Pathological Society
of Great Britain & Ireland

The Journal of Pathology 1st in Pathology

Understanding disease
CENTENARY YEAR
2006

Winter Scientific Meeting

incorporating the Trainees' Programme

3–5 January 2007

UCL

The 191st Meeting of the Pathological Society of Great Britain & Ireland will be held at UCL. Hosted by the Department of Pathology, Royal Free and University College Medical School

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PROGRAMME ACKNOWLEDGEMENTS

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PROGRAMME SYNPOSIS AND TIMETABLE

(Showing times, sessions and venues)

Ⓒ *Cruciform Building (Basement), Gower St.* Ⓜ *UCL Main Building, Gower St.* Ⓡ *Rockefeller Building, University St.*

WEDNESDAY 3 JANUARY 2007

Time	Building & Venue	Session
08.00	Ⓜ–*North Cloisters*	**Registration and Coffee**
09.00–12.00	Ⓒ–*Lecture Theatre 1*	Symposium: *Urological Pathology*
09.00–17.00	Ⓒ–*Cluster Room*	Slide Seminar Competition Case Viewing: *LBC in non-gynaecological cytology* (Win a case of champagne!)
10.30–12.00	Ⓒ–*Lecture Theatre 2*	Sino-British Pathology Forum
10.30–11.00	Ⓜ–*The Cloisters*	Coffee
12.00–12.15	Ⓒ–*Lecture Theatre 1*	Welcome Address: Prof G Williams, UCL
12.15–13.15	Ⓒ–*Lecture Theatre 1*	Academic Pathology Forum
13.15–14.15	Ⓜ–*The Cloisters*	Lunch
14.00–15.00	Ⓜ–*The Cloisters*	Poster Viewing (Abstracts P1–P39)
14.00–15.00	Ⓜ–*The Cloisters*	Trade Exhibition
15.00–18.00	Ⓒ–*Lecture Theatre 1*	Symposium: *Undergraduate Education*
15.00–17.00	Ⓒ–*Lecture Theatre 2*	Oral Communications (Abstracts O1–O6)
15.30–16.00	Ⓜ–*The Cloisters*	Tea (Oral Communications)
16.30–17.00	Ⓜ–*The Cloisters*	Tea (Symposium: *Undergraduate Education*)
18.00–19.30	Ⓜ–*Jeremy Bentham Room*	Welcome Reception

THURSDAY 4 JANUARY 2007

Time	Building & Venue	Session
08.00	Ⓜ–*North Cloisters*	**Registration and Coffee**
09.00–15.00	Ⓒ–*Cluster Room*	Slide Seminar Competition Case Viewing: *LBC in non-gynaecological cytology* (Win a case of champagne!)
09.00–10.30	Ⓒ–*Lecture Theatre 1*	Plenary Oral Presentations (Abstracts PL1–PL6)
10.30–11.00	Ⓜ–*The Cloisters*	Coffee
11.00–13.00	Ⓒ–*Lecture Theatre 1*	Trainees Forum
13.00–14.15	Ⓜ–*The Cloisters*	Lunch
13.00–14.00	Ⓡ–*JF Smith Seminar Room (3rd floor)*	Meet the Experts: *Post Mortem Histology*
13.30–14.30	Ⓜ–*The Cloisters*	Poster Viewing (Abstracts P40–P82)
13.30–14.30	Ⓜ–*The Cloisters*	Trade Exhibition
14.30–17.30	Ⓒ–*Lecture Theatre 1*	Symposium: *Advances in Lymphomas since the advent of the WHO Classification*
16.00–16.30	Ⓜ–*The Cloisters*	Tea
17.30–18.15	Ⓒ–*Lecture Theatre 1*	Pathological Society's 3rd Goudie Lecture: *Our changing view of the genome: implications for Pathology.* Prof PA Hall, Belfast
19.30–20.00	Ⓜ–*The Flaxman Gallery*	Society Dinner Reception
20.00–22.30	Ⓜ–*The Old Refectory*	Society Dinner

FRIDAY 5 JANUARY 2007

Time	Building & Venue	Session
08.00	Ⓜ–*North Cloisters*	**Registration and Coffee**
09.00–12.45	Ⓒ–*Lecture Theatre 2*	Oral Communications (Abstracts O7–O20)
09.30–16.30	Ⓜ–*Gustave Tuck Lecture Theatre*	UK NEQAS for Immunocyotchemistry and FISH Testing
09.30–12.00	Ⓒ–*Lecture Theatre 1*	Slide Seminar Follow-up Symposium: *LBC in non-gynaecological cytology*
10.30–11.00	Ⓜ–*The Cloisters*	Coffee
12.45–14.00	Ⓜ–*The Cloisters*	Lunch
13.00–14.00	Ⓡ–*JF Smith Seminar Room (3rd floor)*	Meet the Experts: *Getting started in Research*
13.00–14.00	Ⓜ–*The Cloisters*	Trade Exhibition
14.00–16.30	Ⓒ–*Lecture Theatre 2*	Trainee Oral Communications (Abstracts O21–O28)
15.00–15.30	Ⓜ–*The Cloisters*	Tea

SCIENTIFIC SESSIONS INFORMATION

Ⓒ *Cruciform Building (Basement), Gower St.* Ⓜ *UCL Main Building, Gower St.* Ⓡ *Rockefeller Building, University St.*

PLENARY ORAL SESSION Ⓒ–*Lecture Theatre 1*

The plenary oral session, in which the 6 highest-ranked submitted oral abstracts will be presented, will be held on **Thursday 4 January, 09.00–10.30 hrs**.

Prize: A prize for the best presentation, donated by the *Journal of Pathology* will be presented at the Society Dinner.

ORAL COMMUNICATIONS Ⓒ–*Lecture Theatre 2*

Oral communication sessions will be held as follows:

Wednesday 3 January, 15.00–17.00
Friday 5 January, 09.00–12.45

Note to presenters: Speakers are reminded that no communication may exceed the time allocated on the programme without the consent of the meeting, obtained through the Chairman.

POSTER VIEWING & ROUNDS Ⓜ–*The Cloisters*

Posters will be displayed throughout the meeting, but dedicated viewing sessions will be on:

Wednesday 3 January, 14.00–15.00
Thursday 4 January, 13.30–14.30

Poster Rounds: Chairmen will review posters during Wednesday 3 January and Thursday 4 January.

Ideally, posters should be in place by **12.00 hrs on Wednesday 3 January** and removed by **15.00 hrs on Friday 5 January**. At least one of the contributors must be in attendance during the viewing period, as indicated in the programme synopsis.

Prizes: Prizes are awarded for the three best posters: The Sir Alastair Currie Prize, Second and Third prizes will be presented at the Society Dinner on Thursday 4 January.

SYMPOSIA

Four symposia will be held:

Wednesday 3 January Ⓒ–*Lecture Theatre 1*
09.00–12.00 *Urological Pathology*
15.00–18.00 *Undergraduate Education*

Thursday 4 January Ⓒ–*Lecture Theatre 1*
14.30–17.30 *Advances in lymphomas since the advent of the WHO Classification*

Friday 5 January Ⓒ–*Lecture Theatre 1*
09.30–12.00 *LBC in non-gynaecological cytology – Slide Seminar Follow-up*

FORA

Wednesday 3 January

10.30–12.00 Sino-British Pathology Forum Ⓒ–*Lecture Theatre 2*
12.15–13.15 Academic Pathology Forum Ⓒ–*Lecture Theatre 1*

TRAINEES PROGRAMME

Thursday 4 January

11.00–13.00 Trainees Forum Ⓒ–*Lecture Theatre 1*
13.00–14.00 Meet the Experts – *Post Mortem Histology* Ⓡ–*JF Smith Seminar Room (3rd floor)*
Expert: Dr PJ Gallagher, Southampton

Friday 5 January

13.00–14.00 Meet the Experts – *Getting started in research* Ⓡ–*JF Smith Seminar Room (3rd floor)*
Experts: Prof NR Lemoine, London and Prof I Tomlinson, London
14.00–16.30 Trainee Oral Communications Ⓒ–*Lecture Theatre 2*

SLIDE SEMINAR – *LBC in non-gynaecological cytology* Ⓒ–*Cluster Room*

Competition: There will be a slide seminar competition and digital images of all cases will be available for preview during the course of the meeting. The images will also become available on the Society's website in due course.

The images will be available for viewing on:
Wednesday 3 January, 09.00–17.00
Thursday 4 January, 09.00–15.00

Prize: A case of champagne will be awarded at the Society Dinner on Thursday 4 January.

Discussion Session: Friday 5 January, 09.30–12.00 Ⓒ–*Lecture Theatre 1*

SOCIETY LECTURE Ⓒ–*Lecture Theatre 1*

Thursday 4 January, 17.30–18.15

The Pathological Society of Great Britain & Ireland's 3rd Goudie Lecture entitled: *Our changing view of the genome: implications for pathology,* will be given by Prof PA Hall, Centre for Cancer Research and Cell Biology, Division of Pathology, Queen's University, Befast.

COMPANION MEETING Ⓜ–*Gustave Tuck Lecture Theatre*

Friday 5 January

09.30–16.30 UK NEQAS for Immunocytochemistry and FISH Testing

TRADE EXHIBITION Ⓜ–*The Cloisters*

Delegates are encouraged to visit the **Trade Exhibition** and are requested to support the companies represented there.

GENERAL ARRANGEMENTS

Ⓒ *Cruciform Building (Basement), Gower St.* Ⓜ *UCL Main Building, Gower St.* Ⓡ *Rockefeller Building, University St.*

REGISTRATION

Registration is via the links on the Society's website: **www.pathsoc.org.uk**
The registration system will issue an automated email acknowledgement. All tickets will be issued on arrival at the Delegate Reception Desk at UCL.

FEES *(Fees include refreshments and lunch)*

Non-concessions

- **Up to and including 27 November 2006:**

Society Members	Whole meeting £180, **or** £80 per day (or part day)
Non-members	Whole meeting £270, **or** £120 per day (or part day)

- **After 27 November 2006:**

Society Members	Whole meeting £270, **or** £120 per day (or part day)
Non-members	Whole meeting £405, **or** £180 per day (or part day)

Concessions – Qualifying Categories

Group A – Society Members
Honorary or Senior Members, Biomedical Scientists/Technicians (all grades), PhD Students, Post-Doctoral Fellows, Trainees.

Group B – Non-Members
Biomedical Scientists/Technicians (all grades), PhD Students, Post-Doctoral Fellows, Trainees.

Group C – Non-Members (at Society Member rates)
Undergraduates.

Groups B & C: *Concessionary delegates **must** provide documentary evidence to qualify for the concessionary Fees. Please send confirmation of your status, signed by your head of training, stating National Training Numbers, where applicable. This must be emailed or faxed to:*
(Email) julie@pathsoc.org.uk *(Fax)* +44(0)20 7976 1267

Concessions

- **Up to and including 27 November 2006:**

Society Members	Whole meeting £50, **or** £25 per day (or part day)
Non-members	Whole meeting £75, **or** £40 per day (or part day)

- **After 27 November 2006:**

Society Members	Whole meeting £75, **or** £40 per day (or part day)
Non-members	Whole meeting £105, **or** £60 per day (or part day)

Society Dinner

- £50 per ticket

ADVANCE REGISTRATION – CLOSING DATE

Advance registration will close on **Monday 18 December 2006**.
After this deadline registration will only be accepted on-site at the meeting.

CANCELLATIONS

Please note that the Society is **unable** to refund registration fees for cancellations **received after Monday 11 December 2006**.

DELEGATE ENROLMENT (AT THE MEETING)

Enrolment at the Delegate Reception Desk will take place at Ⓜ–*North Cloisters* as follows:
Wednesday 3 – Friday 5 January 2007, from 08.00

PRESENTATION CHECKING AND PREVIEW

This will be available at Ⓒ–*Cluster Room*

ORAL PRESENTATIONS AND LECTURES

Electronic presentations must be in Microsoft PowerPoint (PC or Mac). *Versions earlier than 2000 are not acceptable.* Presentations should be submitted **in advance** of the meeting to arrive **no later than 18 December 2006**.

Files may be emailed or a CD posted to Bridgette Smith (telephone: +44(0)20 7679 6304) as follows:

Email: bridgette.smith@ucl.ac.uk *(maximum attachment size is 5 megabytes)*

Post: Bridgette A Smith
PA/Office Manager, Department of Pathology, University College London,
Rockefeller Building, University Street, London WC1E 6JJ

Please **label** the files or CDs with:

- Date and time of your lecture
- Lecture theatre
- Your name

IMPORTANT: **Please bring another copy of your presentation with you to the meeting**.

MESSAGES

During the meeting, messages for delegates may be left on **telephone: +44(0)20 7679 2000 extn 5283**. There will also be a message board located beside the Delegate Reception Desk.

REFRESHMENTS

All refreshments will be served at Ⓜ–*The Cloisters.*

BADGES

Delegates are requested to wear their badges at **all** times.

SMOKING

Smoking is prohibited at all meetings and social events.

DISCLAIMER

The Pathological Society of Great Britain & Ireland cannot be held responsible for any injury or loss sustained during the Meeting.

TRAVEL

Train – Mainline stations
King's Cross, St. Pancras, Euston

Train – Underground stations
Warren Street (Northern Line; Victoria Line)
Euston Square (Hammersmith & City Line; Metropolitan Line; Circle Line)

Car
Parking is almost impossible! NCP car parks are nearby but expensive. Daily Conjestion Charge of £8 will apply.

Air
From London Heathrow take the Piccadilly Line to Green Park, change to the Victoria Line and travel to Warren Street.

ACCOMMODATION

For a list of local hotels, at discounted "UCL rates," see the Society's website: **www.pathsoc.org.uk**

SOCIAL ACTIVITIES

Wednesday 3 January, 18.00–19.30, at Ⓜ–*The Jeremy Bentham Room*
Welcome Reception
Tickets are free – to reserve your ticket please tick the relevant box when registering.

Thursday 4 January, 19.30 for 20.00, at Ⓜ–*The Old Refectory*
Society Dinner
Tickets are £50 each. To reserve your ticket please tick the relevant box when registering.

Local Places of Interest
Please refer to the Internet for information.

CONTINUING PROFESSIONAL DEVELOPMENT (CPD)

This meeting has been approved by **The Royal College of Pathologists** for the purposes of Continuing Professional Development. Credits can be accrued as follows:

For each full day: 7 points
For each half day: 3 points

Certificates
Delegates who are eligible for CPD points should complete the CPD Certificate Request Form which will be provided in their delegate pack at the meeting.

FUTURE MEETINGS

2007	3–6 July	**Glasgow Pathology 2007**: 4th Joint Meeting of the Pathological Society and the British Division of the IAP
2008	7–9 January	Oxford
	1–4 July	Leeds
2009	7–9 January	GKT, London
	30 June–3 July	**Cardiff Pathology 2009**: 5th Joint Meeting of the Pathological Society and the British Division of the IAP
2010	January	Imperial College, London
	29 June–2 July	St Andrews

ENQUIRIES BEFORE THE MEETING

Pathological Society of Great Britain & Ireland
2 Carlton House Terrace, London SW1Y 5AF
Telephone +44 (0)20 7976 1260
Fax +44 (0)20 7976 1267
Email admin@pathsoc.org.uk

08.00 **Ⓜ–North Cloisters**
REGISTRATION

09.00–17.00 **Ⓒ–Cluster Room**
SLIDE SEMINAR COMPETITION CASE VIEWING: *LBC in non-gynaecological cytology* (Win a Case of Champagne!)

09.00–12.00 **Ⓒ–Lecture Theatre 1**
SYMPOSIUM: *Urological Pathology*
Chair: Dr A Freeman, UCLH
Prof S Fleming, University of Dundee

09.00–09.30 *Histopathology and Genetics of Sporadic and Familial Renal Carcinoma*
Prof H Moch, University Hospital, Zurich

09.30–10.00 **[S7]** *Proteomics and Prostate Carcinoma*
Dr L Egevad, International Agency for Research on Cancer, Lyon, France

10.00–10.30 **[S8]** *The value of tissue microarrays in urological pathology*
Dr DM Berney, Barts & The London, Queen Mary School of Medicine & Dentistry, London

10.30–11.00 COFFEE Ⓜ–*The Cloisters*

11.00–11.30 **[S9]** *Evolving a 21st Century Uropathology EQA scheme: from slides to images*
Dr P Harnden, Leeds Teaching Hospitals, Leeds

11.30–12.00 *Growth factors and cell signalling in prostate cancer*
Prof S Fleming, University of Dundee

10.30–12.00 **Ⓒ–Lecture Theatre 2**
SINO-BRITISH PATHOLOGY FORUM
Chair: Prof PA Hall, Queen's University, Belfast

10.30–11.10 *Molecular pathology of pancreatic cancer*
10.30–10.50 Prof C Jie, Peking Union Medical College Hospital, CAMS & PUMC and Deputy President of Peking Union Medical College Hospital, President of Chinese Society of Pathology
10.50–11.10 Prof NR Lemoine, Institute of Cancer & CR-UK Clinical Centre, Bart's & The London School of Medicine (QMUL)

11.10–11.50 *Gastrointestinal stromal tumours*
11.10–11.30 Prof X-z Zhu, Cancer Hospital, Fudan University, Shanghai, China
11.30–11.50 Dr BF Warren, John Radcliffe Hospital, Oxford

11.50–12.00 Final discussion

12.00–12.15 **Ⓒ–Lecture Theatre 1**
WELCOME ADDRESS
Prof G Williams, UCL

12.15–13.15 **Ⓒ–Lecture Theatre 1**

ACADEMIC PATHOLOGY FORUM

Chair: Prof Sir NA Wright, Warden, Barts & The London School of Medicine and Dentistry

The Forum programme will be available on the Society's website in due course.

