were not increased in cases with either steroid dependence (RR 0.86 95%CI 0.32-2.27) or resistance(RR = 0).

Conclusions:

36% of children with CD and 26% with UC required surgery. Commonest indication for surgery in CD was stricture formation followed by sub acute obstruction and fistulous disease. Time to relapse after surgery in CD was 21.3m. With advances in treatment there was a reduction in number of children with UC requiring surgery but no change in those with CD. Increased risk of complications needing surgical intervention was seen in cases with family history of IBD and frequent relapses. There was no increase noted in children with steroid resistance or dependence.

Intestinal alpha-defensin expression in paediatric IBD

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Background:

Reduced alpha-defensin expression has been reported in the terminal ileum (TI) of adult patients with ileal Crohn's disease (CD). However, little is known about alpha-defensin expression in children with chronic inflammatory bowel disease.

Methods:

283 intestinal biopsies were obtained from children with CD, ulcerative colitis (UC) and healthy controls. Absolute mRNA copy numbers for HD5, HD6, IL-8, Villin 1 and Tcf-4 were analyzed by RT-PCR. HD5 immunostaining was performed on biopsy sections and patients genotyped for NOD2 mutations.

Results:

Equal expression levels of alpha-defensins (HD5 and HD6) were found in TI biopsies of children with ileal CD (L1+L3) compared to patients with colonic disease (L2) and healthy controls. In contrast, we found significantly higher levels of alpha-defensins in the TI of children with UC compared to CD and controls. Reduced expression of Tcf-4 was observed exclusively in the duodenum and TI of CD patients with L1+L3 phenotype. We demonstrate significantly increased expression of HD5 and HD6 in the inflamed colon of IBD children (UC and CD) attributable to the presence of metaplastic Paneth cells.

Conclusions:

In this study no difference in alpha-defensin expression was found in the TI of CD children and controls. However, significant reduction of Tcf-4 in L1+L3 phenotype suggests that a possibly impaired PC differentiation may lead to altered HD5 and HD6 expression at some stage of disease. Additionally, substantially increased expression of alpha-defensins in the inflamed colonic mucosa of children with IBD raises the question for their potential involvement in modulating inflammation in these patients.

Introducing minimally invasive surgical approaches in the management of paediatric inflammatory bowel disease – early results and perspectives

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Introduction/Aims:

Surgery is a key component in the holistic management of severe/refractory inflammatory bowel disease (IBD). Minimally invasive surgical (MIS) approaches are well established in adult practice and are being increasingly applied to paediatric populations.

MIS approaches were introduced to our unit after formal governance appraisal under (Royal College of Surgeons) preceptorship by an adult colorectal surgeon experienced in MIS for IBD and colorectal cancer. We report our early experience following adoption of a minimally invasive surgical approach to the management of IBD.

Subjects and Methods: Case notes of all patients (n=16) undergoing 19 major procedures for IBD in the 16 months (May 2009 – September 2010) following the introduction of MIS were reviewed with particular reference to pre-operative management, operative details and post-operative course. All patients were pre-operatively counselled and marked for stoma formation.

Results: There were 16 patients (female n=14, male n=2) with a median age at diagnosis of 13.7yr (IQR 9.7-14.5yr) and surgery at a median time of 1.6yr (IQR 0.8-3.0yr) after diagnosis. The frequency of ulcerative colitis (UC, n=8) and Crohn's disease (CD, n=7) was similar and one colectomy showed indeterminate colitis.

Surgical interventions comprised right hemicolectomy with primary anastomosis (n=3) and subtotal colectomy with either end ileostomy (n=12) or primary ileorectal anastomosis (n=1). Subsequent ileoanal pouch procedure has been performed (n = 3). All but two procedures were performed laparoscopically and one patient was converted to open for technical reasons.

Median length of stay was 8 days (IQR 6-13.5) with a third of cases remaining in hospital less than 1 week. Complications included intra abdominal collections (n=2), persistent rectal bleeding (n=2), rectocutaneous fistula (n=2), prolonged post-operative ileus (n=2) and sub-acute obstruction at the ileostomy (n=1). There were no complications attributable to MIS techniques and none required additional surgical interventions.

Summary/Conclusion:

With planning, good clinical governance and a multi-disciplinary approach it is feasible and safe to introduce MIS techniques in the management of children with IBD in a children's hospital setting. Input from adult colorectal colleagues is vital to establish such a service. Subjective feedback regarding cosmetic benefits and overall experience has been positive.

Magnetic Resonance Enterography (MRE) in adolescents and young adults with Crohn's disease

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Introduction and Aims:

MRE has been increasingly used for evaluation of known and suspected Crohn's disease patients but variable availability and high cost remains a problem in some areas. Young patients with Crohn's disease are reported to be particularly at higher risk of receiving high doses of radiation. There is limited data on the use of MRE in this group. We aimed to assess the effectiveness of use of MRE in adolescents and young adults based on select criteria used in our institution.

Methodology:

Patients with known Crohn's disease diagnosed between 10 to 30 years of age undergoing MRE during a 2-year period were included. All had full endoscopic assessment and were classified based on Montreal classification. Demographics and clinical parameters were recorded. Actual radiation exposure in DAP (Dose Area Product) and milliseverts (mSv) recorded in RadCentre during procedure of all relevant radiological investigations procedures before and after MRE was calculated. Clinician recorded Montreal classification 3 months before MRE and post MRE was recorded in relation to changes to classification in extent (L) and disease behaviour (B). Images were independently reviewed by 2 specialist radiologists. Any change to management within 3 months following MRE was noted. Reported tolerance to procedure was recorded.

Results:

31 patients were included in analysis. Male to female ratio was 1:2. Mean age at diagnosis of Crohn's disease was 17.9 years and at the point of MRE scan was 21.25 years. The mean duration of Crohn's disease follow up pre MRE was 2.6 years and post MRE was 1.28 years. The indications included obstructive symptoms (n=14, 45.1%), assessment of extent (n=15, 48.3%), suspicion of internal fistula (n=1, 3.2%) and non-responsiveness to therapy (n=1, 3.2%). The findings included small bowel stricture (20), stricture with associated abscess (3), colonic stricture (2), thickening (3), fistula (1) and gastric outlet obstruction (1). In 6 patients the MRE was normal. Following MRE 16 patients (51.6%) had upgrading of disease behaviour (B) and 3 of them also had additional disease location (L). In 4 patients the MRE identified longer length of small bowel involvement than recorded before. The average radiation exposure pre MRE was 7.47 mSv and post MRE was 1.56 mSv. In 4 patients the planned management was modified due to additional findings in MRE result. 6 patients did not tolerate oral contrast liquid fully and did not have adequate luminal distension.

Conclusion:

This study describes our experience in the use of MRE in a high risk group of adolescent and young adults with Crohn's disease. Application of specific referral criteria and patient selection may increase pick up rate, improve clinical utility by altering disease classification and extent, reduce radiation exposure and potentially reduce costs. Longer follow up of a larger cohort of patients following introduction of MRE in a hospital is needed to confirm reduction in radiation exposure in this group.

Meta-Analysis of total oesophagogastric dissociation for treatment of gastro-oesophageal reflux disease

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Background:

Total oesophagogastric dissociation (TOGD) is an antireflux procedure developed by Bianchi in 1997 for treatment of gastro-oesophageal reflux disease (GORD) in children with severe neurological impairment (NI). The success of TOGD in the elimination of GORD has allowed it to be considered in two other situations (children with no NI but with anatomical structural anomalies in whom other methods have failed and in adult population with severe NI.)