13.15–14.15 **Ⓜ–The Cloisters**

LUNCH

14.00–15.00 **Ⓜ–The Cloisters**

POSTER PRESENTATIONS, POSTER ROUNDS & TRADE EXHIBITION

CATEGORIES

Autopsy & Forensic **[P1–P4]**
Cellular/Molecular **[P5–P12]**
Education & Audit **[P13–P17]**
Experimental Tumour Pathology **[P18]**
Gastrointestinal **[P19–P26]** *(Note: P24 withdrawn)*
Genitourinary/Renal **[P28–P32]** *(Note: P27 withdrawn)*
Head & Neck **[P33]**
Hepatobiliary/Pancreas **[P34]**
Skin **[P35–P37]**
Technical Advances **[P38–P39]**

Poster Round Chairs:

Categories: Gastrointestinal; Head & Neck; Hepatobiliary/Pancreas; Skin
Dr MJ Arends, Cambridge
Prof Sir NA Wright, London

Categories: Autopsy/Forensic; Education & Audit; Genitourinary/Renal
Dr SS Cross, Sheffield
Prof AJ Howie, London

Categories: Cellular/Molecular; Experimental Tumour Pathology; Technical Advances
Prof CS Herrington, St. Andrews
Prof M Ilyas, Nottingham

15.00–18.00 **Ⓒ–Lecture Theatre 1**

SYMPOSIUM: *Undergraduate Education*

Chair: Prof P Domizio, Barts & The London School of Medicine and Dentistry, Queen Mary, University of London

15.00–15.30 *What pathology should medical students know?*
Dr A Jubb, Medical Student, Leeds

15.30–16.00 **[S1]** *Pathology in a PBL Curriculum*
Dr RFT McMahon, Division of Laboratory & Regenerative Medicine, The University of Manchester

16.00–16.30 **[S2]** *Assessment in pathology*
Dr J Chow, St George's, University of London

16.30–17.00 TEA Ⓜ–*The Cloisters*

17.00–18.00 **DEBATE:** *Medical students DON'T need to learn pathology*
Proponent:
Dr R Arnott, Dean of Medicine, University of Birmingham
Opponent:
[S3] Prof AD Burt, Dean of Clinical Medicine, University of Newcastle-upon-Tyne

15.00–16.00 Ⓒ–Lecture Theatre 2
ORAL COMMUNICATIONS
Categories: Experimental Tumour Pathology; Skin
Chair: Dr A Ramsay, UCL
Prof AH Wyllie, University of Cambridge

15.00 **[O1]** *Apc$^{+/1310T}$ Mice Develop Early-Onset, Severe Gastrointestinal Adenomas*
{P} MG Deheragoda, P Pollard, E Nye, P Seedhar, NA Wright, I Tomlinson

15.15 **[O2]** *Expression of CK17, CK15, CA15.3, ERα, ERβ,1 and ERβ,2 in cutaneous adnexal tumours*
{P} Y Alizadeh, IH Chaudhry, A ShaabanDr SS Cross, Sheffield

15.30–16.00 TEA Ⓜ–*The Cloisters*

16.00–17.00 Ⓒ–Lecture Theatre 2
ORAL COMMUNICATIONS
Categories: Skin; Hepatobiliary/Pancreas; Lymphoreticular
Chair: Dr A Ramsay, UCL
Prof AH Wyllie, University of Cambridge

16.00 **[O6]** *Richter's Transformation of Chronic Lymphocytic Leukaemia*
{P} MA Catherwood, L Venkatraman, M El-Agnaf, TCM Morris

16.15 **[O4]** *IgG4 Immunostaining of Pancreatic and Extrapancreatic Tissue in the Diagnosis of Autoimmune Pancreatitis*
{P} MG Deheragoda, NI Church, M Rodriguez-Justo, P Munson, N Sandanayake, EW Seward, K Miller, M Novelli, S Pereira, ARW Hatfield, GJM Webster

16.30 **[O5]** *Immunohistochemical Study of Plasmacytoid Dendritic Cells in Lymph Nodes Draining Breast Cancer by BDCA2 and CD123 Antibodies*
{P} R Ahmad, H El-Hassi, M Burke, H Singhal, SC Knight, NM Aqel

16.45 **[O3]** *Clinical Diagnosis of Melanoma – Sensitivity and Specificity*
{P} BT Eden-Green, J Chow

18.00–19.30 Ⓜ–The Jeremy Bentham Room
WELCOME RECEPTION

08.00 **Ⓜ–North Cloisters**
REGISTRATION

09.00–15.00 **Ⓒ–Cluster Room**
SLIDE SEMINAR COMPETITION CASE VIEWING: *LBC in non-gynaecological cytology* (Win a Case of Champagne!)

09.00–10.30 **Ⓒ–Lecture Theatre 1**
PLENARY ORAL SESSION
Chair: Prof M Novelli, UCL
Prof M Pignatelli, University of Bristol

09.00 **[PL1]** *Triple negative (ER, PR and HER2 negative) breast cancer: an appraisal of morphology and its prognostic markers*
{P} E Rakha, A Green, I Ellis

09.15 **[PL2]** *CEACAM5&6 as predictors of breast cancer recurrence*
L Maraqa, M Cummings, MB Peter, AM Shaaban, AM Hanby, DJ Scott, K Horgan, **{P}** V Speirs

09.30 **[PL3]** *Post-mortem investigation of sudden unexpected death in infancy: 10-year experience from a single specialist centre*
{P} MA Weber, I Brooke, K Wingrove, RA Risdon, M Malone, NJ Sebire

09.45 **[PL4]** *Quality of surgical resection and short course radiotherapy reduce local recurrence and improve disease free survival in rectal cancer. Preliminary results from the MRC CR07 trial.*
{P} P Quirke, D Sebag-Montefiore, L Thompson, B Steele, B Grieve, S Khanna, J Monson, R Stephens, MRC CR07 Trial Investigators

10.00 **[PL5]** *Modelling the expansion of mutated clones within human colonic crypts and their migration through the colon*
{P} SAC McDonald, P Tadrous, M Bjerknes, M Deheragoda, SJ Leedham, M Rodriguez-Justo, L Greaves, G Elia, M Novelli, DM Turnbull, JAZ Jankowski, NA Wright

10.15 **[PL6]** *Mitochondrial DNA Mutations to investigate cell lineage relations in human liver*
{P} TG Fellous, M Brittan, L Mears, S Bhattacharya, H Kocher, MR Alison

10.30–11.00 COFFEE Ⓜ–*The Cloisters*

11.00–13.00 **Ⓒ–Lecture Theatre 1**
TRAINEES' FORUM
Chair: Dr M Deheragoda, CRUK London Research Institute and UCL
Dr KE Robertson, University of Dundee

11.00–11.30 *DGH or teaching hospital?*
Prof M Novelli, UCL
Dr D Bailey, Wycombe Hospital

11.30–12.00 **[S4]** *Training routes in academic pathology*
Dr M Deheragoda, CRUK London Research Institute and UCL
Dr KE Robertson, University of Dundee

12.00–12.30 **[S5]** *How to be a good teacher*
Prof P Domizio, Barts & The London School of Medicine and Dentistry, Queen Mary, University of London

12.30–13.00 **[S6]** *How to write a scientific paper and get it published*
Prof CS Herrington, University of St Andrews and Editor-in-Chief, *Journal of Pathology*

13.00–14.15 **Ⓜ–The Cloisters**
LUNCH

13.00–14.00 **Ⓡ–JF Smith Seminar Room (3rd floor)**
MEET THE EXPERTS: *Post Mortem Histology*
Chair: Dr PJ Gallagher, University of Southampton
*Note: Lunch for "Meet the Experts" participants **only** will be provided in an area adjacent to the JF Smith Seminar Room*

13.30–14.30 **Ⓜ–The Cloisters**
POSTER PRESENTATIONS, POSTER ROUNDS & TRADE EXHIBITION
CATEGORIES
Breast **[P40–P46]**
Cardiovascular/Pulmonary **[P47–P50]**
Gynaecological **[P51–P57]**
Lymphoreticular **[P58–P66]**
Neonatal/Paediatric **[P67–P78]**
Neuropathology/Opthalmic **[P82]**
Osteoarticular/Soft Tissue **[P79–P81]**

Poster Round Chairs:
Categories: Breast; Gynaecological
Prof IO Ellis, Nottingham
Prof M Young, London

Categories: Neonatal/Paediatric
Dr P Ramani, Bristol
Dr RJ Scott, UCL

Categories: Cardiovascular/Pulmonary; Lymphoreticular; Neuropathology/Opthalmic; Osteoarticular/Soft Tissue
Prof A Dogan, USA
Prof AJ Freemont, Manchester

14.30–17.30 Ⓒ–Lecture Theatre 1
SYMPOSIUM: *Advances in Lymphomas since the advent of the WHO classification*
Chair and Introduction:
Prof P Isaacson, UCL

14.30–15.00 **[S10]** *Advances in B-cell lymphomas since the advent of the WHO classification*
Prof E Jaffe, National Cancer Institute, Bethesda, MD, USA

15.00–15.30 **[S11]** *An up-date on T-cell lymphomas*
Prof A Dogan, Mayo Clinic, Rochester, MN, USA

15.30–16.00 **[S12]** *Hodgkin's lymphoma*
Prof H Stein, Charité Universitätsmedizin Berlin

16.00–16.30 TEA Ⓜ–*The Cloisters*

16.30–17.00 **[S13]** *Immunohistochemical markers of lymphoma*
Prof D Mason, University of Oxford

17.00–17.30 **[S14]** *Molecular biology and molecular markers of lymphoma*
Prof M-Q Du, University of Cambridge

17.30–18.15 Ⓒ–Lecture Theatre 1
THE PATHOLOGICAL SOCIETY'S 3RD GOUDIE LECTURE
Chair: Prof DA Levison, Ninewells Hospital and Medical School, University of Dundee
[S15] *Our changing view of the genome: implications for pathology*
Prof PA Hall, Centre for Cancer Research & Cell Biology, Division of Pathology, Queen's University Belfast

19.30–20.00 Ⓜ–The Flaxman Gallery
SOCIETY DINNER – DRINKS RECEPTION

20.00–22.30 Ⓜ–The Old Refectory
SOCIETY DINNER

08.00 **Ⓜ–North Cloisters**
REGISTRATION

09.00–10.30 **Ⓒ–Lecture Theatre 2**
ORAL COMMUNICATIONS
Categories: Osteoarticular/Soft Tissue; Cardiovascular/Pulmonary; Breast
Chair: Prof AM Flanagan, UCL
Prof RA Walker, University of Leicester

09.00 **[O7]** *Expression and Regulation of Hypoxia-Inducible Factor (HIF) in Osteoclasts and GCTB*
{P} HJ Knowles, NA Athanasou

09.15 **[O8]** *Ossification during Distraction Osteogenesis in patients fitted with Ilizarov Frames*
{P} E Byrne, C Evans, C Hutchinson

09.30 **[O9]** *Idiopathic infantile coronary artery calcification*
{P} MN Sheppard, N Sabire, Y Ho

09.45 **[O10]** *Case report: An unusual case of a primary neuroendocrine tumour of the lung with divergent differentiation presenting with recurrent pneumonia*
{P} M Haris, S Osborne, S Edward, L Davidson, W Merchant, IH Chaudhry

10.00 **[O11]** *Co-ordinate expression and prognostic significance of nuclear receptor co-regulators and Interleukins in human breast cancer*
{P} AR Green, S El-Sheikh, EC Paish, IO Ellis, E Stylianou

10.15 **[O12]** *Altered DNA repair and response protein expression in non-involved cancer – containing breasts*
{P} AJ Batchelder, RA Walker

10.30–11.00 COFFEE Ⓜ–*The Cloisters*

11.00–13.00 **Ⓒ–Lecture Theatre 2**
ORAL COMMUNICATIONS
Categories: Breast
Chair: Prof AM Flanagan, UCL
Prof RA Walker, University of Leicester

11.00 **[O20]** *Her2 expression: correlation of chromogenic in-situ hybridization with immunohistochemistry and fluorescent in-situ hybridization*
{P} M Sohail, N Banu, CJ Calder, S Mungwana, S Florio, F Lewis, M Moorghen, M Pignatelli, A Hanby

11.15 **[O14]** *CISH, a simple, robust and cost-efficient test for HER2 status*
{P} S Di Palma, N Collins, M Kissin, M Cook

11.30 **[O15]** *Low level or loss of detection of acetylated Lys16 and trimethylated Lys20 of Histone H4 and its effect on the malignant Phenotype and patient outcome in breast carcinoma*
{P} SE El Sheikh, AR Green, DM Heery, IO Ellis

11.45 **[O16]** *Expression of BRCA1 protein in breast and ovarian cancers and its prognostic significance*
{P} E Rakha, M Kandil, S El-Shaikh, I Ellis

12.00 **[O17]** *Receptor Status in DCIS is variably and inconsistently reported: a study of 1684 cases from the Sloane Project*
{P} JStJ Thomas, A Hanby, SE Pinder, JC Macartney, IO Ellis, K Clements, H Bishop

12.15 **[O18]** *Risk factors for local recurrence in younger women with breast cancer*
{P} SE Laird, RA Walker, A Stotter

12.30 **[O19]** *Pathological features of primary breast cancer in the elderly – a large series from a single centre*
{P} KL Cheung, AWS Wong, H Parker, VWY Li, L Winterbottom, DAL Morgan, IO Ellis

09.30–12.00 Ⓒ–Lecture Theatre 1
SYMPOSIUM – SLIDE SEMINAR FOLLOW-UP: *LBC in non-gynaecological cytology*
Chair: Dr G Kocjan, UCL

09.30–10.30 **[S16]** *Cases 1–6*
Dr J McCarthy, St Mary's NHS Trust, London

Dr M Griffin, St James's Hospital, Dublin
Prof Dr M Drijkoningen, UZ St Rafaël, Leuven, Belgium

10.30–11.00 COFFEE Ⓜ–*The Cloisters*

11.00–12.00 **[S16]** *Cases 7–12*
Dr J McCarthy, St Mary's NHS Trust, London

Dr M Griffin, St James's Hospital, Dublin
Prof Dr M Drijkoningen, UZ St Rafaël, Leuven, Belgium

12.45–14.00 Ⓜ–The Cloisters
LUNCH & TRADE EXHIBITION
*Note: Lunch for "Meet the Experts" participants **only** will be provided in an area adjacent to the JF Smith Seminar Room*

13.00–14.00 Ⓡ–JF Smith Seminar Room (3rd floor)
MEET THE EXPERTS: *Getting started in research*
Chair: Prof NR Lemoine, Institute of Cancer Research & CR-UK, Barts & The London School of Medicine and Dentistry, Queen Mary's University
Prof I Tomlinson, Molecular & Population Genetics Cancer Research UK, London

14.00–16.30 Ⓒ–Lecture Theatre 2

TRAINEE ORAL COMMUNICATIONS

Chair: Dr M Deheragoda, CRUK London Research Institute and UCL
Dr KE Robertson, University of Dundee

14.00 **[O21]** *Malignant Phyllodes Tumour of the breast with in-situ, invasive and Metaplastic Epithelial Malignancy*
{P} SA Melmore, TR Helliwell

14.15 **[O22]** *Exfoliative cytology – a novel rapid diagnostic tool using breast mammotome core biopsies*
N Dutt, **{P}** C Kaur

14.30 **[O23]** *Amyloidosis of the Submandibular Salivary Glands*
{P} M Tripathi, VM Reddy, TE Giles, TR Helliwell

14.45 **[O24]** *A clinicopathologic study on microvessel density determined by CD34 or CD105 in benign and malignant gastric lesions*
{P} C Li, H Denley, RFT McMahon, V Arora, S Kumar

15.00–15.30 TEA Ⓜ–*The Cloisters*

15.30 **[O25]** *Desmoplasia is accompanied by enhanced vascular maturation in colon cancer*
{P} A Gaumann, S Schmid, S Schulte, F Hofstädter, L Kunz-Schughart

15.45 **[O26]** *Sessile Serrated Polyps in Proximal Colon: our experience*
{P} N Bhatt, HW Chong

16.00 **[O27]** *Eosinophilic oesophagitis in adults*
{P} R Ramakrishnan, H Chong

16.15 **[O28]** *Rapamycin inhibits the spontaneous formation of de novo cancer in p53 knockout mice*
{P} A Gaumann, G Koehl, A Hoehn, M Kovacs, F Hofstädter, HJ Schlitt, EK Geissler

Ⓜ–Gustave Tuck Lecture Theatre
UK NEQAS FOR IMMUNOCYTOCHEMISTRY & FISH TESTING

09.30–13.00 **SESSION 1**
IMPORTANT NEW ADVANCES IN DIAGNOSTIC IMMUNOCYTOCHEMISTRY
Chair: Mr K Miller, University College, London

09.30–10.15 *GI Tract Pathology: The increasing impact of Immunocytochemistry on patient management*
Prof M Novelli, University College London

10.15–11.00 *The utility of IgG4 immunostaining in the diagnosis of pancreatic and extra-pancreatic involvement in autoimmune pancreatitis*
Dr M Deheragoda, University College London

11.00–11.30 COFFEE Ⓜ–*The Cloisters*

11.30–12.15 *The first ever CD33 antibody for formalin-fixed paraffin embedded sections: How helpful is it?*
Dr A Ramsay, University College London Hospitals

12.15–13.00 *Urological Pathology: Today and Tomorrow*
Dr A Freeman, University College London Hospitals

13.00–14.00 **Ⓜ–The Cloisters**
LUNCH

14.00–16.30 **SESSION 2**
UK NEQAS – DEBATE & PARTICIPANT FEEDBACK
Chair: Prof B Jasani, University of Wales College of Medicine

14.00–14.30 *HER-2 Gene Amplification by CISH. The Guildford experience*
Dr S Di Palma, Royal Surrey County Hospital, University of Surrey

14.30–15.20 *UK NEQAS Module for HER-2 FISH testing: overview and feedback*
Dr J Bartlett, Edinburgh Cancer Research Centre

15.20–15.45 TEA Ⓜ–*The Cloisters*

15.45–16.30 *UK NEQAS-ICC & FISH: feedback on performance*
Dr M Ibrahim, UK NEQAS Scheme Manager

16.30 *Summing up and close*

CPD
An application has been submitted to the Royal College of Pathologists and the IBMS.