Aim:

The aim of this meta-analysis is to evaluate the indications for, and statistically analyse the outcome of TOGD.

Method:

We used the search terms: (total) (o)esophago-gastric/gastro-(o)esophageal dissociation/disconnection/separation for (gastro-(o)esophageal) reflux (disease) with no limits to the search database and communicated with the correspondence authors in the individual papers to enquire if any more cases had been performed since their last published article. We set 4 criteria - indications for procedure, operative complications, operative mortality and post-operative recurrence of GORD, and manually reviewed them in the journals. We used Fisher's exact test in Stats-direct to analyze the data.

Results:

In total, 199 published and unpublished cases were performed. 3 groups of patients were identified - 86% were paediatric patients with severe NI, 12.5% were 'normal' paediatric patients with no NI and 1.5% were the adult population with severe NI. For each group, primary and rescue procedures were identified. The indications for TOGD are similar and specific for both the paediatric and adult population with severe NI but are non-specific with special consideration accounted for the 'normal' patients with no NI.

The early operative complications and mortality observed in the paediatric population group with severe NI are not shown to be statistically related to the procedure. No operative complications or mortality were reported by patients in the other 2 groups. No post-operative recurrence of GORD are reported by 3 groups.

Conclusion:

In conclusion, there are clear indications for performing TOGD in the severely NI children and adults. TOGD can also be successfully used in selected clinical situations in non NI patients.

Outcome of Kasai Portoenterostomy in Leeds over 16 years

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Introduction:

In 1994 we developed a standard protocol for the perioperative management of infants undergoing Kasai portoenterostomy (KP) for biliary atresia (BA). Infants received a decreasing dose of dexamethasone from day 5 post-operatively for 15 days, oral antibiotics for 4 weeks and ursodeoxycholic acid and phenobarbitone for 1 year. The aim of this study was to investigate the outcome of KP in a single centre using this standardised protocol.

Methods:

Between January 1994 and May 2010, 113 infants were referred with BA. Twenty three infants were excluded from the analysis; 9 children were referred for primary liver transplant due to late presentation with advanced disease, 4 children died before KP from associated abnormalities and 10 children were not managed by the standard protocol. Patient characteristics, clearance of jaundice, need for liver transplant and patient survival were audited.

Results:

KP was performed on 90 infants who were managed by our standard protocol (44 male, median age at KP was 51 days, range 10-144). Eighty four had type 3 BA and of these 9 had the biliary atresia splenic malformation syndrome. Sixty three children (70%) cleared their jaundice (bilirubin <20µmol/l). This figure was not significantly different between the 2 consecutive surgeons involved in this programme (Surgeon 1, 1994 to Oct 2006, 51 KP. Surgeon 2 started October 2006, 39 KP). Overall at a median follow up of 5.1 years (range 0.5-16 years) 81/90 (90%) children are alive and well. Fifty five children (61%) are alive with their native liver. Twenty six children are alive following a successful liver transplant. Three died after liver transplantation and a further 6 died after KP due to associated abnormalities.

Conclusion: Over 16 years, clearance of jaundice and native liver survival following KP using this protocol consistently compares very favourably to results from the published literature both in the UK and world wide.

Patient empowerment through the use of Patient Held Records – a large scale pilot study

Crook K and Garrick V, on behalf of the RCN and BSPGHAN affiliated Paediatric IBD nurses Group

Introduction:

Patient held records (PHR's) are used regularly in chronic disease management, however, their use in paediatric patients with Inflammatory Bowel Disease (IBD) is not common. A national forum for paediatric IBD nurses allowed practitioners from all over the UK to develop a PHR which could be modified to suit local practice while still providing standardised information for the patient and parents. The prototype record was demonstrated by the authors at BSPGHAN 2009 to ensure that all stakeholders were aware of the project and their input was included in the larger scale roll out of the document. In addition to providing information, the record has also been designed as a working document for the patient to maintain throughout their years with paediatric services. The PHR is a small and easy to carry A5 folder containing patient information, space to write local team/community contacts, document blood results, list investigations and dates etc. It is intended to be the personal property of the patient or parent until the child is able to complete it.

This large scale pilot will represent approximately 30 centres across the UK and is the first of its type for paediatric patients with IBD. Feedback has been requested from patients, parent and healthcare professionals.

Aim;

To produce a working document which includes standardised information, to all paediatric patients with IBD. To empower patients and/or parents to take ownership of their disease and actively participate in the management of their condition through the use of PHR's.

Subjects and Methods: Paediatric IBD nurses from 30 centres across the UK requested inclusion in the pilot. Each nurse was allocated a maximum of 20 records to pilot although many centres did not utilise this amount – in total, 350 PHR's were distributed. There was no randomisation of patients and the PHR was given to either newly diagnosed patients or those diagnosed for some time. In addition each nurse distributed the PHR to a varied age range of patients. Questionnaires were distributed by post to the patient and parent and delivered by hand to the healthcare professional involved in the child's care. Specific questionnaires were designed for each group and the healthcare professional questionnaire was added as a result of feedback from the original demonstration at BSPGHAN 2009

Results:

Preliminary data show 95% of patients and 100% of Health professionals (HP) feel there is a need for this type of information and there is general agreement that the information contained is written appropriately. HP's in particular have highlighted issues around the depth of information in particular sections. There is also conflicting opinion as to whether there should be more specific information (i.e. biologics information, blood test values). Interestingly several long term patients commented that the information contained would be too much for new patients, but this does not appear to be verified by the new patients. In addition, many patients commented on the information being directed at the parent and not the young person themselves. 81% of patients would use the PHR while only 55% of health professionals feel they would use them.

Summary:

Preliminary data show that the PHR may be a useful document in assisting patients in the management of their IBD. 81% of patients agreed they were useful and would use them as a record of their care in the paediatric setting. There were some aspects of the PHR which were not appropriate and these have been identified. Full analysis of the data is expected to highlight aspects of the PHR which could be modified to benefit the user- the patient.

Conclusion:

The pilot data will be used to refine the PHR before being rolled out nationally in 2011. Annual audit will continue to ensure the PHR is meeting the needs of the people using it. While it is recognised that it is challenging to meet the needs of such a varied range of patients, the generic nature of the PHR makes it a flexible document, in a nationally accepted format, which can be modified to suit local practice and specific patient needs.

Perspectives of patients with chronic gastrointestinal conditions and their carers on transition from paediatric to adult health care services: results of a pilot study.

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Introduction/Aim:

Transition from paediatric to adult health care settings has emerged as an important aspect of care. There is limited data on the perspectives of patients with chronic gastrointestinal problems on the process of transition. We aimed to survey the perspectives of patients and their carers who attend our gastroenterology transition clinic.

Methods:

Semi structured questionnaires were sent to patients and their carers. The questions included open and closed questions and were designed to be filled independently by patients and their carers. The items in the questionnaire were ranked using Likert scale from 1-5 with the anchor of 'not important' and 'very important and essential'. The results are described as proportion of respondents. Chi square test and fisher's exact test were used where appropriate.