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Abstracts

Plenary

PL1

Triple negative (ER, PR and HER2 negative) breast cancer: an appraisal of morphology and its prognostic markers

{P} E Rakha, A Green, I Ellis
Nottingham University, Nottingham, United Kingdom

Background: Triple negative (TN) breast cancer (estrogen receptor (ER), progesterone receptor (PR) and HER2 negative) is a high risk group of breast cancer that lacks the benefit of specific therapy which targets these proteins. The aim of this study is to characterize this group and to identify prognostic markers which can identify tumours with the more aggressive behaviour. Methods: we have examined a large and well characterized series of invasive breast carcinoma (n=1944) with a long term clinical follow-up (median 56 months) using tissue microarray. The series were also stained with concurrent immunohistochemical prognostic biomarkers. Results: TN phenotype constituted 16.3% of the informative cases. There were positive associations with larger size, higher grade, pushing margins, poorer Nottingham Prognostic Index, development of recurrence and distant metastasis and shorter survival. In addition, associations were found with loss of expression of androgen (AR), and E-cadherin and positive expression of basal CKs (BP), P-cadherin, p53 and EGFR. In all TN series, tumour size, lymph node (LN) stage and AR were the most useful prognostic markers. In the LN positive subgroup, both size and AR retained their prognostic significance. However, in the LN-negative tumours, BP was the sole prognostic marker identified in this subgroup. Conclusion: TN phenotype is a specific subgroup of breast cancer associated with aggressive behaviour and poor outcome. Assessment of AR and BP, in addition to the established pathologic variables mainly LN and size, can be used to select high- and low-risk patients at the time of primary surgery and can provide valuable information on treatment options in these TN tumours

PL2

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PL3

Post-Mortem Investigation of Sudden Unexpected Death in Infancy: 10-year Experience from a Single Specialist Centre

{P} MA Weber, I Brooke, K Wingrove, RA Risdon, M Malone, NJ Sebire
UCL Institute of Child Health and Great Ormond Street Hospital for Children, London, United Kingdom

Introduction: Sudden unexpected death in infancy (SUDI) constitutes the most common cause of non-neonatal death in the first year of life. Several autopsy protocols have been suggested, all of which include a range of ancillary investigations.
Methods: Retrospective analysis of >1,500 consecutively performed post-mortem examinations, all of which were carried out by specialist paediatric pathologists at a single centre. SUDI was defined as death of an infant aged 7 to 365 days that was sudden and unexpected. A local autopsy protocol was followed that included the use of detailed ancillary investigations. To ensure consistency for data analysis and interpretation, all data extraction, data entry and classification was carried out by a single paediatric pathologist according to clearly defined criteria.
Results: Of 1,516 post-mortem examinations overall, 546 cases presented as SUDI. In a third of infants (180 cases) death was explained by the autopsy findings ("explained SUDI"). The other 366 cases (67%) remained unexplained. Of these, more than 40% were co-sleeping associated deaths. Most deaths occurred in the first 3 months of age, and there was no significant seasonal variation. Of the explained deaths, just over half were infective, most commonly due to pneumonia, whilst the commonest non-infective causes of death included congenital abnormalities, and accidental and non-accidental deaths.
Discussion: This constitutes the largest single institution autopsy study of SUDI. Ten years on from the CESDI study, the ascertainment of a cause of death at autopsy has not changed, with two thirds of SUDI deaths remaining unexplained even after detailed post-mortem examination by a specialist paediatric pathologist in accordance with current guidelines.

PL4

Quality of surgical resection and short course radiotherapy reduce local recurrence and improve disease free survival in rectal cancer. Preliminary results from the MRC CR07 trial.

{P} P Quirke, D Sebag-Montefiore, L Thompson, B Steele, B Grieve, S Khanna, J Monson, Richard Stephens, MRC CR07 Trial Investigators
MRC Clinical Trials Unit, London, United Kingdom

MRC CR07 randomised to surgery alone with chemoradiotherapy for patients with an involved circumferential margin (CRM) or 5x5 radiotherapy. Results at 3 years are local recurrence (LR) dropped from 11% to 5% ($p<0.0001$) and disease free survival (dfs) improved from 75 to 80% ($p=0.03$). Quality of surgery was predefined on the basis of the plane of surgery. The frequency of CRM +ve and the grades of quality of surgery improved through the trial. In all patienents overall LR and dfs were related to plane of surgery. Mesorectal plane (MR) surgery (53%) had improved outcomes over intramesorectral (IM) plane (34%) which in turn did better than muscularis propria plane surgery (MP) (13%). Stage of tumour did not affect the grade of surgery. LR was MR 4%, IM 8%,MP 15% ($p=0.002$) and dfs was MR 83%, IM 78%, MP 73%, ($p=0.04$). By arm of trial, for each grade of surgery the local recurrence rates dropped by a third from MR to IM to MP surgery and for each grade of surgery preoperative short course radiotherapy reduced LR by half over the surgery alone with selective chemoradiotherapy arm. LR for MP surgery in the selective arm was 19% vs 1% for MR surgery plus short course radiotherapy. Overall preoperative radiotherapy improved outcomes over a selective approach, the plane of surgery strongly influenced LR and dfs and preoperative radiotherapy improved outcomes further for any grade of surgery. High quality mesorectal plane surgery and short course preoperative radiotherapy can almost abolish LR and significantly improve survival.
We thank the trial pathologists for their excellent work.

PL5

Modelling the expansion of mutated clones within human colonic crypts and their migration through the colon

{P} SAC McDonald[1], P. Tadrous, M Bjerknes[5], M Deheragoda[2], SJ Leedham[2], M Rodriguez-Justo[3], L Greaves[4], G Elia[2], M Novelli[3], DM Turnbull[4], JAZ Jankowski[1], NA Wright[6]

[1]Oxford University, Oxford, United Kingdom, [2]Cancer Research UK, London, United Kingdom, [3]University College Hospitals London, London, United Kingdom, [4]University of Newcastle upon Tyne, Newcastle, United Kingdom, [5]University of Toronto, Toronto, Canada, [6]Barts and the London School of Medicine and Dentistry, London, United Kingdom

Recent data from our laboratory has shown that mitochondrial DNA (mtDNA) mutations can spread through the human colon by a process of crypt fission, where one crypt is able to divide into two daughters(Proc. Natl. Acad. Sci. 103:714-19).

Here we show how such mutated cells expand through the human colonic crypt by 3D modelling from serial sections throughout single crypts. This highlights that cellular migration within crypts is more complex than originally thought and gives insights into actual stem cell location.

Furthermore, the rate at which normal human crypts undergo fission is unknown. Bjerknes (J. Theor. Biol. 179:381-5) developed a mathematical model by which he calculated the rate at which crypts within aberrant crypt foci were able to expand. This predicts that if an aberrant crypt population was expanding at the same rate as normal crypts then the number of single aberrant crypts should be half of the number of those within foci.

Here we use this model to show that crypts deficient in mitochondrial cytochrome c oxidase (CoxSU1) expand at the same rate as those with normal CoxSU1 expression. We have counted the total number of deficient crypts within tissue sections stained with CoXSU1 from normal colons of 35 patients. 1298 deficient crypts were observed of which 597 were single. This gives a ratio of singletons to patches of 0.46 which are expanding only at 1.15 times faster than positive crypts.

These data suggest that crypts with or without mtDNA mutations expand at the same rate and that this is an appropriate model to calculate the crypt fission rate of the human colon.

PL6

Mitochondrial DNA Mutations to Investigate Cell Lineage Relations in Human Liver

{P} TG Fellous, M Brittan, L Mears, S Bhattacharya, H Kocher, MR Alison

Institute of Cell and Molecular Science, QMUL, London, United Kingdom

Current research on human liver regeneration and stem/progenitor cell biology is hampered by lack of a clonal marker. It is now clear that mitochondrial (mt) DNA mutations occur in human liver stem and progenitor cells, and that these mutations have much potential as a stem cell marker for looking at both the expansion of mutated clones in the liver and for providing a platform for lineage analysis in humans for really the first time. Studying cells with mutations in the cytochrome c oxidase gene (as a cell lineage marker), largely encoded by mtDNA, has revealed patches of COX^{-ve} cells in liver, which are frequently in close proximity to the portal tract and are present in serial sections at least 330μm deep into the tissue. This suggests that clonogenic cells in the normal human liver may proliferate *en masse* from a common niche close to the portal tract. This study highlights a novel means of tracing patterns of cell division and migration in human liver that can be used to study changes in cell behaviour during hepatitis, cirrhosis and neoplasia.

Abstracts

Posters

P1

Sudden Death Due to Undiagnosed Sickle Cell Trait During a Period of Prolonged Religious Fasting

{P} OJ Biedrzycki, M Sheaff
Institute of Pathology, The Royal London Hospital, Whitechapel, London, United Kingdom

Sickle cell trait (SCT) is estimated to occur in 6-10% of Africans and the UK prevalence rate has been estimated at 3.2%. Whilst sudden death in sickle cell disease (SCD) is well known, its occurrence in SCT is rare and requires extremes of physiological stress.
We present a case of a 29 year old black female who died suddenly during a prolonged period of religious fasting. Her previous medical history was unremarkable and there was no family history of SCD. At post-mortem she was found to be dehydrated, and macroscopically the main abnormal finding was a spleen weighing only 20g. Histology revealed splenic auto infarction and extensive vascular congestion with red blood cell sickling in both lungs, and most other organs. There was no myocarditis. Electrophoresis performed on post mortem blood confirmed the proposed initial diagnosis of acute chest syndrome complicating SCT. Blood and urine toxicological examination was negative.
The case highlights a novel scenario of SCT associated sudden death. We discuss the potential pathophysiological mechanisms which may have led to the patient's demise. We also remind pathologists to consider this diagnosis as a cause of death in apparently fit young people of ethnic origin during episodes of physiological stress.

P2

Reversing the slow death of the clinical post mortem examination: developing the post of the Pathology Liaison Nurse.

E Limacher[1], {P} U Carr[2], L Bowker[3], R Y Ball[4]
[1]The Bereavement Office, Norfolk and Norwich University Hospital NHS Trust, Norwich, United Kingdom, [2]Histopathology Department, NNUH NHS Trust, Norwich, United Kingdom, [3]Medicine for the Elderly, NNUH NHS Trust, Norwich, United Kingdom, [4]Histopathology Department, NNUH NHS Trust, Norwich, United Kingdom

Introduction:
Clinical mortem examinations (cPMs) are still valuable in modern medicine and have benefits for bereaved families. To ensure that consent is properly elicited and to relieve the demand on clinicians' time, the Trust in Norwich established a Pathology Liaison Nurse (PLN) post.
Design:
PLN post: The PLN was to liase with families and medical staff. The post was evaluated at the end of a trial year. Opinions of consultants and families were sought using questionnaires.
Review of cPMs: The numbers of adult deaths in hospital were determined and adult cPM rate (cPMR) was calculated (number of cPMs divided by the total number of deaths). Coroner's cases were excluded.
Results:
Opinions of consultants and families: The surveys suggested that the PLN provided a valuable service to both the Trust and bereaved families.
Reversing the trend: The number of cPMs had declined by 80% from 167 in 1997 (cPMR = 8.4%) to 34 in 2003 (cPMR = 1.4%). This trend was reversed in 2004 and 2005 following the appointment of the PLN, with 45 cPMs (cPMR = 1.8%) and 58 cPMs (cPMR= 2.4%), respectively.
Conclusion:
The development of the PLN post has been associated with a reversal in the decline in the adult cPMR. Our study shows that the death of the cPM is not inevitable and there is potential for further improvement.

P3

A CASE OF AORTODUODENAL FISTULA FIRST DIAGNOSED ON AUTOPSY EXAMINATION

{P} A Naveed, B Benatar
Tameside General Hospital, Ashton, Manchester, United Kingdom

Primary aortoenteric fistula is rare and is usually caused by an untreated abdominal aortic aneurysm. The diagnosis of aorto-duodenal fistula may not be made until autopsy examination.
We present a case of an 84-year-old man with history of transient ischaemic attacks and hypertension presented with offensive smelling diarrhoea, abdominal pain, vomiting, intermittent confusion, and lethargy. He died shortly after admission followed by a sudden episode of extensive hematemesis in an otherwise stable patient. Autopsy examination was carried out, where we found an aorto duodenal fistula that remained silent during life and was only diagnosed on autopsy.
This case emphasizes the difficulty of making a clinical diagnosis of primary aortoduodenal fistula and importance of autopsy examination to diagnose such unusual cases, which may have an impact on our clinical practice.

P4

A Rare Autopsy Case of Fatal Thyrotoxicosis in a Young Woman

{P} P F Boyle, S Lucas, S George
St Thomas' Hospital, London, United Kingdom

Thyrotoxicosis is a rare cause of death: ONS in 2004 recorded 140 deaths due to thyrotoxicosis in UK, none between 20 – 30 years. We report the case of a young women, known hyperthyroid, who following two weeks withdrawal of Carbimazole treatment suffered three cardiac arrests and died.
HISTORY: 28 year old Nigerian woman presented with a short history of diarrhoea, vomiting, fever, confusion and palpitations having arrived in the UK 2 weeks previously. Initial blood tests revealed 3% malarial parasitaemia, T3 > 46 nmol/l (N= 4.8-11.6) and TSH of < 0.01 mIU/l (N= 0.4-6.2). Shortly after admission she suffered a cardiac arrest. Despite intensive care support and following two further cardiac arrests she died.
HISTOLOGY: There were no malarial parasites within any organ, including the brain. The heart showed contraction band necrosis from cardiac arrest and resuscitation. The thyroid was diffusely enlarged with extremely hyperplastic follicles. There was myocyte degeneration within the psoas muscle consistent with proximal thyrotoxic myopathy. The brain had global red neurone degeneration consistent with hypoxic ischaemic encephalopathy. The bone marrow showed marked haemophagocytosis- probably malaria driven.
CONCLUSION: We report the death of a young woman via cardiac arrest the most likely cause being a fatal arrhythmia secondary to thyrotoxicosis.

P5

The Actin-Bundling Protein Fascin is Overexpressed in Inflammatory Bowel Disease

{P} D Qualtrough, D Littlejohns, M Pignatelli
University of Bristol, Bristol, United Kingdom

Fascin, an actin-bundling protein, is not expressed by normal colonic epithelial cells but is upregulated in colorectal tumours where it promotes cell motility and invasion. Analysis of the fascin promoter suggests that its expression may be induced by inflammatory mediators.

Immunohistochemical analysis of inflammatory bowel disease (IBD) specimens showed fascin expression in both ulcerative colitis (34/34) and Crohn's colitis (7/7). Its expression correlated with the degree of inflammatory activity. Highly expressing foci were observed at the edges of ulcers where flattened, motile epithelial cells are actively involved in epithelial restitution.

We studied the effect of therapeutic modalities used in the treatment of IBD on the expression of fascin in SW480 and HT29 colon carcinoma cells by western blotting. Non-steroidal anti-inflammatory drugs (NSAIDs) reduced fascin expression (60%) in both cell lines, whereas butyrate (a fermentation product of resistant starch and potential treatment for IBD) increased its expression 2-7 fold.

These data suggest that Fascin expression could be of importance in IBD and that its regulation by NSAIDs and butyrate may affect motility and the epithelial restitution of colonic mucosa.

P6

Expression of Transporter Proteins in Rat Placentation

R Stratton, T Aldridge, J Noakes, D Moore, C Sadler, A Hargreaves, {P} J Wright
Syngenta, CTL, Cheshire, United Kingdom

ATP-binding cassette (ABC) transporters are a large super family of transmembrane proteins, which mediate trafficking of a wide variety of substrates in an ATP dependant manner across membranes and are fundamental to protecting the foetus from xenobiotics exposure. We investigated the expression profiles of 3 ABC transporters; p-Glycoprotein (p-Gp), Multidrug resistance associated protein 2 (MRP2) and Breast cancer resistance protein (BCRP) in rat placenta.

Han Wister rats were time mated and foetal gestational days 6 -21 were investigated by IHC, Immunoblotting and genomics.

p-Gp protein and mRNA were found to be expressed in rat placenta from day 13 increasing up to day 20. MRP2 and BCRP proteins were found to be expressed from day 14 and day 12 respectively, increasing up to day 20.

Human placental expression of p-Gp is reported to be greatest within the first trimester and decreasing over time, in contrast to the rat. Human placental expression of BCRP is reported to remain constant throughout pregnancy again in contrast to the rat.

These species differences need to be considered when choosing an animal model to investigate foetal exposure to xenobiotics in relation to human risk assessment.

P7

Inhibition of COX-2 with NS-398 decreases colon cancer cell motility through blocking epidermal growth factor receptor transactivation: possibilities for combination therapy

{P} M Pignatelli, N Banu, A Buda, S Chell, D Elder, M Moorghen, C Paraskeva, D Qualtrough
University of Bristol, Bristol, United Kingdom

The use of NSAIDs has proved of great interest in the prevention and treatment of colorectal cancer. Overexpression of COX-2 and prostaglandin production promote metastasis and have been shown to increase cell motility in vitro. We investigated whether specific inhibition of COX-2 with NS-398 inhibited the motility of colorectal cancer cells and whether this was modulated through EGFR transactivation. A trans-well filter assay was used to study cell motility. Expression of COX-2, EGFR phosphorylation and PGE_2 receptors was assessed by Western blot and RT-PCR. NS-398 significantly reduced PGE_2 levels and reduced cell migration in HT29 and HCA7 colorectal cancer cells and this effect was rescued by addition of PGE_2. Specific inhibition of COX-2 with NS-398 reduces EGFR phosphorylation. Inhibition of EGFR activity with AG1478 reduced PGE_2-stimulated motility, demonstrating that PGE_2 acts via the EGFR signalling pathway. The novel combination of NS-398 and AG1478 dramatically reduced migration of colorectal cancer cells. The data presented here indicate that use of NS-398 in chemoprevention and adjuvant therapy for colorectal cancer may work in part, through the inhibition of cell motility. Our data suggests that the combined use of NSAIDs with EGFR antagonists could be explored further for future use in the clinic.