Results:

The patient group included 15 with celiac disease and 10 with inflammatory bowel disease. 25 patients and 23 of the respective carers completed the questionnaire. The proposed age for initiation of transfer discussion was 16 years by majority of patients and 17 by the parents but both groups felt age 18 as appropriate to complete transfer. Vast majority of patients (20/25) and carers (22/23) felt the facility of dedicated transition clinic as beneficial (p=ns). Both patients and carers considered adequate transfer of clinical information between the paediatric and adult teams (mean scores 4.33 and 4.9 respectively) and ensuring full understanding of the condition and its treatment (mean scores 4.0 and 4.71 respectively) as the most important aspects in preparation (p=ns). In relation to disease status both patients and carers rated a controlled disease state as very important at the time of transfer and wished to have direct access to either clinical team when needed. The average importance scores on concerns and anxieties regarding the process of transition varied between patients and their carers (see table).

Items of concern	Mean score patients (max=5)	Mean score carers (max=5)	Scoring maximum in importance patients (n=25)	Scoring maximum in importance carers (n=23)	P value
Lack of knowledge of adult team	3.48	4.64	7	16	<0.001
Uncomfortable in meeting new team	2.7	4.2	3	12	<0.001
Adult team less sympathetic to needs	3.45	4.43	7	14	<0.001
Suboptimal access to medical team	3.45	4.38	5	12	<0.001
Condition flaring up more frequently	2.9	4.09	5	10	<0.07
Overcrowding of adult services	3.33	3.95	7	9	ns
Adult clinic environment	3.2	4.0	6	9	<0.02
Admission Adult wards	3.04	4.29	5	13	< 0.04
Attend independently	2.71	3.64	7	8	ns
Making decisions independently	3.58	4.0	10	11	ns

Conclusion: The results of our pilot survey describe the importance of both organisational and individual disease related factors for a successful transition from a user perspective. Considering these will be essential in developing and improving the transition services.

Prevalence of anaemia in children with inflammatory bowel disease.

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Background:

Anaemia is the most frequent complication of Inflammatory bowel disease (IBD) affecting about 20% of adult patients at any one time; half of whom are iron deficient (IDA)(1,2). Few studies have reported the prevalence of anaemia in children with gastrointestinal (GI) complaints and or IBD, where dietary restrictions may conceivably worsen iron deficiency.

Aims and Objectives:

We aimed to compare the prevalence of anaemia in IBD with a group of GI disease controls, and identify disease characteristics that predict anaemia.

Methods:

We conducted a retrospective case-control study. Using electronic case note review we identified 46 consecutive paediatric IBD patients attending our tertiary Paediatric Gastroenterology Unit, (20 ulcerative colitis (UC), 2 indeterminate colitis and 24 Crohn's (CD)). 40 children with GI complaints with no underlying organic pathology were used as controls. Anaemia was defined using WHO criteria (1), patients with co-existing haemoglobinopathies were excluded. Disease activity was defined by global clinician's assessment and/or CRP>5 mg/l. Disease extent and behaviour were recorded according to the Montreal classification. Differences between the IBD group and controls were sought using Fisher's exact test and Mann Whitney-U test.

Results:

There was no significant difference between the median ages (range) of the IBD group compared with controls 13(5-16), 12(5-16)yrs respectively. Prevalence of anaemia in the IBD group was 71.7% (33/46) and significantly greater than in the controls 17.5% (7/40) (p<0.001), too few patients had haematinics or iron studies to determine type of anaemia. Mean haemoglobin in the anaemic UC and CD group was 10.2 (8.0-11.9) compared to 10.6 (8.2-12.4)g/dl respectively. Overall only 6% (2/33) of the anaemic group were treated with oral iron. Using univariate analysis, neither gender, disease type, extent, duration or activity; were found to be predictive of anaemia in IBD.

Conclusion: Anaemia is much more common in children with IBD. Despite this few children have their anaemia adequately assessed and fewer receive specific treatment. Further studies are needed to assess the prevalence of ID anaemia and anaemia of chronic disease and the impact of iron supplementation and erythropoietin on symptoms of anaemia, quality of life and disease activity.

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Pubertal Timing in Children with Inflammatory Bowel DiseaseMason A¹, Malik S¹, Russell², Bishop J², McGrogan P², Ahmed SF¹¹Developmental Endocrinology Research Group, RHSC, Glasgow, UK;²Department of Paediatric Gastroenterology, RHSC, Glasgow, UK**Background:**

Pubertal onset and progression is thought to be commonly affected in adolescents with crohn's disease (CD) and ulcerative colitis (UC). However, the extent of this effect has rarely been quantified.

Aims: To determine the impact of CD and UC on pubertal timing in a retrospective study of peak height velocity and a prospective study documenting pubertal status and skeletal maturation.

Methods:

Two groups of patients with IBD were studied. The first was a retrospective cohort of 67 children: CD-M(30); CD-F(11); UC-M(14) and UC-F(12) and the second was a prospective cohort of 55 children: CD-M(21); CD-F(17); UC-M(12) and UC-F(5) with median age at baseline of 13.9, 13.9, 13.4 and 13.2 yrs respectively. Age at Peak Height Velocity (APHV) defined tempo of the growth spurt and puberty in the first cohort whereas data on pubertal assessment, age at menarche and bone age were collected in the second cohort.

Results:

Group	Median APHV(range) [yrs]	Median Delay APHV (range) [yrs]
CDM	14.31 (12.4; 16.3)	0.31 (-1.6; 2.3)
CDF	12.75 (10.3; 13.8)	0.75 (-1.7; 1.8)
UCM	13.66 (12.8; 15.7)	-0.34 (-1.2; 1.7)
UCF	12.2 (10.1; 14)	-0.2 (-1.9; 2)

A statistically significant negative impact on APHV ($p=0.001$), was seen in the CD-M group only. The median delay in APHV in CD-M was 0.31 years (range -1.6; 2.3). Median ESR showed a significant association with delay in APHV in the whole group ($r,0.329$; $p=0.018$). In the prospective cohort, the median bone age delay in CD was 0.7 yrs (range -2.2, 3.2). A statistically significant negative impact was only seen on skeletal maturation ($p=0.001$) in the CD group. Age of menarche and timing of entry into puberty, defined as G2, were not delayed relative to the normal population. Conclusion: Pubertal delay does exist, with those at greatest risk being males with CD with active disease but, in most cases, it is not particularly marked.

Redo Gastrostomy: Our experience

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Background:

Insertion of gastrostomy has become a popular choice for children with feeding problems. With the passage of time gastrostomies require revision for various reasons. The aims of this study are to report our experience of the revision of gastrostomies, to ascertain the reasons for revision and to discuss any measures which may prevent the need for revision.

Methods:

We conducted a retrospective review of all the patients requiring revision of gastrostomy by the senior author between 2005 and 2010. The patients had had their original operation in several different hospitals, between 1997 and 2008. We excluded those patients requiring an operation for an acute complication or required revision for subsequent fundoplication. The patients' hospital notes were reviewed to ascertain the reasons for revision and a literature search was done to find any ways to prevent these.

Results:

There were 11 patients who required revision of gastrostomy. Epithelialisation of the gastrostomy tract with gastric mucosa reaching the skin, which resulted in excessive leakage of gastric juice and feed, was the commonest reason for the revision of gastrostomy (7 out of 11). Other reasons were migration of the gastrostomy exit site towards the rib cage (2/11) and Buried Bumper Syndrome (2/11). The mean interval for the epithelialisation of the tract was 98 months since the insertion of the gastrostomy. The mean for other complications were 25 months for buried bumper syndrome and 93 months for migration of the exit site.