P8

Notch Signalling is Altered in Colorectal Tumours and Can Influence Malignant Progression

{P} P Rees, M Pignatelli, D Qualtrough
University of Bristol, Bristol, United Kingdom

Notch is a highly conserved developmental signalling pathway expressed in adult intestinal epithelium. Aberrant Notch activation is oncogenic in a number of tissues but its role in intestinal tumourigenesis is undefined. A common feature of Notch in embryogenesis is participation in processes that involve selective changes in adhesion including the epithelial to mesenchymal transition (EMT), a process thought to be important in colorectal tumour invasion.

In this study we analysed Notch1 (N1) and E-cadherin (as a marker of EMT) in 9 colorectal carcinoma (CaCo2, HCA7/C29, HCT15, HCT116, HT29, JW2, LS174T, SW480, SW620) and in 4 adenoma-derived cell lines (RG/C2, AN/C1, AA/C1, BH/C1) by western blotting. N1 expression was increased in the carcinoma cell lines (especially SW480 and SW620) compared with the adenomas, which were either negative (RG/C2, BH/C1) or low expressors (AA/C1, AN/C1). A hallmark of EMT and tumour invasion is a decrease in the epithelial marker E-cadherin. There was an inverse relationship between E-cadherin and N1 expression in all adenoma and carcinoma derived cell lines examined. In vivo, 5/10 adenocarcinoma tissue samples showed N1 immunoreactivity compared to 2/8 adenomas. These findings highlight Notch as a regulator on EMT in colonic tumours and its possible role in colorectal tumour progression.

P9

PKC ZETA ALTERNATIVE SPLICING IN PROSTATE CANCER

{P} S J Ireland, C S Foster, C M Gosden
University of Liverpool, Liverpool, United Kingdom

The human Protein Kinase C zeta gene is located, at 1p36.32-1p36.3. The gene encodes isoforms of the enzyme that are regulators of many homeostatic signalling mechanisms responsible for co-ordinating changes that modulate cellular phenotypes. Through the mechanism of alternative splicing, variants of PKC zeta are believed to exert a range of physiological effects including epithelial cell invasiveness and development of metastases.

The data examine the splice variants of PKC zeta present in prostate cell lines and matched normal and tumour tissues as assessed by genome walking. Real Time PCR data shows the increase in expression of two PKC zeta splice variants (a and r) as malignancy progresses.

An Antisense knockdown of PKC zeta in PC3-M and Du145 cell lines shows that cells with a reduced expression of PKC zeta exhibit reduced invasion capacity and proliferation rate.

IHC staining of 955 prostate tissues (TA-PG tissue microarray) shows splice variants of PKC zeta have different subcellular localisation. Tumour samples show a higher level of positive PKC zeta staining than normal samples. Increase in expression of nuclear splice variant r was early event in the progression of prostate cancer. The changes in cytoplasmic splice variant a suggest a change in function. Survival analysis showed that positive PKC zeta staining is related to poor survival compared with negative staining. Staining for PKC zeta is both diagnostic and prognostic.

Splice variants of PKC zeta through their position in key signalling pathways present themselves as new therapeutic targets.

P10

The Characterisation and Culture of Human Foetal Kidneys

{P} D.K. Franklin, N.A. Hanley, P.S. Bass, J.E. Collins
School of Medicine University of Southampton, Southampton, United Kingdom

Renal tubules differentiate from metanephric mesenchymal progenitor cells. The human kidney, at 7 to 10 weeks gestational age, is forming many new nephron units in rapidly enlarging developing kidneys. This important resource allows mapping of foetal expression of many known stem cell markers, established from work mainly in mouse. The aim of this study was to stain human foetal kidneys with stem cell and differentiation markers and to assess the capacity of tissue to survive and differentiate in culture. Staining was positive for N-cadherin in the nephrogenic mesenchyme and in nascent proximal tubules which also stained with claudin 2. Epithelial membrane antigen (EMA) and E-cadherin were stained in nascent distal tubules. Dispase disaggregated foetal tissue formed cell monolayers that were positive for differentiation markers, corresponding to fixed tissue. Cells were also positive for stem cell markers CD133, Cdx1, Pax 2, Oct 4, TRA1-60, β-catenin and SSEA-4. Cultured explants of foetal tissue formed tubules in Matrigel, while collagenase disaggregated tissue formed cysts showing that these preparations have developmental potential in vitro. Improved understanding of the mechanisms that renal progenitor cells use to survive and differentiate may lead to new therapies aimed at promoting or enhancing the repair of diseased adult kidneys.

P11

The Effect of Cyclosporine A and TGF-β1 on Differentiation of Primary Human Renal Tubular Epithelial Cells

A Kirk, {P} D.K. Franklin, S.K. Campbell, M.A. Hardyman, P.S. Bass, J.C. Mason, J.E. Collins
School of Medicine, University of Southampton, Southampton, United Kingdom

The widely used immunosuppressant Cyclosporine A (CsA) stimulates the production of TGF-β in renal tubular epithelial cells (RTEC). The aim was to characterize the effects of CsA and TGF-β1 on the differentiation of cultured primary RTEC. Antibody staining was observed on tissue sections, with N-cadherin and claudin 2 localised in subapical cell junctional areas of proximal tubules and E cadherin and epithelial membrane antigen (EMA) in distal tubules. Primary RTEC in serum-free medium were treated with CsA or TGF-β1 for 72 hours and stained for N-cadherin, claudin 2, E-cadherin, alpha smooth muscle actin (αSMA) and EMA. Most cells were N-cadherin and claudin 2 positive suggesting that they were of proximal phenotype. Smaller percentages of cells stained for E-cadherin and EMA. Cells lost their membrane staining for claudin 2 in response to CsA and TGF- β1, whereas N-cadherin became redistributed in the membrane. All cells retained cytokeratin, EMA and αSMA although their morphology became more flattened and elongated with alignment of actin filaments. These results suggest that tight and adherens junctions of primary human RTEC are changed or lost upon treatment with CsA and TGF-β1. In vivo these effects would likely compromise the function of existing healthy tubules

P12

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P13

The Anatomy of a Trainee-driven Digital Atlas of Pathology

{P} AJ Saenz, V Ko, MW Lawlor, AB Farris, A Vasilyev
Massachusetts General Hospital and Harvard Medical School, Boston, MA, United States

Background: Digital pathological images can enrich a trainee's education in pathology. We undertook a project to acquire a database of gross and microscopic images of pathology to fulfill this need.
Methods: The two main components of this project are the digital camera/microscope (Olympus DP70 camera) and the database application (PostgreSQL and custom Java servlets), which is accessible with a Java-enabled web browser.
Results: The overall system has many novel properties. The database is accessible via the hospital intranet, allowing users to add, edit, search, and view cases. It takes ~5 minutes to capture and save several pictures, and have them available for viewing. The database is secured with a username/password and all changes are logged and reversible. The database is structured after 'real' pathology cases, which allows for a logical organization (for search and display) of images; cases can have several parts, parts have blocks and gross images, and blocks have microscopic images.
Conclusions: While the imaging and database technologies are not new, the overall architecture of the system is notable for allowing efficient contribution of cases. This project is unique in that users can easily add their own cases, allowing this project to be entirely resident driven. The project has been successful to date with ~750 cases, ~3400 images, and ~3.0GB of data in less than one year. Given the high volume of interesting pathology cases at this institution, there are still many opportunities for growth.

P14

Audit to Compare the Turnaround Times Before and After the Involvement of Private Laboratory

{P} M Batra, R Williams
Wrexham Maelor Hospital, Wrexham, United Kingdom

Turnaround time (TAT) is a visible parameter of efficiency of pathology service and a common benchmark by which the performance of pathologists is judged by themselves and by the clinicians.
Aim
To compare the TATs between May and Nov 2005 to look at the impact of use of private laboratories in sharing the workload.
Methods
The biopsies and resection specimens were subdivided into various categories according to site. The average TAT was calculated and the data was compared between 2 months.
Results
A total of 777 and 926 samples were received in May and November respectively. Despite the involvement of private laboratories, overall TAT was significantly longer in November (5 days) compared to May (4.24 days). The average TAT for biopsy samples was 4.22 and 5.17 days for resection specimens was 4.48 and 3.93 days during May and November respectively. The TAT was significantly longer for lung, prostate and bladder biopsies during November.
The changes recommended were:
To appoint more medical staff in the department to make the working of department efficient and economically viable
To investigate the cause of excessive TAT for prostate, bladder and lung biopsies and improve the same.

P15

A Departmental Audit to Assess the Accuracy of Penile Cancer Reporting

{P} M Batra, C O'Brien
Morriston Hospital, Swansea NHS Trust, Swansea, United Kingdom,

Thorough reporting of penile cancer is necessary for determining patient management and prognosis. Major prognostic factors are tumour size, growth pattern, histologic subtype, grade, depth, TNM stage and margin status.
AIM: To assess the content of pathology reports for penile cancer specimens, the standard based on a minimum dataset derived from the literature.
METHODS: Histopathology reports of penile cancer specimens received between 2002-2005 were evaluated [19 invasive cancer, 5 carcinoma in situ (CIS)].
RESULTS: Histologic type was described in all cases; tumour size, grade and anatomic site in >84%; level of invasion in 74%; involvement of margins in 79% of invasive cancer and 60% of CIS. Growth pattern and depth measurement were given in 32%; vascular/perineural invasion and TNM staging in 42% and 37% respectively.
CONCLUSIONS: The majority of reports mentioned histologic type, tumour size, anatomic site and grade and most included level of invasion and margin status of invasive tumours. However the reporting of TNM staging, pattern of growth, depth of invasion and margin status of carcinoma in situ were inadequate.
Consistent reporting of this dataset is recommended.

P16

Control charts - A simple visually informative method of comparing performance in pathology audit and quality assurance

{P} K Kalyanasundaram[1], D.C Rowlands[1], M. A Mohammed[2]
[1]Department of Histopathology, Royal Wolverhampton Hospitals NHS Trust, Wolverhampton, United Kingdom, [2]Department of Public Health and Epidemiology, University of Birmingham, Birmingham, United Kingdom

Control charts were developed by Shewhart as a quality control tool that graphically distinguishes special or exceptional variation from chance variation in performance. This is crucial, because the actions required to address each of these variations are different. Chance variation can only be reduced by changes to the underlying process, whereas a special cause requires investigatory work to find the factors responsible for the variation. Control charts can compare variation between a group of individuals or institutions as well as variation over time. Control charts are thus more informative than the traditional bar chart or scatter diagram which are commonly used to express the differences found by audit and quality assurance processes. Various types of control chart can be used to display either continuous (e.g. tumour size) or discontinuous (e.g. tumour grade) variables.
We illustrate the utility of control charts at two levels – within a department and within a region. We analysed the variation in tumour grading on biopsies of bladder and prostate tumours by consultants in one medium sized histopathology department. We have also compared grading of breast cancers between the eighteen major laboratories in the West Midlands. We were able to distinguish between chance causes of variation (which require a change to the process) and possible special causes of variation which require further investigation.

P17

Pilot Workforce Survey Using a Commercial Web Based Survey Instrument

{P} S Holden, DFR Griffiths
University Hospital of Wales, Cardiff, United Kingdom

The shortfall in the histopathology workforce in the UK is well known; an increase in trainee numbers is anticipated to improve the situation. However, it is not known by how much each trainee will contribute to the workforce when qualified.
A survey was designed in order to determine the type of department and post trainees would like to work in, and the proportion of a full time workload they expect to contribute. SurveyMonkey, a commercially available web-based programme, was used to distribute to the survey via email. All the histopathology trainees within the Wales Deanery were sent a link inviting them to complete the survey anonymously.
SurveyMonkey was then used to collate the answers. 82% of trainees replied. Important factors influencing choice of post were geographical location and type of department. Very small and very large departments are unlikely to be popular. 66.7% expect to work full time. On average each of this group of trainees plan to contribute 92% of a full time post over the next 10 years.
The method of delivering the survey proved effective, and the results obtained may be of use to departments who wish to make available posts more attractive to current trainees.

P18

Effect of Unsaturated Fatty Acids on Schistosomasis-associated Lesions

{P} NY Asaad, MM El-Sobky, SM Selim
Pathology, Menoufyia University, Egypt

Aim: To study the effect of diet level of unsaturated fatty acid (FA) on worm burden, liver egg count and the pathology of schistosomiasis. Experimental design: Eighty male swiss albino mice were infected with 120 cercariae of S. mansoni per mouse. Mice were divided into two groups; first group was offered standard diet (SD) and the second was given 20% pure corn oil as unsaturated FA (FD). Worm perfusion and ova count/ gm liver tissue was carried out. Tissue sections from both lung and kidney were examined with the aid of matrix metalloproteinases-2 (MMP-2) immunostaining to study the pathologic changes.
Results : FD mice demonstrated statistically lower worm burden and egg count/gm liver tissue than SD group. Also, FD group showed statistically higher peribronchial and perivascular inflammation, alveolitis and interstitial pneumonia in lung tissues and an increase in mesangial cells and matrix and tubular vacuolar change in kidney tissues than SD group. In FD group, MMP-2 was expressed in a diffuse pattern in 77.5% and 55% of lung and kidney tissues, versus 30% and 15% in SD mice group, respectively.
Conclusions: This study provides evidence that diet of unsaturated FA could increase natural elimination of lung stage schistosomula leading to decrease in the worm and egg burden and modulate the inflammatory and the immune response to S. mansoni infection.

P19

Duodenal Biopsies – Are Numbers important?

{P} D Dey, W Taylor
University Hospital of Aintree, Liverpool, United Kingdom

Four biopsies are generally recommended from four quadrants of duodenum for investigation of anaemia, weight loss and diarrhoea. We examined the number of duodenal biopsies taken in cases for investigation of anaemia, weight loss and diarrhoea at each endoscopy and looked whether less than adequate number of duodenal biopsies were responsible for issuing equivocal reports.
Histology reports and endoscopy reports of 101 patients were reviewed for number of duodenal biopsies, name of endoscopists, diagnosis and equivocal reports.
In only 40% (41/101) of the biopsies the endoscopists had taken four or greater than four biopsies. In the remaining 60% (61/102) of cases less than four biopsies had been taken.
An equivocal report had to be issued in one case in which only three biopsies were taken. The features in the biopsy raised the possibility of coeliac disease but did not justify a firm diagnosis of coeliac disease. Three cases had increased intraepithelial lymphocytes but only in one of them were less than four biopsies were taken.
Ignorance of the guidelines by both Medical and Nurse endoscopists combined with tissue malorientation and artefact may result in issuing equivocal reports.
Recognition of villous atrophy is more likely to be affected by a smaller number of biopsies than recognition of increased intraepithelial lymphocytes.

P20

TTF-1 REACTIVITY IN COLORECTAL ADENOCARCINOMA

{P} E Sarkady[1], E.W. Benbow[2]
[1]Wythenshawe Hospital, Manchester, United Kingdom, [2]Manchester Royal Infirmary, Manchester, United Kingdom

AIM: Lymph node metastases from a colorectal primary adenocarcinoma were immunoreactive for TTF-1, prompting further stains. These demonstrated that the primary carcinoma, and part of the villous adenoma it arose from, were also positive. As part of a subsequent audit, we re-stained other TTF-1 positive cases, and studied TTF-1 staining of further primary colonic carcinomas, both with our usual Novocastra antibody (clone SPT24) and an additional reagent from Dako (clone 8G7G1/1).
METHODS: Eleven cases of invasive colonic adenocarcinoma were selected from the archive. Immunohistochemical staining for TTF-1 was carried out with both the Novocastra and Dako clone under the same standard conditions. A further 11 cases of lung and lymph node were randomly selected, where the TTF-1 reaction had been previously found positive, and stained with both clones.
RESULTS: Of the 11 cases of colonic adenocarcinoma, four showed positivity in the epithelial cell component with the Novocastra clone, but none with the Dako clone. None of the 11 randomly selected blocks with previous TTF-1 positivity showed a negative reaction, though reactions with the Novocastra clone were stronger in all cases.
DISCUSSION: Our results indicate differences in sensitivity between the two antibodies, and show that the diagnostic utility of TTF-1 detection depends on the antibody used. The Novocastra reagent has a significant false positive rate for colorectal adenocarcinomas under routine conditions, and metastatic deposits may thus be misinterpreted.

P21

A Case of Oesophageal Carcinosarcoma with Adenocarcinoma Differentiation and Sarcomatous Metastasis

{P} AD Christian, AG Douglas-Jones
University Hospital of Wales, Cardiff, United Kingdom

Carcinosarcomas of the oesophagus are rare tumours, clinically presenting as polypoid exophytic masses with squamous cell and spindle cell components.

We present the case of a 63 year old man with epigastric discomfort and weight loss. On endoscopy an ulcer with raised rolled edges was found in the lower oesophagus. A biopsy was performed which showed a small fragment of a highly pleomorphic malignant tumour composed of aggregates of plump epithelioid and spindle cells with high mitotic activity. Immunohistochemical staining showed vimentin positivity and weak cytokeratin positivity. Initial diagnosis was of a malignant fibrous histiocytoma.

Gastro-oesophageal resection showed a 3 by 2cm polypoid tumour in the lower oesophagus. The tumour was composed of spindle – sarcomatous elements with adjacent adenocarcinoma. Tumour invaded through muscularis propria, with lymph node deposits of sarcomatous elements (6 out of 12 nodes). Immunohistochemical staining showed positivity for p53 and AE1/AE3 in both elements of the tumour, consistent with a carcinosarcoma.

This unusual tumour showed adenocarcinoma as the carcinomatous component. Positive p53 staining in both elements of the tumour suggests a single monoclonal origin for this tumour. Metastases from carcinosarcomas tend to be of the carcinomatous element whereas, in this case, the lymph nodes contained metastatic sarcoma.

P22

Immunohistochemistry Shows No Difference in E cadherin Expression Pattern Between Early and Late Onset Gastric Cancer

{P} C R Parkinson[1], T E Buffart[2], A Gill[1], E Morrison[4], B Carvalho[2], C J H van de Velde[3], G A Meijer[2], N C T van Grieken[2], P Quirke[1], H Grabsch[1]
[1]Pathology and Tumour Biology, Leeds Institute of Molecular Medicine, Leeds, United Kingdom, [2]Dept of Pathology, VU University Medical Center, Amsterdam, Netherlands, [3]Dept of Surgery, Leiden University Medical Center, Leiden, Netherlands, [4]Cancer Research UK Clinical Centre at Leeds, Leeds Institute of Molecular Medicine, Leeds, United Kingdom

We have demonstrated that early onset gastric cancer has a different array comparative genomic hybridisation (CGH) profile compared to late onset GC. The expression and distribution of E cadherin (CDH1) are often abnormal in GC. Very few studies have compared CDH1 expression in early and late onset GC and results from these studies are contradictory.

We investigated CDH1 expression by immunohistochemistry on tissue microarrays constructed from sporadic GC of 77 patients younger than 50 years and 163 older patients. Staining pattern was classified as normal (complete membranous staining), abnormal (reduced membranous or cytoplasmic staining) or negative and correlated with patient age, clinicopathological data, survival data and CDH1 copy number from array (CGH) data.

CDH1 expression pattern was markedly heterogeneous even within the same TMA core. 18% of the cases showed normal expression, 70% abnormal expression and 12% were negative. Higher number of lymph node metastases and higher stage were both related to a higher frequency of tumour cells with abnormal CDH1 expression. CDH1 expression was more often abnormal in diffuse type GC. Abnormal CDH1 expression was more often associated with a high grade of differentiation. No association was found between CDH1 expression pattern and patient age, survival, CGH copy number or any other clinicopathological parameter.

Our study confirms the relationship between CDH1 expression, tumour progression and tumour differentiation in GC, but does not support a relationship between CDH1 expression pattern, patient prognosis or age of diagnosis. Furthermore, our array CGH data indicate that a mechanism other than CDH1 copy number change could be responsible for abnormal CDH1 staining pattern in GC.

P23

Coincident Granular Cell Tumour of the Stomach with Invasive Adenocarcinoma: A Case Report and Review of Literature

{P} SP Sah, JN Thompson, AC Wotherspoon
The Royal Marsden Hospital, London, United Kingdom

Background: Granular cell tumour (GCT) is relatively uncommon benign neural tumour. Approximately 5% to 9% of GCTs occur in the gastrointestinal tract, most commonly in oesophagus. Gastric localization is very rare and only six cases have been reported since 1996.

Case Report: A 49-year-old man presented with 4 months' history of weight loss and dysphagia. Endoscopic examination revealed an exophytic tumour at oesophago-gastric junction. Following 4 cycles of pre-operative neoadjuvant chemotherapy he underwent an oesophago-gastrectomy. The resected specimen showed a tumour involving distal oesophagus and proximal stomach. Sections from tumour revealed an invasive moderately differentiated adenocarcinoma of intestinal type (pT3N0Mx). Within muscularis propria of the stomach, in the region of the adenocarcinoma, a circumscribed lesion measuring 1.5 x 1.2 cm was seen. The lesion composed of oval to polygonal cells with a small central nucleus and abundant granular cytoplasm. The cytoplasmic granules were positive for periodic acid-Schiff. The cells stained for S-100 protein and NSE. Morphologic and immunohistochemical findings favoured a benign GCT infiltrated by adjacent adenocarcinoma at places. The patient is doing well after a follow up of 3 and half years.

Conclusion: We report a rare case of GCT colocalized with an invasive adenocarcinoma of the stomach.

P24

Poster withdrawn

P25

An Interesting Case of Indigestion

{P} R Arora, P Pichman
West Herts Hospital NHS Trust, Northwood, London, United Kingdom

Pancreatic heterotopia or aberrant pancreatic tissue in not an uncommon condition in the antrun and pyloric canal. Most of these are however unsymptomatic. Some which become symptomatic require surgical resection.They can mimic other upper gastrointestinal pathologies endoscopically and histopathologically.

We present an interesting case of distal gastrectomy performed for symptoms of indigestion and pyloric obstruction in a 70 year old male. Macroscopically there was a 12mm firm area at the antrum which on histology showed islands of varying sizes of glandular structures within the muscularis propira which were interspersed with smooth muscle and fibrous tissue. Occasional foci of heterotopic pancreatic tissue including acinar cells and neuroendoocrine islet-like cells were seen. These apprearences are of adenomyoma or myoepithelial hamartoma which is thought to be a congenital abnormality due to separation of fragments of pancreatic tissue from the main mass of the pancreas during rotation of the forgut.

P26

Evaluation of Genomic Instability in Sporadic Colorectal Cancers: Array-Comparative Genomic Hybridisation Outperforms Flow Cytometric Analysis

{P} G Poulogiannis[1], K Ichimura[1], NG Miller[1], IM Frayling[2], RG Morris[3], DJ Harrison[3], VP Collins[1], A Ibrahim[1], AH Wyllie[1], MJ Arends[1]
[1]University of Cambridge, Pathology Department, Cambridge, United Kingdom, [2]University Hospital of Wales, Institute of Medical Genetics, Cardiff, United Kingdom, [3]University of Edinburgh, Pathology Department, Edinburgh, United Kingdom

Colorectal cancers (CRCs) show at least two patterns of genomic instability: chromosomal instability resulting in aneuploidy, and microsatellite instability (usually occurring in near-diploid CRCs), with inactivation of the DNA mismatch repair (MMR) pathway, and sometimes both patterns or neither. In this study, we evaluated chromosomal instability in >100 sporadic CRCs using 1Mb array-comparative genomic hybridisation (aCGH) to assess DNA copy number alterations of the whole genome with arrays of 2904 cloned DNA inserts (mean clone size 152kb) spaced on average 0.97 Mb apart. The quantitative assessment of DNA copy number changes by aCGH identified many genomic abnormalities ranging from copy number variations of entire chromosomes and chromosomal arms to small micro-deletions and micro-gains of chromosomal subregions. The overall DNA content of these CRCs was also evaluated by the quantitative assessment of propidium iodide labelled tumour nuclei by flow cytometry (FCM). Comparison of FCM DNA histograms with aCGH analyses showed that a significant proportion of tumours with a near-diploid DNA content by FCM exhibited >1000 DNA copy number changes by aCGH indicating widespread chromosomal instability. This discrepancy is largely due to tumours displaying approximately equivalent numbers of DNA gains and losses resulting in an overall near-diploid DNA content. Most (>85%) MMR defective CRCs showed near-diploidy with few DNA breakpoints by aCGH. Furthermore, we developed a computational method to correlate aCGH-detected DNA copy number changes in CRCs with published changes in the expression levels of genes localised to the relevant chromosomal regions in order to identify novel putative oncogenes, such as LIVIN that showed copy number gains in ~70% of CRCs. We conclude that flow cytometric analysis of DNA ploidy underestimates chromosomal instability in CRCs, whereas aCGH provides a more accurate evaluation of chromosomal instability and can identify novel putative cancer-related genes.

P27

Poster withdrawn

P28

The Predictive Value for Adenocarcinoma of HGPIN and Atypical Small Acinar Proliferation (ASAP) in Prostate Needle Biopsies

L Hatsell, {P} N Mayer
University Hospitals of Leicester NHS Trust, Leicester, United Kingdom

Background and Aims: High grade prostatic intraepithelial neoplasia (HGPIN) is characterised by architecturally benign prostatic glands lined by cytologically atypical cells. Atypical small acinar proliferation (ASAP), rather than being a specific diagnostic entity, is a term used to describe a focus of glands which are suspicious for adenocarcinoma but for a variety of reasons fall below the threshold for a definite cancer diagnosis. In this retrospective audit of prostate needle biopsies, we compared our own diagnostic rates of HGPIN and ASAP and their predictive values for a subsequent diagnosis of adenocarcinoma against published standards. **Methods:** We identified 162 biopsies with an initial diagnosis of HGPIN and/or ASAP and determined how many of these had adenocarcinoma on re-biopsy. We compared this with a control group with a benign first biopsy. **Results:** In 2004 and 2005, HGPIN accounted for 6.9% and 5.8% of all prostate biopsies, respectively. Our 'suspicious rate' (ASAP and ASAP/HGPIN) was 2.6% in 2004 and 2.3% in 2005. The predictive value for adenocarcinoma in the HGPIN group was 15% which was similar to the control group of 13% (P=0.746). The predictive value for ASAP was 24% (P=0.286) and combined ASAP/HGPIN 33% (P=0.150). **Conclusion:** Our diagnostic rates for HGPIN and ASAP are within recommended guidelines. The predictive value for adenocarcinoma in the isolated HGPIN group is virtually the same as in the control group who had a benign first biopsy. The predictive value of ASAP and ASAP/HGPIN is higher (although failing to reach statistical significance).These results are in keeping with recent published series and suggest a diagnosis of isolated HGPIN does not justify immediate re-biopsy whereas ASAP or combined ASAP/HGPIN probably does.

P29

Utility of Polyclonal anti-PSA and 34betaE12 Immunostaining For Differentiating Prostatic Carcinoma from Urothelial Carcinoma

{P} M Varma, B Jasani, PN Mathews, SN Datta, MB Amin
[1]*University Hospital of Wales, Cardiff, United Kingdom,* [2]*Emory University, Atlanta, United States*

PSA and 34βE12 immunohistochemistry has been shown to be useful for differentiating high-grade prostatic adenocarcinoma (Pca) from Urothelial carcinoma (Uca). Polyclonal antibody to PSA (pPSA) has been reported to be more sensitive than monoclonal anti-PSA in high-grade PCa.

However, published studies examined only morphologically unequivocal cases. We retrospectively evaluated the utility of pPSA and 34βE12 immunostaining in 16 cases that had been signed out as "poorly differentiated carcinoma: ?PCa,?Uca" after immunostaining with monoclonal antibodies to PSA, PSAP and/or CEA.

Using pPSA and 34βE12, a definite diagnosis could be established in 15 (93.8%) of the 16 originally equivocal cases [9 Pca (pPSA+, 34βE12 -), 6 Uca (pPSA-, 34βE12 +)]. In 2 of these cases the possibility of synchronous PCa and UCa had originally been considered in view of patchy immunoreactivity with monoclonal anti-PSA, but pPSA showed diffuse positivity establishing a diagnosis of PCa. The remaining case was negative for pPSA and 34βE12, and an extended immunohistochemical panel was also non-diagnostic. Clinical findings in this case favored UCa but no follow-up was available.

Our findings confirm the clinical utility of a simple immunohistochemical panel composed of pPSA and 34βE12 for differentiating high-grade Pca from Uca.

P30

Microwave Pre-treatment Improves the Sensitivity of 34betaE12 as a Marker for High-grade Urothelial Carcinoma

{P} M Varma, S Wozniak, B Jasani
University Hospital of Wales, Cardiff, United Kingdom

Histopathologic distinction between high-grade urothelial carcinoma (HG-UCa) and prostate adenocarcinoma is critical for appropriate therapy.

High molecular weight cytokeratin monoclonal antibody, 34βE12 has been shown to be a sensitive marker for HG-UCa. A recent study found the sensitivity of 34βE12 immunostaining in HG-UC to be significantly greater with the use of microwave heat retrieval, as compared to enzyme predigestion.

We describe two cases (1 TURP, 1 prostate needle biopsy) in which the lower sensitivity of 34βE12 immunoreactivity after enzyme predigestion resulted in diagnostic difficulty. In both cases, the poorly differentiated carcinoma was negative for PSA and with 34βE12 used after enzyme predigestion at outside institutions and the overall appearances were considered most in keeping with prostate cancer.

On repeat immunostaining in our department, in both cases the tumour cells were negative for PSA and PSAP but diffusely and intensely positive on 34βE12 immunostaining performed after microwave pretreatment. Based on the morphology and immunoprofile, a diagnosis of HG-UCa was made on both cases. This diagnosis was confirmed following cystoprostatectomy in one case, no relevant follow-up is available to date on the other case.

We conclude that heat retrieval is the pre-treatment of choice when 34βE12 immunostaining is performed to confirm a diagnosis of urothelial carcinoma.

P31

An Evaluation of the Clinical Utility of Pelvic Lymph Node Frozen Section Examination Prior to Radical Prostatectomy

{P} LJ Aitken, H Kynaston, DFR Griffiths, M Varma
University Hospital of Wales, Cardiff, United Kingdom

In the current era of PSA screening, prostate cancer deposits within pelvic lymph nodes of patients considered for radical prostatectomy are generally small and the utility of frozen section (F/S) examination of these lymph nodes prior to radical prostatectomy is uncertain.

In our institution, 101 pelvic lymph node F/S examinations prior to planned radical prostatectomy were performed between 1996 and 2005. The lymph nodes were partially submitted for F/S examination and entirely submitted after fixation for definitive histology.

Metastatic tumour was found in only 2 (2%) of the cases while there were 3 false negative cases. The remaining 96 cases were negative on F/S and definitive histology.

Review of the 3 false negative cases confirmed the absence of metastatic tumour in the cryostat sections. Tumour deposits were found only in paraffin sections from deeper levels of cryostat blocks in two cases and only in additional blocks submitted after fixation in the third case. Thus, two of the three false negative cases would have been missed even if the nodes had been submitted in total for F/S examination.

We conclude that pelvic lymph node frozen section examination prior to radical prostatectomy is not cost effective.

P32

Bone Marrow-Derived Renal Parenchymal Cells Respond Poorly to the Renotropic Actions of Epidermal Growth Factor

T-H Yen[3], MR Alison[2], RA Goodlad[1], WR Otto[1], HT Cook[5], NA Wright[1], **{P}** R Poulsom[1]
[1]*Cancer Research UK - London Research Institute, London, United Kingdom,* [2]*Queen Mary's School of Medicine and Dentistry, London, United Kingdom,* [3]*Chang Gung Memorial Hospital, Taipei, Taiwan,* [4]*Chang Gung University, Taoyuan, Taiwan,* [5]*Imperial College, London, United Kingdom*

A small percentage of regenerating epithelial cells are derived from bone marrow (BM) cells following different types of renal injury. We reported previously that these enter S-phase of the cell cycle to assist regeneration, but we are concerned that they may not respond normally to growth controls, and be undesirable rather than useful for organ regeneration.

We tested whether BM-derived epithelial cells respond to epidermal growth factor (EGF) in lethally irradiated female mice transplanted with male whole BM cells. Six-weeks later they received pegylated colony stimulating factor (p-GCSF), EGF, and $HgCl_2$ singly or in combination, and were killed after 4 days, with tritiated thymidine given one hour earlier to label cells in S-phase.

Tubular injury scores and serum urea nitrogen levels were high after $HgCl_2$ injection and reached uremia, but EGF protected from such extreme damage. To explore the cell origin underlying this rescue, kidney sections were subjected to a "four-in-one" analytical technique for identification of cell origin, tubular phenotype, tubular basement membrane and S-phase status.

Transplanted BM contributed ~ 1% of proximal tubular epithelium in undamaged kidneys, ~ 3% in $HgCl_2$-damaged kidneys, but without further increase after either EGF or p-GCSF injection. Only ~ 0.5% proximal tubular cells were in S-phase without damage, increasing to ~ 7-8% after $HgCl_2$, and to ~ 15% for EGF+$HgCl_2$ mice. BM contributed ~ 1 in 15 of the S-phase proximal tubular cells after $HgCl_2$, but only ~ 1 in 30 after EGF+ $HgCl_2$ treatment.

Thus, BM-derived tubular cells are compromised in their ability to respond to a normal renal growth factor, and thus have a selective disadvantage that might cause them to be lost.

P33

Low Grade Adenocarcinoma of the External Auditory Meatus (EAM) Metastatic to Lung and Spine with Epithelial and Myoepithelial Differentiation.

{P} MAU Rahman, AG Douglas-Jones
University Hospital of Wales, Cardiff, United Kingdom

Glandular tumours of the external auditory meatus (EAM) are rare and at least some have been thought to arise from the ceruminous glands lining the ear canal leading to the term "Ceruminoma". The glandular neoplasms are a diverse group with differing histological appearances and biological behaviour. More specific classification is desirable and adenoma, cylindroma, adenoid cystic carcinoma, mucoepidermoid carcinoma and ceruminous adenocarcinoma have been described.
We present a case of low grade adenocarcinoma of the EAM presenting in a man of 35 who developed pulmonary metastasis after one year and metastatic tumour in the spinal cord after 17 years. Histologically, the primary and metastatic pulmonary lesion showed a nodular appearance with tubules , cords and gland-like structures whereas the lesion in the spine showed a more solid growth pattern. On immunohistochemistry for AE1/AE3, S100, Calponin, SMA and P63 all cases showed a biphasic epithelial/myoepithelial cell population. The intensity and distribution of the myoepithelial markers was different at the 3 sites with more evidence of myoepithelial differentiation in the late metastasis in the spine.
This case illustrates the unusual biological behaviour of these tumours which has been previously described and also the variable _expression of myoepithelial differentiation markers in this tumour.