Conclusion:

We believe the incidence of revision of gastrostomy could be reduced if proper measures are taken at the time of insertion and subsequently, during routine care. Avoiding epithelialisation is very difficult and may be minimised by aggressive and generous use of silver nitrate. The site needs to be as far from the rib edge as is possible. Use of a gastrostomy button instead of a tube eliminates buried bumper syndrome.

Relapse Rate Following Azathioprine Withdrawal in Maintaining Remission for Crohn's Disease: A Systematic Review and Meta-analysis

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Background:

The use of azathioprine (AZA) and 6-mercaptopurine (6-MP) for maintaining remission in Crohn's disease is well established. The duration of using these medications is not clear.

Aim:

The aim of this systematic review and meta-analysis was to examine whether Aza/6-MP can be safely withdrawn in patients with Crohn's disease who have been in remission

Methods:

The following databases were searched: MEDLINE (1950- September 2010), EMBASE (1980- September 2010), CINHAL (1981- September 2010), PubMed (1950- September 2010) and the Cochrane Central Register of Controlled Trials (CENTRAL). Randomised controlled and cohort studies comparing azathioprine continuation versus placebo or no treatment were eligible for inclusion. Primary outcomes were relapse rate following discontinuation of AZA / 6-MP at 6, 12, 18 months, 5 years and 10 years. Secondary outcome was any reported side effects. Two independent reviewers performed data extraction and quality assessment of the included trials. Data from the included trials were pooled and analysed using a random effects model.

Results:

Five studies met the inclusion criteria with 256 patients and 168 controls. Stopping azathioprine/6-MP was found to significantly increase the risk of relapse at 6, 12 and 18 months with pooled odds ratios of 0.29 (95% CI 0.15-0.56), 0.25 (95% CI 0.11-0.56) and 0.26 (95% CI 0.12-0.52) respectively. Two trials examined relapse rate at 5 years with pooled OR 0.53 (95% CI 0.13-2.21). No trials looking at relapse rates beyond 5 years were identified. Side effects reported in all studies were documented, showing serious but rare side effects in the Aza/6-MP group.

Conclusions:

There is a clear benefit of continuing Aza/6-MP for at least 18 months to maintain remission for Crohn's disease patients who established remission. There is not enough evidence to provide a clear guidance on whether to continue Aza/6-MP treatment or not beyond 18 months. Well-designed randomised controlled trials addressing this issue are needed.

Response in the 2 years following a course of Exclusive Enteral Nutrition in a cohort of >100 paediatric Crohn's disease patients

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Introduction:

Exclusive enteral nutrition (EEN) is an effective first line treatment for induction of clinical remission in paediatric Crohn's disease (CD). However there is a paucity of data regarding the long term follow up of patients beyond the treatment course.

Aim:

To explore the short and long term effects of EEN including anthropometric parameters in children with CD. The secondary aim was to evaluate factors during the baseline EEN course that predicted subsequent disease outcomes.

Methods:

A retrospective medical and dietetic case note review in newly diagnosed CD children (<16 y) who started a primary course of 8 weeks of EEN. Data on demographics, anthropometry, disease characteristics, inflammatory markers and disease activity indices were taken at diagnosis, 4 and 8 weeks on EEN and at 6, 12 and 24 months post diagnosis. Clinical response to EEN was characterised according to the global physician assessment. Anthropometry was expressed as z-scores. All patients included completed at least their initial course of EEN.

Results:

160 CD patients were identified of whom 110 were included for further analysis (males 68; median age: 11.2 years at diagnosis). At diagnosis 34% were thin ($\leq 2SD$), 1% obese ($\geq 2SD$), 10% had short stature ($\leq -2SD$) and 25% were underweight ($\leq 2SD$). In the initial course of EEN there were significant improvements in weight and BMI z-score as well as in inflammatory markers. By four weeks of EEN weight and BMI z-score had increased significantly (-1.1 cf. -0.6 and -1.3 cf. -0.4 respectively, $p < 0.02$) with a smaller but still significant increase between 4 and 8 weeks (-0.6 cf. -0.4 and -0.4 cf. -0.05 respectively, $p < 0.05$). Children with active disease after 8 weeks of EEN ($n = 12$) gained significantly less weight than those who entered remission (2.2 vs. 5.0kg respectively, $p < 0.05$). There was a strong negative correlation between weight or BMI z-score at diagnosis and magnitude of change at the end of EEN ($r = -0.76$, $p < 0.0001$).

44 patients successfully completed a 2nd course of EEN within the 2 year follow up period where median weight gain significantly improved again but was less than the initial course (3.3 vs. 5.1kg respectively, $p < 0.05$). There was again a significant increase in weight and BMI ($p < 0.05$). BMI z-score at diagnosis was the strongest predictor of BMI z-score at any time point of the follow up. The size of weight or BMI z-score change at the end of the initial EEN did not predict time elapsed to a subsequent clinical relapse or anthropometry and growth status at 6, 12, and 24 months. At 24 months, 9% were short, 5% were underweight and 1% had low BMI. Height z score had dropped from -0.6 at diagnosis to -0.8 at 24 months follow up.

Conclusion:

Weight and BMI is increasing through both primary and secondary courses of EEN but the change is smaller at the second half of the course or at secondary course. The amount of weight gained was increased in those who achieved remission and lowest in those who still had active disease. The size of weight gain is not a predictor of time to relapse or anthropometry and growth at follow up to 2 years.

Roux-en-Y: the route to successful long-term jejunal feeding

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Background and aim:

Established nutrition support teams (NST) are dealing with an emerging group of children with poor and worsening upper GI dysmotility. This presents as vomiting, retching, poor feed toleration and poor weight gain. These are a challenging group of children to meet sufficient nutrition and hydration requirements in order to promote appropriate growth and development, who often need jejunal rather than gastric home enteral tube feeding (HETF). We aimed to review the need for and outcome of medium to long-term jejunal feeding within our NST experience.

Methods:

A retrospective cohort study (using database and clinical note review) of use of PEG-J, transgastric gastrojejunostomy (GJ) tubes and surgical roux-en-Y jejunostomy in a tertiary paediatric centre serving a population of 1.25million people. Nasojejunal feeding tubes were only used for short-term jejunal feeding as a guide to need for and utility of this feeding route. All children receiving HETF under 18years of age during the period 01.01.02-30.09.10 were included.

Results:

A total of 795 children received HETF during the study period. Thirty-three (4%) required medium to long-term jejunal feeding, achieved by placement of a PEG-J tube in 4, GJ tube in 25, or an initial surgical roux-en-Y jejunostomy in 4. Twenty-five children had 71 GJ tubes placed endoscopically or radiologically. There was one major complication, namely death following intussusception of small bowel around the GJ tube. 43 of the 71 tubes needed to be changed for minor complications which included burst balloons in 16 (37%), holes in the Y-port or tube in 10 (23%), and fungal infection in 4 (9%). Proximal tube migration was a problem with both GJ and PEG-J tubes. Of the 29 children who were either PEG-J or GJ tube fed, 7 (24%) returned to gastric feeding, 5 (17%) died due to their underlying profound neurodisability and 8 (27%) continue with GJ or PEG-J, 2 of whom are awaiting formation of roux-en-Y jejunostomy. The remaining 9 (31%) demonstrated a need for long-term jejunal feeding and had a surgical roux-en-Y jejunostomy formed. 13 children in total had formation of roux-en-Y jejunostomy during the study period, at a median (range) age of 3yrs 4months (7mths-17yrs 10months). 11 (85%) of these children have an underlying neurodisability, and 7 (53%) had previous fundoplication. In terms of outcomes of this group, 9 (69%) continue with only minor complications of stomal infection and leakage, 2 (15%) died due to underlying condition, 1 (8%) moved out of area and 1 (8%) transitioned successfully to adult services.