P34

Identifying Pancreatic Cancer Stem Cells

{P} N J Guppy[1], M Brittan[1], M R Alison[1], W Otto[2]
[1]Centre for Diabetes and Metabolic Medicine, Institute of Cellular and Molecular Science, QMUL, London, United Kingdom, [2]Department of Histopathology, CRUK, London, United Kingdom

Cancer stem cells (CSCs) have been found in leukaemia and some solid tumours; retaining many properties and markers of normal adult stem cells, and thought to be uniquely responsible for initiating and maintaining tumours. Pancreatic adenocarcinoma is the 5th commonest cause of UK cancer deaths, with the lowest survival rate of all cancers. A pancreatic CSC is an attractive therapeutic target, yet a definitive stem cell remains unidentified within normal or malignant pancreatic tissue.
Two stable human pancreatic ductal adenocarcinoma cell lines (Panc-1 and Capan-2) were studied in vitro. Presence of two reported features of adult stem cells was explored: aldehyde dehydrogenase (ALDH) activity was evaluated by flow cytometric (FACS) analysis using Aldefluor, and ABC-transporter activity was investigated by Hoechst 33342 efflux assay, an established technique for revealing the side population (SP). ALDH-bright and SP cells were isolated via FACS and relative colony-forming potential assessed.
A subpopulation with high ALDH activity and an SP were present in both lines. Comparative clonogenity was significantly increased for ALDH-bright Panc-1 cells and for Capan-2 SP cells versus controls. However, the increase in Capan-2 SP clonogenicity may be artefactual, as Hoechst exposure significantly affects proliferation and clonogenicity in the non-SP fraction, a fact ignored by most investigators. Further studies must be performed before conclusions may be drawn as to the “stemness” of the SP fraction.

P35

Cutaneous lymphadenoma: An unusual adnexal tumour with prominent lymphocytic infiltrate

{P} A Biswas[1], D Gey van Pittius[1], M Stephens[1], BB Tan[2]
[1]Department of Histopathology, University Hospital of North Staffordshire, Stoke-on-Trent, United Kingdom, [2]Department of Dermatology,University Hospital of North Staffordshire, Stoke-on-Trent, United Kingdom

Background: Cutaneous lymphadenoma is a rare and unusual adnexal tumour with distinctive histological features. Less than 50 cases have been reported till date and controversy exists about its histogenesis and correct designation.
Case report: A 65 year old man presented with a slowly growing 10 x 6 mm skin nodule on the right cheek. Histology showed a well circumscribed dermal nodule composed of multiple round to irregular lobules of basaloid cells showing peripheral palisading. Also present within and outside the lobules was a dense mononuclear inflammatory infiltrate composed predominantly of mature T lymphocytes and numerous S 100 and CD1a positive cells. Scattered large Reed Sternberg like cells stained weakly with CD68 but were CD30 negative. Focally, there was perilobular condensation of stroma and subtle differentiation into follicular germ and papillae. No sweat glandular differentiation was apparent on CEA and EMA immunohistochemistry.
Conclusion : The morphology and immunohistochemical profile is supportive of a folliculo-sebaceous-apocrine, rather than an eccrine line of differentiation. Cytokines produced by intralobular dendritic cells may be responsible for the intimate association between the epithelial and inflammatory cells in these tumours. Our findings provide support for the currently held view that cutaneous lymphadenoma is probably a variant of trichoblastoma.

P36

A case of childhood primary cutaneous anaplastic large cell lymphoma with spontaneous regression

{P} A Biswas[1], D Gey van Pittius[1], M Stephens[1], BB Tan[2]
[1]Department of Histopathology, University Hospital of North Staffordshire, Stoke-on-Trent, United Kingdom, [2]Department of Dermatology, University Hospital of North Staffordshire, Stoke-on-Trent, United Kingdom

Primary cutaneous CD 30+ anaplastic large cell lymphoma (ALCL), unlike its primary nodal counterpart is exceptionally rare in the paediatric population. We report a case of primary cutaneous ALCL in a child which resolved spontaneously.
An 8 year old girl presented with a solitary 20x10 mm ulcerated skin lesion on the areola. An incisional biopsy revealed a pandermal infiltrate of CD 30+ large pleomorphic lymphoid cells arranged in a strikingly perivascular distribution. Staining for ALK-1 protein was negative. The epidermis was acanthotic and showed focal ulceration. The features were typical of a cutaneous CD30+ lymphoproliferative disorder. Complete staging investigations did not reveal any extracutaneous disease or new skin lesions. A specific diagnosis of primary cutaneous ALCL was made. The lesion resolved almost completely in 4 weeks and this was confirmed by a repeat biopsy. The child is being managed by close follow-up and remains well 6 months later.
The importance of good clinico-pathological correlation is highlighted. Perivascular cuffing of large lymphoid cells, as seen here, is a well recognised clue for nodal ALCL but is not widely described in primary cutaneous ALCL. Clear treatment guidelines do not exist in this age group and long term follow-up is mandatory.

P37

Immunohistochemical study of HSP60 in cutaneous lichen planus compared to normal skin and psoriasis vulgaris.

L Mansour[1], Z Abd El-Samad[2], M Sherif[1], {P} D Shaaban[1], A Abdellatif[1]
[1]*Department of Dermatology, Tanta University, Tanta, Egypt,* [2]*Department of Pathology, Tanta University, Tanta, Egypt*

Background Lichen planus (LP) is a relatively common papulosquamous dermatosis for which the exact aetiology remains obscure. Cell mediated immunity plays an important role in its pathogenesis. Heat shock proteins (HSPs) are expressed by most living cells and have fundamental importance in cutaneous biology. Although an altered expression of certain HSPs were reported in oral LP, their expression in cutaneous LP has not been fully investigated. In this study, we aimed at investigating the role of HSP60 in the pathogenesis of LP by studying its expression in cutaneous LP when compared to that of normal skin and psoriasis.
Materials and Methods Formalin-fixed paraffin- embedded skin biopsies from LP patients (n=25), psoriasis patients (n=25) and normal controls (n=10) were included in the study. Antibodies to HSPs 60 were applied immunohistochemically. An immunoreactivity intensity distribution index (IRIDI) was calculated for epidermal cells and the dermal infiltrate.
Results The main IRIDI score in the basal, suprabasal and superficial epidermal layers of LP was significantly higher than that of normal skin but not different from that of psoriasis vulgaris. Regarding the inflammatory cells, HSP60 score was higher in LP than in psoriasis.
Conclusion HSP 60 may have a role in the pathogenesis of LP.

P38

Enhanced Clonogenicity of Side Population Cells may be an Artefact of Hoechst 33342-related Alterations in Cell Kinetics

{P} N J Guppy[1], M Brittan[1], M R Alison[1], W Otto[2]
[1]*Centre for Diabetes and Metabolic Medicine, Institute of Cellular and Molecular Science, QMUL, London, United Kingdom,* [2]*Department of Histopathology, CRUK, London, United Kingdom*

Isolation of a "side population" (SP) via flow cytometric Hoechst 33342 efflux assay is a popular tool for adult stem cell identification. High ABC-transporter activity confers the enhanced dye efflux seen in SP cells and resistance to cytotoxic drugs in vivo. However, it has been suggested that enhanced clonogenicity and proliferative capacity exhibited by SP cells versus non-SP cells isolated in this way may be an artefact of Hoechst overload, as Hoechst may inhibit proliferation in vitro in a dose-dependent manner.

To investigate this possibility, SP and non-SP cells were isolated from two pancreatic adenocarcinoma lines (Panc-1, Capan-2) via the standard Hoechst efflux assay. Relative clonogenicity and proliferation of viable SP, non-SP, and whole populations exposed to Hoechst ± reserpine (an inhibitor of ABC-transporters), reserpine alone or neither were examined.

Capan-2 SP cells were significantly more clonogenic than the Hoechst-exposed whole population control. However, in whole populations, Hoechst exposure produced significant decreases in clonogenicity and population doubling rate, exacerbated by addition of reserpine. Conversely, Panc-1 cells showed no significant differences in clonogenicity or proliferation rate between treatments or sub-fractions.

The relatively high clonogenicity of Capan-2 SP cells may be an artefact of dye-related effects on cell kinetics, and attribution to intrinsic properties cannot be implied. Therefore, SP studies using this method must be interpreted with caution.

P39

Affinity is not the Only Factor

{P} VA Reid, J Doherty, G McIntosh, S Cowell, M Lee, M Rees
Vision BioSystems, Newcastle upon Tyne, United Kingdom

Recently there has been a broad interest into the effect and contribution of antibody affinity on the quality of immunohistochemistry (IHC). Here we investigate the affect of affinity on IHC using Biacore® analysis. Biacore® utilises the phenomenon of surface plasmon resonance (SPR) to measure changes in the refractive index (RI) which is determined by the quantity of bound antibody-antigen at the chip surface resulting in a real time kinetic measure. We also compare directly the affinity of equal concentrations of market leading rabbit and mouse monoclonal antibodies for the same target antigens using Biacore® and IHC analyses. Our studies have focussed on several important antibodies, including those to estrogen receptor, progesterone receptor, CD3 and CD8. We conclude that although antibody affinity can influence IHC intensity for some target epitopes, there is clearly a complex interplay between affinity, epitope availability and specificity, which ultimately determines antibody performance. Furthermore, we have also shown that antibody host species is largely irrelevant in terms of generating high affinity antibodies for use in immunohistochemistry. This is largely epitope dependent and varies depending on the target, and how it is presented to the host species immune system.

P40

Role of vascular endothelial cell growth factors in progression of human breast cancer

{P} RAA Mohammed[1], A Green[2], EC. Paish[2], IO Ellis[2], SG Martin[1]
[1]*University of Nottingham, Clinical Oncology Department, Nottingham, United Kingdom,* [2]*University of Nottingham, Histopathology Department, Nottnigham, United Kingdom*

Background: Vascular endothelial cell growth factors (VEGF)-A, VEGF-C and VEGF-D have angiogenic and lymphangiogenic functions in experimental studies however their role in the progression of human breast cancer is still unclear.
Aims: To study the prognostic value of the expression of VEGF-A, -C and -D in breast cancer.
Methods: Paraffin embedded sections of 177 invasive breast cancer, with 10 years follow up, were stained immunohistochemically with the lymphatic marker, podoplanin to assess lymph vessel density (LVD), VEGF-A, VEGF-C and VEGF-D. Expression of growth factors was correlated with clinicopathological criteria and LVD.
Results: High expression of VEGF-A and -C but not of VEGF-D were associated with high LVD (P= 0.047, <0.001 and 0.187 respectively), presence of LN metastasis (P= 0.017, <0.001 and 1.000 respectively), distant metastasis (P= 0.010, 0.008 and 0.805 respectively) and shorter overall survival (P= 0.029, 0.028 and 1.000 respectively).
Conclusions: Breast cancers that express high levels of VEGF-A and -C are characterized by a worse prognosis. This may be due to increased lymphangiogenesis that increases the probability of malignant cell dissemination. VEGF-A and -C may be helpful in the identification of a subset of lymphangiogenic breast cancers that have a higher probability of recurrence and metastatic spread.

P41

Outcome of Screen Detected Breast Lesions with False Positive Pre-operative Core Biopsy or FNAC

{P} Y F Baber, J Dove, D Ravichandran
Luton NHS Foundation Trust, Luton, United Kingdom

The objective was to study the outcome of patients with screen detected breast lesions in whom pre-operative core biopsy and/or FNAC were reported as suspicious or definitely malignant but the final histology of the excised lesion was benign.
Between April 1998 and March 2004 40 patients were identified from the Bedfordshire and Hertfordshire Breast Screening Centre database. The mean age was 56 years(50-78). Mammographic abnormalities were microcalcification in 17, soft tissue lesion in 19 and both in 4. Thirty-five patients had both FNAC and CB and 5 had FNAC only.
All cytology, core biopsies and final excisions, where available, were reviewed on 33 patients.
The median follow up period following surgery was 36 months. No patient had been diagnosed with breast cancer in this period.
In conclusion, "false positive" core biopsy or FNAC is uncommon in screen detected lesions and this data suggests that these patients are not at a higher risk of being diagnosed with a malignancy following this episode and may be returned to routine screening.

P42

Glycan Profiles of Breast Cancer: Distinguishing Invasive from In-Situ

{P} A Leathem[1], H Lacey[1], M Dwek[2]
[1]*University College London, London, United Kingdom,* [2]*University of Westminster, London, United Kingdom*

Glycans, or complex-sugar chains on the surface of cells, provide important signals for cell-cell interaction, such as fertilization, cell adhesion and immune recognition. Changes in the glycans of normal cells have been described in many cancers, some probably related to invasive and metastatic behaviour. We are developing methods to compare the glycans of healthy and cancer tissues and discovered differences between glycans of In-Situ and Invasive breast cancer tissues.
Intact glycans were released from tissues using anhydrous hydrazine and and, after labelling with a fluorescent tag, were separated on a range of High Performance Liquid Chromatography matrices.
The profiles of Invasive and In-Situ cancers were mapped and show several differences, particularly in the diversity of sialylated and neutral oligosaccharides and the number of sialylated structures. We are trying to separate and characterize these structures. This may help us follow in-situ to invasive behaviour and provide a simple biomarker to aid in diagnosis.

P43

Hidden Danger: Carcinoma Arising in Accessory Breast Tissue in a BRCA2 Germline Mutation Carrier.

{P} H G Shenoy, M B Peter, S A Lane, K Horgan, A M Hanby
Leeds General Infirmary, Leeds,West Yorkshire, United Kingdom

A 43-year-old lady with a family history of breast cancer presented with a right axillary lump. Excision revealed two lymph nodes infiltrated with undifferentiated carcinoma (ERα positive). Investigation failed to identify the primary tumour but an occult primary breast cancer was assumed and treatment with adjuvant chemotherapy followed. Subsequent genetic assessment showed she had a germline BRCA2 mutation. She opted for bilateral prophylactic mastectomies, a right axillary node clearance and bilateral oophoretomies- all of which showed benign histology.

20 months later, she noted a small superficial lump in the skin of the cleared axilla. A clinical diagnosis of a benign skin adnexal lesion was made. Excision showed a 10mm Invasive Ductal Carcinoma (ERα+ve, PR-ve, Her-2+ve) with extensive high grade DCIS within accessory breast tissue. Further excision of remaining axillary tissue revealed residual high grade DCIS and five negative lymph nodes. A retrospective history revealed that she had a right axillary swelling during breast-feeding and regression on cessation.

This case underlines the possibility that even after risk-reducing surgery, affected kindred with a risk of heritable breast cancer may develop breast cancer in any accessory breast tissue found along the milk-line; which extends from the axilla to the vulva.

P44

Adenoid Cystic Carcinoma (ACC) of the Breast – A Report of a Case with Long Follow-up

{P} MB Peter, HG Shenoy, K Horgan, AM Shaaban
Leeds General Infirmary, Leeds, West Yorkshire, United Kingdom

ACC is a rare mammary neoplasm representing <1% of breast carcinomas. It comprises various proportions of glands and stromal or basement membrane elements. In contrast to its salivary counterpart, mammary ACC carries an excellent prognosis. Its rarity and structural heterogeneity limit our knowledge to diagnose and treat it. Here, we present a case of mammary ACC with a 7-year follow-up.

A 62-year-old asymptomatic female was found to have a 7mm spiculate lesion in the left breast on screening mammography. FNAC showed large cohesive sheets of epithelial cells with regular hyperchromatic nuclei. There was associated dense hyaline basement membrane-like material forming branching cords in the centre of the groups and in areas having a more spherical or globular outline. On diagnostic excision, a 21 mm ACC with solid areas and an infiltrative pattern was found. Vascular invasion was absent. The tumour was ERα and PR negative. Myoepithelial cells were SMA and CK14 positive, while the hyaline material stained positive for Laminin and type IV collagen.

Further excision, for close margins, with an axillary clearance was done; both were free from neoplasia. Radiotherapy, but no endocrine therapy or chemotherapy was administered. Clinico-radiological follow-up for 7 years has not shown any recurrence.

P45

ISOLATED CALCIFICATIONS DETECTED BY SCREENING MAMMOGRAPHY: RADIOLOGIC-PATHOLOGIC CORRELATION

{P} CM Brodie[1], A O'Doherty[2], C Quinn[1]
[1]*Department of Histopathology, St. Vincent's University Hospital, Dublin, Ireland,* [2]*Department of Radiology, St. Vincent's University Hospital,, Dublin, Ireland*

Introduction: Screening mammography frequently detects isolated mammographic calcification. The associated histologic correlates and incidence of malignancy are not well characterised.
Methods: Needle core biopsies (NCBs) for isolated mammographic calcification at screening mammography submitted to the histopathology department from November 2000 to February 2004 were retrieved. Mammograms were coded by the consultant radiologist according to the R – coding classification system (R1 negative, R2 benign, R3 probably benign, R4 suspicious of malignancy, R5 malignant). The R code was correlated with histology on NCB (if benign – 49 cases) and/or on subsequent excision (atypical or malignant NCB – 110 cases).
Results: 159 patients with mammographic calcification were detected. Appearances were coded as R3 in 73 (47%), R4 in 48 (30%) and R5 in 37 (23%). Final histologic diagnoses were benign, atypical or malignant (table 1).

	Benign	Atypical	Malignant	Total
R3	41	9	24	74
R4	17	4	27	48
R5	2	1	34	37
Total	60	14	85	159

Table 1.
The positive predictive value (PPV) for malignancy of R5 calcification was 92%, R4 calcifications 56% and R3 calcifications 33%.
Conclusion: R5 mammographic calcifications are strongly predictive of malignancy. Indeterminate mammographic calcifications (R3 and R4) have a lower but substantial incidence of malignancy.