Conclusions:

It is possible to provide medium to long-term jejunal feeding via PEG-J or GJ tubes to the group of children with profound and worsening GI dysmotility who have prolonged hospital admissions for problems with both establishment of and successful use of HETF. However, this is not without many time-consuming practical challenges, in particular the urgent need to change the tube when it malfunctions. Formation of a surgical roux-en-Y jejunostomy provides a more secure and relatively complication free means of providing long-term jejunal feeding to these children.

Screening investigations to exclude liver disease in neonates with conjugated jaundice: current practice in England and Wales

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Background:

Cholestasis is a common problem in extreme preterm infants and generally seen as a reversible complication of prolonged parenteral nutrition. In addition they are exposed to further cholestatic insults which may include hypoxia, interrupted enteral feeds, drug toxicity and sepsis. In May 2010, NICE has issued guidelines emphasizing the identification of neonatal conjugated jaundice (>25 mmol/L), but further assessment and investigations were outside its remit. BSPGHAN issued specific guidelines in 2007 for stepwise approach in these investigations. However, several investigations are performed to exclude underlying liver pathology. Opinions differ about the diagnostic utility of such investigations.

Aim:

To evaluate practice related to investigation of conjugated jaundice in the neonatal units across England and Wales.

Method:

A standard questionnaire was sent to lead neonatal paediatricians of all neonatal units in England and Wales. Questions included definition of conjugated jaundice, bilirubin cut off which prompted investigations and tests performed. Clinicians were also requested to give their opinion on the yield of these investigations.

Results:

102/194 neonatal units (52%), responded (33 level 3, 50 level 2 and 19 level 1 units). 96 units (94%) performed conjugated jaundice screen and 6 units (6%) did not. 77 units (75%) had a written policy. 46% of the responders defined conjugated jaundice as conjugated bilirubin >15% of total bilirubin and 49% as >20% of total bilirubin and 5% of units did not have a clear definition. Conjugated bilirubin levels which prompted investigations varied between units with 28 (30%) using conjugated bilirubin >20% of total, 33(36%) a conjugated bilirubin >15% of total and 20 (21%) with no definite threshold. Majority (>76%) of units performed LFTs, TFTs, GGT, Galactosaemia screen, -1 antitrypsin and liver ultrasound. In addition to above investigations 2/3rd of units performed urine culture, hepatitis serology, 1/3rd performed urine organic acids, NH3 and lactate. 19 units performed CF genetics and 23 HIDA scan. 71% of responders (which included 2 out of 3 paediatric liver units) thought 'diagnostic yield' from these tests was 'poor' and 44% based this on their personal view, 27% on local data and 18% on anecdotal evidence.

Conclusion:

Our study identified a wide variation in definition and investigation of conjugated jaundice in neonates. Most neonatal paediatricians believe yield from these investigations is poor. Further studies are needed to support or refute this view. National consensus guidelines need to be developed to standardize practice.

Synbiotics for Inflammatory Bowel Disease: Useful in Adults but Problematic in Paediatrics

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Introduction/Background:

Alterations in the colonic mucosal bacteria (microbiota) are thought central to the pathogenesis of inflammatory bowel disease (IBD). Limited data from adult studies suggests that modification of the microbiota by targeted use of probiotic agents alongside specific prebiotics (collectively termed synbiotics) can positively impact on both ulcerative colitis (UC)¹ and Crohn's disease (CD)².

Aim:

To determine the feasibility of using a synbiotic comprised of Synergy 1 (inulin oligofructose prebiotic), and Bifidobacterium longum (probiotic) in children with IBD by assessing the acceptance and tolerability of the synbiotic.

Subjects and Methods:

Patients with known IBD aged between 6 and 16 years under paediatric follow-up were approached for inclusion in this study (funded by CICRA). Children were excluded if they had used any other prebiotic/probiotic agent in the preceding two weeks, if they were using systemic antibiotics or if they had a severe exacerbation of their IBD. Patients were withdrawn from the study if they commenced antibiotics or an alternative prebiotic/probiotic or if they wished to discontinue their involvement. Study participation involved taking the probiotic (8X1011 freeze-dried, viable B. longum in a gelatin capsule) and prebiotic agents (3.5g Synergy 1 powder) twice daily for 3 months. At trial onset, a pre-study questionnaire was completed along with a physician's global assessment (PGA) of their IBD state. Repeat questionnaires were provided for completion and mail back at 1 week, 1 month, 2 months and 3 months. A participant was deemed to have completed the trial if they successfully completed the synbiotic course and returned all questionnaires.

Results:

23 children were recruited to the study, of whom 11 (48%) were male. The median age of recruits was 13.4 years (7.8 to 16.6 years). 11 patients had a diagnosis of CD, 6 had UC and 4 had inflammatory bowel disease unspecified. The median duration from diagnosis to enrolment was 2.8 years (0.3 to 10.3 years). PGA was "inactive" in 19, "mild" in 3, "moderate" in 1 and "severe" in 1 patient at enrolment. Only 3 of the first 17 patients completed the study as intended. There was an awareness within the study team from patient feedback that the prebiotic was poorly tolerated, therefore the last 6 participants undertook a modified version of the protocol with a tapered introduction of the prebiotic: none in week 1, once daily in week 2, then twice daily (full dose) from week 3 onwards. Despite this alteration, only 2 of these 6 participants completed the modified study. The completion rate overall was 5/23 (22%). The reasons for withdrawal were as follows: 6 diarrhoea/potential IBD flare-up, 6 stopped returning questionnaires, 4 required antibiotics (1 for Clostridium difficile in stools), 1 advised by their general practitioner because of a rash, 1 felt unwell on prebiotic and completed on probiotic only and 1 whose parent stopped therapy after noticing "no difference" in their child's condition.

Summary and Conclusion:

Although the use of synbiotics has shown promise in limited adult studies, including the Scottish adult UC and CD population, this small feasibility study in a cohort of fairly well paediatric IBD patients has shown that tolerability of these agents is poor in children. We suspect the high drop-out rate was due to poor tolerance of the prebiotic agent used, but further studies are necessary with the specific aim of assessing tolerance of different prebiotic and probiotic agents in paediatric IBD before larger trials studying efficacy can be undertaken.

1 Furrie E, Macfarlane S, Kennedy A, et al. Gut 2005; 54: 242-9.

2 Steed H, Macfarlane GT, Blackett KL, et al. Aliment Pharmacol Ther 2010; 32: 872-83.

The incidence of childhood coeliac disease in Scotland- the first year of the SPSU Coeliac project

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Aim:

To establish the incidence of coeliac disease (CD) (<16 years) in Scotland using the Scottish Paediatric Surveillance Unit (SPSU) e-reporting system and through strategic contacts within the three Tertiary GI Regions -West (W), East (E) and North (N) of Scotland.

Subjects and Methods- The SPSU began e-mailing SPS members in September 2009- the question was how many new cases of CD were diagnosed by members in the preceding month. Regular e-mail contact was maintained throughout the study period. Only cases diagnosed from 1.09.09 to 31.08.10 were included in the study. Minimum incidence rates for each region were calculated using population data from the General Register Office (GRO) for Scotland.

Results:

There has been steady reporting of new cases. Double reporting happened in 13 cases. These have been cross-checked and duplicate cases excluded using sex, age and postcode data. Four cases were furthermore excluded as a biopsy to confirm diagnosis was not performed (2W, 1N, 1E). A total of 94 new cases of CD were reported (38E: 39W: 17N), male to female ratio was 1:2. Mean (SD) age at presentation was 7.9 (±4.1) years. 57% of patients had abdominal pain, 31% diarrhoea and 15% were asymptomatic. 24% of cases were actively screened for CD (60% had Type 1 diabetes). 30% had a first degree relative with CD. There were no significant differences in age at presentation (p=0.79), asymptomatic cases (p=0.29) and those actively screened (p=0.77) between tertiary regions. Of the 94 patients, 90 (94 %) were scoped by a paediatric gastroenterologist, one by an adult gastroenterologist (W) and 3 by paediatric surgeons (N). The under 16 populations within each catchment area are 504,973 in West, 230,323 in North and 240,664 East Scotland (GRO). The calculated incidence of CD is 7.7 West, 7.4 North and 15.8 East per 100 000 population.

Conclusions:

The study has successfully captured 94 new cases of CD within the Scottish population. There is some uniformity in terms of screened groups, presenting symptoms and number of asymptomatic patients between regions. The majority have diagnosis confirmed endoscopically in an appropriate paediatric setting. There is a stark difference, however, in the number of cases diagnosed per head of population, with a rate more than twice the West and North being diagnosed in the East of Scotland (Lothian, Fife and Borders). The reasons for this are unlikely to be due to different population genetics, given the homogeneity of the population. Further analysis is required to establish why.

The Long and The Short of It. Experiences of a Paediatric Multi Disciplinary Regional Intestinal Failure Team (RIFT)

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Background:

Transition to enteral feeding in the complex and heterogeneous group of patients with intestinal failure is of key importance in promoting pro adaptive changes.

A coordinated team approach is essential, however management can be challenging, demanding of resources, and standards of care Nationally have been described as being patchy. It has been suggested that discharge for Home Parenteral Nutrition (HPN) should occur from 2-4 months (60-120 days) of age in clinically stable patients (1).

Aim:

To report our team's experience over the last 2 years (2008 and 2009) of patients with long term intestinal failure highlighting impact on clinical resources and nutritional outcomes.

Method:

In-patients with intestinal failure are seen by the whole RIFT team (including consultant gastroenterologist, consultant surgeon, specialist dietitian, pharmacist and speech therapist) once a week to review all the aspects of care. Patients are then reviewed in smaller teams throughout the week. A dietetic data base records RIFT activities and from this we identified those patients seen with intestinal failure who received PN for >28 days and the number of team contacts. A review of the medical notes and in-patients admission data was completed to identify length of stay. A surgical database recording surgical procedures on these patients was also reviewed. We investigated the number of contacts with the whole team. We excluded individual specialist and smaller group contacts to the patient.

Results:

We identified 6 patients under the team's care in 2008 and 11 patients in 2009. Total numbers of whole team individual patient contacts were 45 and 86 in 2008 and 2009 respectively (average number during the child's stay was 7.5 in 2008 and 8 in 2009). Source of referral for these patients was primarily from our Level 3 NNU which represented 50% of patient referral in 2008 and 70% in 2009. Other sources of referral were from outside transfers and from term infants presenting direct at The Children's Hospital. On referral to the team the majority of patients were on exclusive PN and this proportion remained similar between 2008 and 2009 (~70%). There was a small increase in patients who had already started some trophic feeds (2/6 versus 5/11 respectively). Nutritional outcome on discharge showed a large improvement in patients establishing on oral diet alone (i.e. no artificial tube or PN support) to meet all requirements from 25% in 2008 to 50% in 2009. Discharge within 2-4 months recommended was achieved in 1 patient in 2008 and 2 patients in 2009. Average length of stay for the patients in 2008 was 142 days and 159 days in 2009. Discharging at 3 months (mid point of recommendations) represented 156 potential bed days saving in 2008 and 560 in 2009.

Summary & Conclusions:

This data highlights the complex nature and high demand on resources associated with this patient group. These children represent long and expensive hospital stays as in-patients requiring intervention from a multi disciplinary team. Managing this small but highly vulnerable patient group in increasing numbers has provided invaluable experience and our results indicate our success in establishing full oral feeds with no associated large increase in average length of stay. However, the recommended discharge time is currently not being achieved in part due to many remaining unstable within this timeframe but also due to resource implications. This highlights the need for improving efficiency of support and setting up HPN but also has implications for community care. Where possible this would represent a considerable potential clinical (e.g. reduced line infection rate) and financial benefit in addition to the social and emotional advantage to children and their families.

References:

1) BSPGHAN Intestinal Failure Working group final report. March 2007

The relationship between C-reactive protein genotype and inflammatory bowel disease phenotype and its diagnostic utility at diagnosis: a pilot study.

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Background:

With regards to inflammatory bowel disease (IBD) over 50 serum and faecal biomarkers have been proposed to date. C-reactive protein (CRP) is an acute phase reactant which is commonly used in paediatric practice to inform clinicians at IBD diagnosis and during the patient's clinical course. However, it is now becoming clear that many of these biomarkers may not only allow disease monitoring but may also contribute to disease phenotype.

Aim:

A pilot study to assess the relationship between CRP genotype and IBD phenotype and also the diagnostic utility of serum CRP levels at IBD diagnosis.

Methods:

Five single nucleotide polymorphisms (SNPs) were used to haplotype-tag the CRP gene on chromosome 1q. Two additional SNPs which had previously been shown to influence serum CRP levels were also identified. These SNPs were then genotyped on the Illumina platform by TaqMan analysis in 330 Scottish early-onset IBD patients (<17yrs). Additional phenotypic characteristics and laboratory values were obtained from an extensive paediatric Scotland-wide database and case note review. Statistical analysis was carried out using Haploview and R.

Results:

The study group consisted of 219(66%) patients with Crohn's disease (CD), 78(24%) with ulcerative colitis (UC) and 33(10%) with inflammatory bowel disease unspecified (IBDU). There was a male:female ratio of 1.24 and the mean age(\pm SD) at diagnosis was 11.0yrs(\pm 3.1). Only 168 (51%) IBD patients demonstrated a rise in CRP above the normal range (i.e. the reference range specifically used in each paediatric clinical chemistry laboratory) at diagnosis. This compared to 65% for ESR (>20mm/hr; p =<0.001) and 91% for faecal calprotectin (>100ug/g; p =<0.001). Patients with CD were significantly more likely to have a raised serum CRP at diagnosis compared to those with UC (p =<0.001) however there was no significant difference in CD patients with ileal or colonic disease. No differences existed in serum CRP levels between males and females. With regard to CRP genotype five haplotypes were identified (A,B,C,D,E) with a frequency of greater than 5%. Haplotype B was significantly less common in CD patients compared to UC (p =0.002) and also in males with IBD (p =0.0436). Haplotype C was less common in males with CD (p =0.0373) with Haplotype D under-represented in patients with ileal CD (p =0.0263). The SNP rs1205 (which lies in a regulatory region of the CRP gene) was also significantly different in CD versus UC patients (p =0.0114).