P46

Bilateral Inflammatory Breast Cancer : A Case Report

{P} YA Masannat[1], MB Peter[1], P Turton[2], AM Shaaban[1]
[1]*Leeds General Infirmary, Leeds, United Kingdom,* [2]*St James University Hospital, Leeds, United Kingdom*

Breast cancer is bilateral in 3-4% of cases. Inflammatory breast cancer makes up 1-3% of primary breast tumours, classically presenting with signs of inflammation. The pathological type of the tumour varies but the classical skin biopsy finding is malignant invasion of dermal lymphatics. We report a case of bilateral inflammatory cancer.
A 61-year-old lady with history of previous malignancy in the left breast presented with left breast lump, erythema, peau d'orange and skin changes. A core biopsy showed a necrotic malignant epithelial tumour (ER-ve, PR-ve) with basal differentiation. She then had neoadjuvant chemotherapy followed by a mastectomy and axillary clearance which showed no residual neoplasia and negative lymph nodes.
However 6 months later, she presented with a similar lesion in the right breast; which on core biopsy was proven to be another inflammatory cancer (Ductal NST, ER-ve, PR-ve, Her-2-ve). A skin biopsy showed intralymphatic infiltration. She then received a different form of neoadjuvant chemotherapy followed by a right mastectomy and axillary clearance. Histological analysis revealed no residual neoplasia and negative nodes. The patient is alive and free from recurrence.
This is an unusual case of 2 rare cancers in the same patient with complete regression after neoadjuvant chemotherapy.

P47

Four unusual cases of thoracic vasculitis

{P} M Jansen[1], L Burke[1], M Bolster[1], MN Sheppard[2]
[1]*Dept of Histopathology, Cork University Hospital, Cork, Ireland,* [2]*Dept Histopathology, Royal Brompton and Harefield NHS Trust, Imperial College, London, United Kingdom*

Four cardiopulmonary vasculitic complications of 4 different diseases, all with an autoimmune basis. Two of these cases presented clinically and radiologically with evidence of pulmonary thrombo-embolic disease. One with an antecedant history of Wegener's granulomatosis, following "embolectomy", had a giant cell vasculitis affecting the large pulmonary elastic arteries. The second case of "pulmonary thrombothrombo-embolic disease" had giant cell vasculitis affecting widespread small peripheral pulmonary arterial vessels. The association with positive serology for anticardiolipin antibodies has not been previously reported. Third case was Cogan's syndrome, complicated by descending acute and chronic aortitis, a rarely reported phenomenon, with co-existant acute endocarditis of the aortic valve leaflets. Fourth case was an acute and chronic aortitis associated with relapsing polychondritis. Both of these cases occurred despite aggressive immunosuppressive regimen including cyclophosphamide with an apparent clinical response in one case. If patients develop new symptoms related to the cardiovascular system they should be clinically investigated, regardless of apparently inactive disease. It was similar with the Wegener's case, where the patient developed pulmonary vasculitis despite therapy. All these cases emphasize the continued importance of histology and the post mortem examination in elucidating previously undetected or unsuspected disease.

P48

Multiple combined sclerosing haemangiomas and tumourlets. A report of two patients with bilateral disease.

{P} R Saluja[1], S Pomplun[2], AG Nicholson[1], MN Sheppard[1]
[1]*Royal Brompton and Harefield NHS Trust, London,* [2]*Kings College London, London*

Sclerosing haemangiomas (SH) are rare typically solitary benign pulmonary tumours which have occasionally been described in association with foci of neuroendocrine (NE) proliferation, this ranging from tumourlets to carcinoid. We present two cases where both components, SH and tumourlets, were multiple and bilateral in nature.
The two patients (female, aged 43 years and male, aged 47 years) both presented with non-productive cough and wheeze, one patient having a history of melanoma. Imaging showed bilateral multiple nodular opacities. Surgical lung biopsies showed multiple SH of variable sizes, up to 4mm and multiple tumourlets, with some nodules comprising both cell types. In one case, there was obliterative bronchiolitis focally associated with tumourlets. In the second case, there were additional papillomatous foci, interpreted as an early growth phase of SH rather than a further tumour type, and also localised foci of goblet cell hyperplasia.
Conclusion: This study documents an very rare pattern of presentation for SH and tumourlets where they present throughout the lungs, in combination or separately, to mimic disseminated malignancy. Given the precedent for NE proliferations being associated with SH, there may be a relationship between the two types of cell growth, either originating from different pathways from the same stem cell or with SH promoting NE growth by an unknown mechanism.

P49

T-Regulatory Cells are Increased in the Cellular Infiltrates of Hypersensitivity Pneumonitis

{P} DA Oble, RL Kradin
Massachusetts General Hospital, Boston, MA, United States

Hypersensitivity pneumonitis (HP) represents a pulmonary immune response to inhaled antigens characterized by peribronchiolar and interstitial T-lymphoid infiltration and microgranulomas. T regulatory cells (Treg) play a role in down-regulating cellular immunity and can be identified by their expression of FOXP3. We identified Treg and other lymphoid subsets in situ in five cases of biopsy-proven HP, non-specific interstitial pneumonitis (NSIP) and normal lung. While an increased number of CD3 cells were present in HP relative to NSIP ($p=0.03$), the CD4/CD8 ratios for HP and NSIP were comparable (1.5 and 1.4, respectively). Interestingly, HP showed increased FoxP3 positive Treg compared to NSIP ($p=0.02$). We conclude that HP is specifically characterized by an increase in Treg in situ. Further studies to elucidate the role of this lymphoid subset are in progress.

P50

This abstract is not available
for publication
until after presentation
at the Meeting

P51

Malignant Clear Cell Hidradenoma of the Vulva: A Case Report and Review of the Literature

{P} OJ Biedrzycki[1], B Rufford[2], DPJ Barton[2], C Jameson[1]
[1]*Department of Histopathology, The Royal Marsden Hospital, London,*
[2]*Department of Gynaecology, The Royal Mardsen Hospital, London*

Clear cell hidradenoma (CCH) is a rare tumour derived from eccrine sweat glands with a predilection for the head, face and upper extremities. Its biological behaviour is unpredictable, although frank malignant transformation is reportedly rare (6.7% in one review). Malignant clear cell hidradenoma (MCCH) exists only as case reports or very small series in the literature.
We present a 39yr old female who underwent marsupialisation of a presumed left vulval Bartholin's gland cyst. She had no significant past medical history and her smear history was normal. Microscopy revealed a tumour with the features of CCH; no atypia, necrosis or mitoses were seen. Ten months later, she developed enlarging left groin nodes, one of which contained a metastatic clear cell tumour. Radiology did not reveal any other primary source and the diagnosis of MCCH was confirmed by expert review. A re-excision of the vulval primary site was performed which contained residual tumour. She is currently free of any further recurrence nine months after excision of the lymph node metastasis.
The case highlights the difficulty in predicting the behaviour of CCH from histology alone and the importance of considering MCCH in the differential diagnosis of a lymph node containing a metastatic clear cell tumour.

P52

Pathological findings associated with the presence of a Mirena coil at hysterectomy

{P} H Rizkalla, M Higgins, P Kelehan, C O'Herlihy
Departments of Pathology, Obstetrics and Gynaecology, National Maternity Hospital, Dublin, Ireland

The Mirena intra-uterine system (IUS) has changed the management of women with menorrhagia. Sometimes IUS treatment fails and patients undergo hysterectomy. We have reviewed the histopathological findings of the uteri of fifty women undergoing hysterectomy, 48 of which had a clinical history of abnormal uterine bleeding following unsuccessful IUS treatment. The mean patient age was 42.7 years. The majority of women (60%) had the expected appearance of atrophic endometrial glands and pseudodecidual stromal reaction. Thirty hysterectomy specimens contained benign leiomyomata with reduced reactivity in the enlarged uterine cavity and incomplete suppression of the endometrium. Fourteen specimens had adenomyosis, of which eight also had fibroids. One specimen had, an atypical polypoid adenomyoma of the endometrium and fibroids. Four cases had invasive cervical squamous cell carcinoma. Two specimens had endometrial hyperplasia where the IUS was unsuccessful. Two specimens showed intrauterine misplacement of the IUS. Seven specimens showed no histological abnormalities.
In conclusion, Although IUS can be used successfully in the treatment of menorrhagia due to uterine fibroids; in our series the majority of hysterectomies following failed IUS suppression of menorrhagia contained uterine fibroids. Specimens with cervical carcinoma highlighted the need to consider cervical causes in the investigation of abnormal uterine bleeding.

P53

Audit of PPV of cervical biopsies: compliance with National Guidelines

{P} S Deen, JR Patel, RH Hammond, D Nunns, KW Williamson
Nottingham University Hospital, Nottingham, United Kingdom

The NHSCSP guidelines for colposcopy indicate that a biopsy should be carried out unless an excisional treatment is planned, when the cytology indicates persisting moderate dyskaryosis or worse. The clinical practice for colposcopy directed punch biopsies varies between submitting one pot with one or more biopsies from the worst area (team 1) or submitting two pots from suspected areas of CIN (team 2). Whilst the latter practice may show the distribution of the disease around the cervix, it also produces an extra specimen to be dealt with by the department.
Aim: Do we need to identify biopsy sites separately in different pots?
Methods: We audited the reported data of cases received from January- March 2006 for team 1 and from November 2005- March 2006 (team 2) that had more than one pot. All cases followed by a LLETZ. Cases with one biopsy only from team 2 or without a following LLETZ were excluded. The PPV of CIN for the cervical smear and individual cervical biopsies (as biopsy one and biopsy two) has been calculated.
Results: 70 cases fulfilled the stated criteria. Tabulated results bearing in mind different teams of reporting pathologists.

	Colposcopy PPV	Smear PPV	Biopsy 1 PPV	Biopsy 2 PPV
Team 1	0.83	0.86	0.68	00
Team 2	0.87	0.76	0.84	0.84

Conclusion: 1) The PPV of both biopsies is the same suggesting that perhaps there is no need to identify them separately.
2) The inevitable question is that do we need a biopsy? This is considering that 56 out of the total 120 cases were suspected high grade at colposcopy.
3) Re-audit with independent review of the histological picture of the biopsies and loops.

P54

Is Microscopic Examination of Hysterectomy Specimens Performed for Clinically Benign Disease Necessary?

{P} TD Andrews, H Monaghan
Royal Infirmary of Edinburgh, Edinburgh, United Kingdom

Introduction: The recent Royal College of Pathologists report "Histopathology of Limited or no clinical value" raises the possibility that Pathologists' time could be saved by macroscopic examination only of hysterectomy specimens for certain benign processes, however, the authors conclude that further study is needed in this area. We present the results of an audit of 5 years experience of hysterectomy specimens undertaken for clinically benign disease.
Materials and Methods: The reports of all hysterectomy specimens removed for benign disease, over a 5-year period, were reviewed and cases showing a significant abnormality reviewed.
Results: Of 851 cases, only 14 (1.6%) of these showed a significant unexpected abnormality, including 2 invasive cancers and 7 cases of CIN. If hysterectomy was performed for menorrhagia and was macroscopically normal, or if the patient had a normal smear history and a negative endometrial biopsy in the 12 months prior to hysterectomy there were no significant unexpected findings.
Discussion: Although the chance of finding an unexpected abnormality in a hysterectomy specimen for benign disease is low, 9 (1.1%) of cases did contain either pre-invasive or invasive disease, therefore we recommend that all specimens should be examined microscopically, however, excessive block taking is unnecessary.

P55

Endometrial Small Cell Carcinoma With Endometrioid, Serous Papillary and Clear Cell Components

{P} NP West, N Wilkinson
St. James' University Hospital, Leeds, United Kingdom

Endometrial carcinomas with a neuroendocrine small cell component are rare. These tumours may occur admixed with other components but to date there is only one previous case report of a mixed serous papillary and small cell carcinoma of the endometrium. We report a case of endometrial carcinoma showing mixed small cell, endometrioid, serous papillary and clear cell components.

The patient was a 69 year old female who presented with post-menopausal bleeding. A hysteroscopy was performed and histology of the curettings revealed an endometrioid adenocarcinoma with small foci of small cell and high grade serous carcinoma. She then proceeded to a staging laparotomy.

Macroscopically the endocervix and uterine cavity were replaced by tumour. Microscopically the tumour was predominantly a small cell carcinoma with areas of moderately differentiated endometrioid, high grade serous and clear cell carcinoma. No sarcomatous elements were identified. There was evidence of serosal involvement and vascular space permeation by mixed serous papillary and small cell carcinoma. Two out of ten lymph nodes showed microscopic deposits of pure serous papillary carcinoma.

This unusual tumour is the first case report in the English literature of an endometrial small cell carcinoma admixed with endometrioid, serous papillary and clear cell components.

P56

Stereological Analysis of Villous Trophoblast in Intra Uterine Growth Restricted Placentae

{P} KL Widdows[1], C Jayadewa[2], JCP Kingdom[1], PD Sibbons[1], T Ansari[1]
[1]*Department of Surgical Research, NPIMR, Harrow, United Kingdom,*
[2]*Dept. Obs & Gyn, Mount Sinai Hospital, University of Toronto, Toronto, Canada*

IUGR placentae are characterised by altered villous and vascular morphology. Alterations in the morphology of the villous membrane are yet to be described for IUGR placentae but it is hypothesised that altered trophoblast differentiation and proliferation may lead to perturbed maternofetal exchange and ultimately compromised fetal growth.
Placentae samples were obtained uniform-randomly from preterm control (n=6) and preterm IUGR (n=6) pregnancies. 5µm and 25µm formalin-fixed paraffin embedded sections were stained with H&E. Stereological analysis included volume, total number and density estimates of cytotrophoblast and syncytiotrophoblast nuclei for both study groups.
Placental volume was significantly decreased in the IUGR group compared with controls (p=0.015). Significant reductions were observed for both the volume (V) and total number (N_{TOT}) of cytotrophoblast (p=0.009, p=0.004) and syncytiotrophoblast nuclei (p=0.009, p=0.004) in the IUGR group when compared with controls. The density of the cytotrophoblast and syncytiotrophoblast remained unchanged in the IUGR group compared with controls.
IUGR placentae exhibit unaltered functional intergrity in terms of membrane morphology and the reduction in the total number of trophoblast nuclei is likely due to a smaller IUGR placentae.

P57

Primary Fallopian Tube Carcinoma- A Case Report

{P} L Radhakrishnan, AQ Ganjifrockwala, A Howat, W Salman, Z Twaij, H Stringfellow, A Al-Dawoud
Department of Histopathology, Burnley General Hospital,East Lancashire Hospitals NHS Trust. Royal Preston Hospital, Burnley and Preston, United Kingdom

Background: Malignant neoplasms of the fallopian tube (FT) are the rarest of the gynaecological cancers (0.3-1.1%). While cancers metastatic to the FT occur frequently from ovarian, endometrial and other sources, primary cancers are a rarity.
Case report: We report a case of a 56 year old woman who presented with CIN III and a past history of breast cancer. Imaging revealed an enlarged, solid and nodular left ovary. A total abdominal hysterectomy with bilateral salpingo-oophorectomy and omentectomy was performed.
Macroscopically, there was presence of a mass occupying the middle portion of the FT and extending into the mesosalpinx. On sectioning a solid, cream coloured tumour mass was seen measuring 6 x 4 x 2.5cms compressing the ovary.
Microscopically, the left FT showed extensive infiltration of the wall and mesosalpinx by a poorly differentiated adenocarcinoma showing areas of serous and clear cell differentiation. The tubal epithelium showed presence of carcinoma in situ which was in continuation with the invasive cancer. The tumour adhered to the left ovary but showed no evidence of direct extension to the ovary. The above features suggested a diagnosis of a primary adenocarcinoma of the FT.
Conclusion: Although Fallopian tubes are frequently involved in benign gynaecological conditions, primary malignant involvement is rare, and because of its rarity, lack of diagnostic accuracy, non presenting symptoms and physical findings, primary fallopian tube carcinoma is a diagnostic difficulty.

P58

Comparison Between Flow Cytometry and Trephine Bone Marrow Biopsy in the Detection of Lymphoid and Plasma Cell Infiltrations

{P} A Sandouka, E Raweily, L Jone, M Semple
Epsom & St Helier University Hospitals NHS Trust, Surrey, United Kingdom

Objective: To assess the diagnostic value of bone marrow trephine biopsies (BMB) and flow cytometry (FC) in the assessment of bone marrow infiltration in plasma cell disorders (PCD) and other lymphoid disorders (LD).
Methods: We have reviewed retrospectively 101 diagnostic and follow up bone marrow specimens from a series of patients in whom BMB and FC data were available. Of these, there were 30 specimens from patients with PCD and 71 specimens from patients with other LD.
Results: In PCD there was significant disagreement between the two investigations in 63.3% of samples. In 13.3% of samples there was complete agreement. In 23.3% of specimens there was a non significant disagreement, these were almost all in the monoclonal gammopathy of uncertain significance (MGUS) category. This makes a total of 86.6% disagreement in the monoclonal plasma cell disorders category. In contrast, in other LD, complete agreement was 90.1%, complete disagreement 2.8% and insignificant differences in 7.1%.
Conclusions: BMB is the better method for the detection of infiltration in PCD. While a much less marked difference in sensitivities of BMB and FC to PCD has been reported before, the cause of this marked difference in our figures need to be clarified.

P59

The utility of PWS44, an anti-CD33 antibody active in paraffin-embedded tissue, in routine haematopathology practice

{P} A D Ramsay, P Munson, I Proctor
University College London, London, United Kingdom

Antibody PWS44 (Novocastra, UK) recognises the CD33 transmembrane glycoprotein on cells of myeloid and monocytic cells lineage in paraffin-embedded tissues. Anti-CD33 is routinely used in flow cytometry but until now has not been available for histological use. We report on the utility of this antibody in a specialist haematopathology unit.

We applied PWS44 to 70 haematopathological specimens (54 bone marrow biopsies, 13 lymph nodes and 3 other sites). There was strong membrane staining on almost all myeloid and monocytic cells, from precursor forms through to mature cells. All 25 cases of acute myeloid leukaemia were positive, as were myeloid cells in 5 cases of myelodysplastic syndrome, 3 cases of chronic myeloid leukaemia and one case of granulocytic sarcoma. 1 of 5 cases of T-lymphoblastic lymphoma was positive as was one of 3 cases of B-lymphoblastic lymphoma. Three Burkitt lymphoma cases were negative. Reed-Sternberg cells in classical Hodgkin lymphoma were positive in 1 of 5 cases. Overall PWS44 was useful in the recognition of acute leukaemias derived from myeloid or monocytic cells, especially where CD117 or myeloperoxidase expression was absent, but the extent of staining of normal marrow cells meant that assessment of subtle infiltrates or dysplastic changes was difficult.