Conclusions:

It can be seen that although serum CRP levels based on normal laboratory concentrations have little diagnostic value when used in isolation during the investigation of suspected IBD, there are significant differences between IBD phenotypes. In addition significant differences in CRP genotype exist between CD and UC. This information along with further large scale studies may enable serum CRP levels to be used more effectively in the assessment of paediatric IBD patients.

The role of cytomegalovirus in inflammatory bowel disease: a systematic review.Henderson P^{1,2}, Wilson DC^{1,2}¹Department of Paediatric Gastroenterology, Hepatology and Nutrition, Royal Hospital for Sick Children, Edinburgh. ²Child Life and Health, University of Edinburgh, Edinburgh.**Introduction:**

Cytomegalovirus (CMV) has been widely implicated in the aetiopathogenesis, exacerbation and treatment refractoriness of inflammatory bowel disease (IBD). In addition, recent research showing that NOD2 and TLR2 (genes in which germline mutations give rise to increased IBD susceptibility) both act as viral pattern recognition receptors has stimulated a renewed interest in the role of this common virus in IBD.

Aim and Methods:

To study the evidence for the role of CMV in IBD by formal systematic review. An electronic database search (up to Nov 2009) of the Cochrane Library, Medline, Embase and the British Nursing Index and Archive was performed with keywords related to IBD and cytomegalovirus in addition to searches on PubMed, other online indexes and foreign language periodical databases. A hand search of reference lists of articles was also performed along with reviews of major gastroenterology journals and meeting abstracts. The papers identified were then reviewed and the level of evidence (EL) was assessed using the Scottish Intercollegiate Guidelines Network (SIGN) methodology (www.sign.ac.uk).

Results:

The initial database searches produced 264 hits and after review of their abstracts a total of 69 papers were identified; a further 77 papers were sourced from their reference lists. A total of 108 were included and comprised 3 systematic reviews, 12 case-control studies (EL 2-), 5 cohort studies (EL 2-), 20 case series (EL 3) and 68 case reports. The literature search in the only methodological robust systematic review (EL 1+) ended in 2002 with the two subsequent systematic reviews demonstrating major weaknesses (EL 1-). The remaining studies varied widely with regard to the population studied, the method of CMV detection and the clinical details presented. Analysing the case-control studies that tested biopsy or surgical specimens the overall incidence of CMV detection was 32/100 in IBD and 12/100 in controls ($p=0.001$). There was some consensus that CMV contributed to steroid-refractory disease and anecdotal evidence that the treatment of CMV-related relapses with antiviral therapy may be beneficial.

Conclusion:

The evidence surrounding the role of CMV in IBD is poor. Few studies have been of sufficient quality to provide convincing evidence of CMV as an aetiopathological factor in active IBD or that the use of antivirals should be routinely used in those in which CMV disease is suspected. A prospective randomised controlled trial of antiviral therapy for those found to have active CMV, by a variety of accurate investigations, should be considered to ascertain the benefits of treating this prevalent pathogen.

The role of endoscopy in under 1 year olds referred for faltering growth and diarrhoea

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Introduction/ Background:

Gastrointestinal (GI) endoscopy is an increasingly common procedure in young infants with persistent gut symptoms. Only scant data exists of the usefulness of intestinal mucosal histology in young children referred for faltering growth (FTT) and diarrhoea.

Aim:

The aim of this study was to identify all children under one year of age referred for FTT and diarrhea who underwent GI endoscopy and review histological outcomes.

Subjects and Methods:

Intestinal mucosal biopsies were obtained and analytical histological findings were recorded in 198 cases (median age 202 days, age range 26-364 days) in a total of 175 infants less than 12 months old (98 males, 77 females) that were referred to a single paediatric gastrointestinal tertiary unit during the period June 1987- August 2007 due to FTT and diarrhoea.

Results:

A total of 102 gastroscopies, 83 jejunal biopsies and 85 colonoscopies were performed in our selected group of patients in the specified time period. The procedure failed to produce adequate samples in 5/198 cases (2.5%), was normal in 50/198 cases (25.2%), whereas abnormalities were found in 143/198 cases (72.2%). In the latter group, villous atrophy was the most common histological finding evident in 94/134 small bowel biopsies (70.1%); inflammatory cell infiltration was also present in 41/94 cases (43.6%), with tissue eosinophilia in 21/41 (51.2%). When colonic biopsies were taken, inflammation was found in 33/67 cases (49.2%), with eosinophilic component in 16/33 of those (48.5%). 4/193 (0.02%) patients were diagnosed with microvillous inclusion disease, 4/193 (2%) with autoimmune GI disease, 1/193 (0.5%) with graft-versus-host disease post bone marrow transplantation, 3/193 (1%) with tufting enteropathy and 1/193 (0.5%) with disaccharidase deficiency.

Conclusion:

Young infants with faltering growth and on-going diarrhoea are most likely to have histological abnormalities in upper and lower gastrointestinal endoscopy, which makes this investigation a valuable tool in directing their treatment.

The value of MRI in terminal ileal Crohn's disease: assessment and inter observer agreement

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Background:

Magnetic Resonance Imaging (MRI) is becoming increasingly employed to delineate mid gut disease in place of barium follow-through for Crohn's disease (CD). While objective comparisons are not readily available for jejunal and proximal ileal disease, terminal ileal endoscopy and biopsy findings may validate MRI findings of this area.

Aims:

We aimed to assess terminal ileal changes in patients with CD using MRI.

Methods:

Paediatric patients with CD received contrast enhanced MRI of the small bowel and endoscopy with biopsy of the terminal ileum. Patients were imaged in the supine position using a 1.5 T MRI scanner. Once adequate bowel distension was achieved with polyethylene glycol, Fast Field Echo (FFE) and T1 thrive Spectral Selection Attenuated Inversion Recovery (SPAIR) sequences in coronal and axial orientations from the diaphragm to the groins were obtained. Further images were obtained 3 and 5 minutes post gadolinium injection. MRI images were reported by two radiologists working independently who were blinded to the endoscopic and histological findings. Terminal Ileal biopsy was considered gold standard to identify CD in this region. Reported MRI abnormalities were compared against the same. Interobserver agreement on MRI findings were analysed using the Cohen's Kappa statistical method.

Results:

Among the 18 patients who had MRI for this indication (9 male, 9 female; Mean age 12.1 years), abnormal ileum was identified by biopsy in 12/18 cases; Between the two reporters, sensitivity of MRI was between 50% - 67% and specificity 83-100%. The positive predictive value was 89%- 100% and the negative predictive value was 50%-56%. Concordance of terminal ileal findings between radiologists was 83.33% (K= 0.667, good agreement). Bowel wall thickening (K= 0.769) and contrast enhancement (K= 0.667) also showed good agreement. Luminal dilation identification was in perfect agreement (K=1.00). Poor agreement was found between identification of stenosis and extra-mural findings.

Conclusion:

A strong specificity and positive predictive value for MRI identification of terminal ileal CD is encouraging. Intra-observer variation was evident at a level that suggests reasonable reliability in MRI small bowel interpretation. MRI ability to identify bowel wall thickening, contrast enhancement and luminal dilation was good to perfect.

Transoral incisionless fundoplication for treatment of pediatric GERD: 12-months results of a feasibility study

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Objective:

Transoral incisionless fundoplication (TIF) using EsophyX was evaluated for the treatment of pediatric gastroesophageal reflux disease using subjective and objective outcomes.

Methods and procedures:

Inclusion criteria were chronic and symptomatic GERD, refractory to or dependent on high dose proton pump inhibitor (PPI) therapy. Exclusion criteria were >18 years of age, dysphagia, obesity, previous upper intestinal surgery, or hiatus hernia > 2cm. Pre-procedure assessment consisted of upper GI endoscopy, 24-h esophageal pH, and Quality of Life in Reflux and Dyspepsia (QOLRAD) questionnaire. The TIF procedure reconstructed the antireflux barrier through augmentation of the GE junction tightness. The TIF procedure was performed using EsophyX following a standardized TIF2 protocol.

Results:

Ten patients [8 male, median age 12 (range 9-16) years, weight 43.7 (28.0-91.0) kg] underwent TIF because they suffered from GERD for 45 (24-70) months, had documented gastroesophageal reflux by abnormal pH-metry (pH<4 for >6% of time) or esophagitis (LA grade A or B), and were on antisecretory medication. Median operative time was 42 (25-94) min. In all patients a wrap of 270 degrees and 1-3 cm in length was achieved. The first two patients experienced pneumomediastinum shown on CT scan, but no leak was revealed on barium swallow. One of these two patients was treated for possible mediastinitis and discharged after 5 days of intravenous antibiotics. CO2 insufflation was employed on subsequent patients and resulted in no further complications. At each 6-month and 12-month follow-up, reflux index was significantly reduced and QOLRAD scores higher and 80% of patients discontinued PPIs completely.

Patient ID	Reflux Index			QOLRAD Score			PPI Usage	
	Pre-TIF	Month 6	Month 12	Pre-TIF	Month 6	Month 12	Month 6	Month 12
001	9.4	6.3	8.7	71	175	175	None	None
002	18.4	3.5	14.2	146	172	172	None	None
003	37.0	27.9	28.2	86	175	175	None	None
004	18.7	13.4	3.8	104	127	135	Daily	Daily
005	7.3	3.8	5.8	54	171	173	None	None
006	6.1	7.5	7.5	56	25	25	Daily	Daily
007	10.3	8.4	9.6	65	145	150	None	None
008	13.4	3.8	8.7	68	169	139	None	None
009	5.7	2.2	6.0	122	155	167	None	None
010	20.0	3.6	4.0	80	175	175	None	None
<i>n</i>	10	10	10	10	10	10	10	10
Ave	14.6	8.0	9.7	85.7	148.1	148.9		
SD	9.5	7.7	7.2	30.1	46.4	46.0		
%Normalized		60%	40%				80%	80%
<i>t test</i>		0.002	0.02		0.001	0.001		

Conclusion: The TIF procedure using EsophyX was feasible and safe in children. Subjective and objective outcomes at one year were significantly improved, and PPIs were discontinued by 80% of patients.

Trends in UK paediatric home parenteral nutrition and implications for service development.

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There has been a rising demand for home parenteral nutrition (HPN) services for children over the past 20 years. In order to help plan a strategy for delivery of care at regional level, our aim was to carry out a national point prevalence survey of HPN during February 2010.

Paediatric gastroenterologists in 33 hospitals known to have provided HPN services were identified from their membership of the British Society of Paediatric Gastroenterology, Hepatology and Nutrition and participation in the British Intestinal Failure Survey (BIFS). Anonymised data on children currently receiving, or about to be discharged on, HPN were collated by the BIFS administrator and results compared with a similar study performed by the British Paediatric Surveillance Unit in 1993. Trends in underlying diagnosis were explored using the BIFS database for 2006-2009.

Results:

Colleagues from all 33 (100%) Trusts responded: 167 patients were reported of whom 139 were already established on HPN, four times as many as in 1993, and 28 were about to be discharged home for the first time. Six young people were older than 16 years, but remained under the care of a paediatrician. The regional point prevalence of HPN varied from 1.76 to 41.4 per million, with a mean of 13.7 patients per million. Short bowel syndrome had increased from 27% to 63% of cases.

Conclusions:

The large overall increase in numbers of HPN patients suggests that a national strategy needs to be developed for the management of chronic IF.

Use of an interferon- γ release assay to screen for latent tuberculosis (TB) in children with inflammatory bowel disease (IBD)

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Introduction: Use of anti-TNF α biological agents (Infliximab and adalimumab) has been associated with the reactivation of latent tuberculosis. As a result, it is recommended that children should be evaluated for TB prior to treatment with one of these agents. The long established Tuberculin skin test (TST) has a number of limitations, some of which have been overcome by the use of blood based interferon- γ release assays such as the T-spot test. However, the optimal method for diagnosing latent TB infection remains unclear, particularly in immunocompromised children.

Method: We performed a retrospective study of paediatric patients with IBD undergoing screening for TB prior to commencing biological therapy. Clinical data collected included gender, age, disease diagnosis, date of diagnosis, immunosuppression therapy at time of T-spot, and white cell/neutrophil counts. The outcome of the procedure was documented and reason for failure investigated. We also looked at what other investigations for TB had been performed. As a comparison population to our children with IBD, data on children who underwent TB testing at our local paediatric TB clinic were also collected

Results:

19 children with IBD were identified as currently receiving or about commence biological therapy. 3 had not undergone T-Spot testing and were excluded, leaving 16 children (M=8). All patients were on concurrent treatment with an immunomodulatory agent (azathioprine or methotrexate) at the time of commencing biological treatment.

In the comparison population, 22 children (M=14) were identified who underwent T-spot testing at the TB clinic between March and April 2010. The majority were being screened due to TB contact. None of these children had a defined immune deficiency or were on immunomodulator therapy.

There was no difference in gender between IBD and comparison group. However, children in the comparison group were significantly younger ($p = 0.0002$). Venesection in both groups was carried out by the same staff and the T Spot analysis was performed in the same laboratory in both IBD and comparison groups.

Of the 16 children with IBD, 8 (50%) had invalid results. Of the 50% with failed assays, all were 'inconclusive' due to insufficient peripheral blood mononuclear cell yields.

Only 3 (13.63%) tests from the comparison group were 'inconclusive' due to insufficient peripheral blood mononuclear cell yields, though a further 3 were 'indeterminate' due to poor response in the positive control for the test. Children with IBD were significantly more likely to have a failed T Spot test ($p=0.02$). In the IBD patients, neither the total white cell count nor the neutrophil count were significantly different between those with inconclusive results and those with valid results at the time of T-spot testing. Unfortunately patients in the comparison group did not have a full blood count checked at the time of T-Spot testing.

Conclusion:

Although limited by small patient numbers, these results suggest significant limitations in the use of T spot testing to screen for latent TB in children with IBD. The failure is likely to be due to the concurrent treatment with immunomodulatory drugs. More research is required to determine the most appropriate method of screening for TB in this patient group.

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