P60

Immunohistochemical staining of bone marrow for CD33 in patients with acute myeloid leukaemia – a comparison with flow cytometry

{P} I Proctor, P Munson, AD Ramsay
University College London, London, United Kingdom

CD33 is a transmembrane glycoprotein expressed by cells of myeloid lineage but not by pluripotent stem cells, B-cells or T-cells. Anti-CD33 monoclonal antibodies for flow cytometry have been available for some years and play an important role in the diagnosis of acute myeloid leukaemia (AML) and in assessing CD33 status prior to treatment with Mylotarg. Until now no anti-CD33 monoclonal antibodies were available for use in paraffin embedded tissue.
We report on the efficacy of a new monoclonal antibody PWS44 (Novocastra, UK) which recognises CD33 expressed in paraffin embedded tissue. Using PWS44 we examined CD33 expression in paraffin embedded bone marrow trephine biopsies from 25 patients with AML and compared this to the CD33 flow cytometry findings.
PWS44 immunohistochemistry was positive in all cases of AML, although the staining intensity was variable. In 3 patients reported as CD33 negative by flow cytometry, PWS44 staining was strongly positive.
These results show that PWS44 is able to identify CD33+ve cells in AML in paraffin embedded tissue, and that cases reported as negative with flow cytometry may show CD33 expression in paraffin section. This is a potentially significant observation considering the importance of assessing CD33 status in patients prior to treatment with Mylotarg.

P61

Bone Marrow Trephine Findings in AML with Multi-lineage Dysplasia

{P} N Ngo, IA Lampert, KN Naresh
Hammersmith Hospital & Imperial College, London, United Kingdom

Objective: To identify characteristic features in bone marrow trephines of acute myeloid leukaemia (AML) with multi-lineage dysplasia.
Patients and Methods: A retrospective analysis of the bone marrow trephine features was performed in 14 patients. The cases were subdivided into two groups: (a) AML with background multilineage dysplasia (AML-MD) (11), (b) Myelodysplastic syndrome which subsequently transformed to AML (MD-AML) (3).
Results: 9/11 AML-MD patients had hypercellular marrow and increased proportion of precursor cells could be identified on morphology and CD34/HLADR/CD117 immunostains. Four cases showed trilineage dysplasia and five cases showed bilineage dysplasia. Most had increased reticulin. Megakaryocytes were increased in number in 7 cases and were dysplastic in all cases but one (marked in seven). The three MD-AML cases show frank features of AML with increased numbers of precursor cells with appropriate immunophenotype and all of them showed persistent dysmegakaryopoiesis, and increased numbers of megakaryocytes, apoptoses and reticulin.
Conclusion: Assessment of an increased proportion of immature myeloid cells by their morphology and immunophenotype and appreciation of dysplastic features in the haemopoeitic lineages based on morphological features can aid in the diagnosis of AML with multilineage dysplasia in bone marrow trephine sections.

P62

Bone Marrow Trephine Findings in CMML

{P} N Ngo, IA Lampert, KN Naresh
Hammersmith Hospital & Imperial College, London, United Kingdom

Objective: To identify characteristic features in bone marrow trephines of CMML (Chronic Myelomonocytic Leukaemia).
Patients and Methods: A retrospective analysis of the bone marrow trephine features was performed in 22 patients. All patients had a sustained raise in peripheral blood monocyte count of over $1X10^9$/L.
Results: The average age of the patients is 67.7yr. The mean peripheral blood monocyte count was 5.84 $x10^9$/L. All the CMML patients had hypercellular marrow with an abnormally high M:E ratio (in excess of 4 in most cases). 15 of the cases had noticeably increased numbers of monocytes on H&E staining, while in the other 7 cases the monocytes were identified by CD68 (PGM-1) staining. The CD34 count was marginally elevated. CMML2 was diagnosed in two cases where the CD34 count was 5% and 10%. The number of megakaryocytes were increased in 11 cases and dysmegakaryopoiesis was present in 14 cases. Most (20 cases) had increased reticulin.
Conclusion: Appreciation of hypercellularity, high M:E ratio, increased proportion of monocytic cells (either on morphology or aided by CD68 (PGM-1) and presence of dysmegakaryopoiesis can aid in the diagnosis of CMML in bone marrow trephine sections.

P63

Analysis of vitrectomy and chorioretinal biopsies in the diagnosis of primary intraocular lymphoma

{P} S. E. Coupland, H. Stein
[1]*University of Liverpool, Liverpool, United Kingdom,* [2]*Charite University Medicine, Berlin, Germany*

Primary intraocular lymphoma (PIOL) is an aggressive lymphoma difficult to diagnose clinically and histopathologically. We evaluated the histopathological diagnoses established following vitrectomy and chorioretinal biopsy in patients with clinically-suspected PIOL.
Evaluated were 125 consecutive diagnostic vitrectomies and 15 chorioretinal biopsies from 107 patients. All specimens were examined using conventional and immunohistological stains, and IgH-PCR. The clinical data were collected and compared.
The 107 patients comprised 67 women and 40 men, with mean age of 62 years. Most vitrectomies were diagnosed with "reactive inflammation", but 22 (18%) as "malignant lymphoma". Chorioretinal biopsies led to diagnoses of PIOL in 12 patients, and of 3 reactive lesions. 20/22 malignant lymphomas were diffuse large B-cell lymphoma; one, PIOL-T-cell type, and another, a choroidal MALT lymphoma. Comparison of diagnoses with follow-up resulted in concordance in 96% cases and "false negative" diagnoses in 4%. The PIOL patients were treated with radiotherapy, chemotherapy or both. At follow-up, 9/22 patients had CNS manifestations, and 11 had died.
PIOL diagnostic is often difficult, requiring experienced interpretation of cytology, immunocytology and IgH-PCR. Although cytological examination of vitreous aspirates remains the first-line diagnostic procedure, adjunct methods and additional chorioretinal biopsies increase the chance of diagnosing or excluding a PIOL.

P64

FOLLICULAR LYMPHOMA GRADE 3: A CONTINUUM OR TWO DIFFERENT ENTITIES?

{P} C Brodie[2], D Horncastle[1], J Mehta[1], K Naresh[1]
[1]*Department of Histopathology, Hammersmith Hospital, London, United Kingdom,* [2]*Department of Histopathology, Charing Cross Hospital, London, United Kingdom*

Introduction: Follicular lymphoma grade 3 (FL3) is a B cell lymphoma, subdivided to FL grade 3a (FL3a) and grade 3b (FL3b) by the presence of centrocytes. The aim of the study is to investigate other differences between FL3a and FL3b.
Methods: A tissue microarray was constructed from paraffin blocks of cases of FL3 accessioned from January 1993 until April 2005 and immunohistochemically stained for CD20, CD3 and CD10, bcl-6, bcl-2, Ki-67, MUM-1, FOX-P1, CDK-2, p53, PKCγ, cyclin D2 and c-myc.
Results: 14 cases of FL3a and 5 of FL3b were retrieved. FL3a had a mean proliferation fraction of 40% and FL3b 65% on Ki-67 staining. The immunohistochemical staining pattern and comparison is shown in table 1 (cases with positive staining in >30% of cells). The difference in expression of FOX-P1 is statistically significant.
Table 1:

	Grade 3a (14)	Grade 3b (5)
CD10	12	2
Bcl-6	13	5
Bcl-2	13	5
MUM-1	7	4
FOXP1	2	4
p53	11	5
PKC-gamma	7	1
Cyclin D2	0	2
c-MYC	5	1

Conclusion: There is a contrast in immunohistochemical profile of FL3a and FL3b, even in this small series. Whether this is biologically or clinically important is unclear.

P65

IMMUNOPHENOTYPIC VARIATION WITHIN CASES OF MULTIPLE MYELOMA

{P} C Brodie[1], D Horncastle[1], C Giles[2], A Rahemtulla[2], K Naresh[1]
[1]*Department of Histopathology, Hammersmith Hospital,, London, United Kingdom,* [2]*Department of Haematology, Hammersmith Hospital, London, United Kingdom*

Introduction: The immunophenotype of multiple myeloma cells resembles normal plasma cells, with frequent expression of CD38, CD138, CD79a and epithelial membrane antigen (EMA) but with aberrant expression of CD56 and cyclin D1. Variation in immunophenotypic profile within cases has not been characterised.
Methods: Multiple myeloma cases with sequential bone marrow biopsies, accessioned by the histopathology department between October 2002 and December 2005, were retrieved. Expression of CD138, kappa, lambda, CD20, CD79a, CD56, cyclin D1 and EMA was recorded for each biopsy. Expression in serial biopsies was compared and analysed with respect to prospectively recorded clinical data including date of relapse, date of progression and status at last follow-up.
Results: 51 cases of multiple myeloma were assessed. All biopsies expressed CD138. Expression of kappa (38) and lambda (13) remained constant in successive biopsies. 21 cases (41%) showed a change in expression of one or more antigen. CD20 expression changed in 4 cases, CD79a changed in 8, CD56 in 3, cyclin D1 in 3 and EMA in 6. There were potentially significant associations between changes in the immunophenotype and disease outcome.
Conclusions: Variability in immunophenotype within cases of multiple myeloma is not an uncommon phenomenon and could have bearing on disease outcome.

P66

T-cell Receptor Gene Rearrangements in Hodgkin's Lymphoma

{P} L Venkatraman[1], MA Catherwood[2], P Kettle[1]
[1]*Royal Victoria Hospital, Belfast Northern Ireland, United Kingdom,* [2]*Belfast City Hospital, Belfast Northern Ireland, United Kingdom*

Introduction: B or T-cell clonality in Classic Hodgkin's lymphoma (CHL) is detected by polymerase chain reaction (PCR) of the microdissected Hodgkin-Reed Sternberg cells (H-RS) but seldom demonstrable by whole tissue DNA PCR. This aids the distinction between CHL, peripheral T-cell lymphoma (PTCL) and T-cell rich B-cell lymphoma.
Patients and methods: We report 3 cases that were morphologically CHL but had clonal TCR gene rearrangements, resulting in diagnostic uncertainty. Case 1 (58yrs, male) stage IIA nodular sclerosing CHL. Case 2 (29 yrs, female) stage IV CHL diagnosed on a lymph node needle aspirate and a bone marrow biopsy. Case 3 (39yrs, female) stage III(2) mixed cellularity CHL noted on preoperative investigations for rectal adenocarcinoma. Cases had predominantly mononuclear LCA-, CD15-CD30+, EBV-, Alk-1- Hodgkin cells. T-cell antigens were not expressed in cases 1 and 2; a proportion of Hodgkin cells in case 3 were CD3+ and CD4+. Whole tissue PCR revealed clonal TCR gamma (case 2) and TCR beta (cases 1 and 3) rearrangements. All received chemotherapy for CHL. Two patients are disease free after a short follow-up. Case 3 transformed to a high grade CD30+ T cell lymphoma 6 months after diagnosis and died 4 months later.
Conclusion: The presence of clonal TCR on whole tissue DNA in H-RS cells suggests a Hodgkin like PTCL rather than CHL

P67

Sudden Unexpected Death in the First Week of Life: Autopsy Series from a Single Specialist Centre

{P} MA Weber, DJ Fowler, N Baxter, MT Ashworth, M Malone, NJ Sebire
UCL Institute of Child Health and Great Ormond Street Hospital for Children, London, United Kingdom

Introduction: Sudden unexpected death in the first week of life (sudden unexpected neonatal death or SUND) shares many features with SUDI but is usually not formally included in the SUDI group, which is limited to post-perinatal deaths. The aim of this study was to review all SUND autopsies performed in a single specialist centre over a 10-year period, from 1996-2005.
Methods: Retrospective analysis of >1,500 consecutively performed post-mortem examinations, all of which were carried out by specialist paediatric pathologists. The autopsies were performed according to a local protocol that included the use of detailed ancillary investigations.
Results: Of 1,516 post-mortem examinations overall, 180 were neonatal deaths in the first week of life, of which 55 (31%) presented as SUND. Almost half (49%) of these were explained following post-mortem examination; the remainder were unexplained, and a third of these were associated with co-sleeping. Of the explained deaths, over 40% were associated with previously undiagnosed congenital abnormalities, with almost all of these due to clinically undetected congenital heart disease. In addition, there were three deaths from unsuspected metabolic disease, including two medium chain acyl-CoA deficiencies. There were no accidental or non-accidental deaths in this age group.
Discussion: There are distinct differences between SUND and SUDI, with significantly more explained deaths in the former. Compared to SUDI, a much higher proportion of SUND are due to congenital abnormalities, whilst the majority of explained SUDI are reported to be infection related.

P68

Causes of Paediatric Death: Results of >1,500 Autopsies from a Single Specialist Centre

{P} MA Weber, I Brooke, MT Ashworth, RA Risdon, M Malone, NJ Sebire
UCL Institute of Child Health and Great Ormond Street Hospital for Children, London, United Kingdom

Introduction: It is now recommended that perinatal and paediatric post-mortem examinations are performed by specialist paediatric pathologists. This is an audit of all paediatric autopsies from a single specialist institution over a 10-year period.
Methods: Retrospective analysis of >1,500 consecutively performed autopsies in a single centre from 1996 to 2005, all of which were carried out by specialist paediatric pathologists to a common protocol.
Results: There were 1,516 post-mortem examinations; excluding stillbirths and abortions, more than 70% were of infants <1 year of age. Overall, there were 987 (65%) coronial autopsies and 529 (35%) consented hospital autopsies. 601 cases presented as sudden and unexpected death in the first year of life, with a further 254 cases of sudden unexpected death in children >1 year of age. Whilst autopsy numbers have risen steadily during the study period, from 129 cases per annum in 1996 to 285 cases in 2005, the percentage of consented hospital post-mortems has decreased to 26% in 2005. Overall, 52% of all non-perinatal coronial deaths were explained by the autopsy findings, whereas the commonest indication for hospital autopsies was congenital abnormalities.
Discussion: The increase in autopsy numbers in this centre is likely to be a reflection of the current national trend to ensure that all paediatric autopsies are performed in a specialist unit. The high proportion of sudden and unexpected deaths, and of congenital abnormalities, highlights the need of a specialist pathology service for the investigation of paediatric deaths.

P69

Rib Fractures Identified at Post-Mortem Examination in Infancy: Experience from a Single Centre

{P} MA Weber, RA Risdon, C Hall, M Malone, NJ Sebire
UCL Institute of Child Health and Great Ormond Street Hospital for Children, London, United Kingdom

Introduction: Rib fractures may be associated with non-accidental injury (NAI) in infancy, but the possible significance of fresh fractures in relation to resuscitation remains undetermined. At post-mortem examination, the detection and confirmation of rib fractures is therefore important in this patient group. At our centre we have had a policy of performing radiological skeletal surveys and specific post-mortem examination of the ribs for this purpose.
Methods: As part of a larger review of paediatric post-mortem examinations, all cases presenting with sudden unexpected death in infancy (SUDI) were identified, and the anonymised records were searched to identify all cases in which rib fractures were recorded.
Results: Over a 10-year period, 546 post-mortem examinations were performed for the indication of SUDI, including 96 forensic autopsies. Rib fractures were identified in 25 (5%) of cases. In 15 (3%) these were healing or healed fractures, and of these, 8 (53%) demonstrated additional features consistent with death due to NAI. In 10 (2%) there were only fresh rib fractures with no surrounding tissue reaction histologically; in 7 (70%) of these there were no other injuries, suggesting resuscitation related trauma. Compared to healed/healing fractures, which were apparent on skeletal survey in 93%, fresh rib fractures were only detected in 44%.
Discussion: Rib fractures are uncommon in infancy and may indicate NAI, particularly when healed or healing. Fresh rib fractures may be missed on skeletal survey, but can be reliably detected at post-mortem examination following stripping of the pleura and detailed examination of each rib. Fractures should be examined histologically when present to aid in confirmation of timing in relation to death.

P70

Myocarditis Presenting as Sudden Unexpected Death in Childhood: An Autopsy Series

{P} MA Weber, DJ Fowler, MT Ashworth, M Malone, NJ Sebire
UCL Institute of Child Health and Great Ormond Street Hospital for Children, London, United Kingdom

Introduction: Myocarditis is a recognised cause of cardiac failure in childhood, often presenting with non-specific features of 'cardiomyopathy'. The frequency of myocarditis as a cause of sudden unexpected death across the paediatric age range is uncertain.
Methods: A structured review of the results of all autopsies carried out in a single paediatric centre over a 10-year period, including the results of all investigations performed as part of the centre's policy for the post-mortem investigation of paediatric deaths.
Results: During the study period there were 1,516 autopsies carried out in children aged 0-18 years. The final cause of death was histologically proven myocarditis in 28 cases, of which 20 (71%) presented as sudden unexpected death (age range 19 days to 15 years, median 14 months). In 10 of the 20 sudden deaths there were macroscopic abnormalities, including a dilated and/or enlarged heart in five children. In contrast, in the other 10 cases the post-mortem examination was macroscopically unremarkable and myocarditis was only revealed on routine histological examination of the heart. In only four cases (20%) were viral particles isolated, which included parvovirus in two, and enterovirus in the other two. The histological features were similar in all cases, with an interstitial inflammatory cell infiltrate, predominantly lymphocytic, with focal myocyte necrosis and interstitial oedema.
Discussion: Histologically proven myocarditis is an uncommon cause of sudden unexpected death in childhood, representing 2.4% of cases in this unselected series. The peak age is <1 year, and in half of the cases there may no macroscopic abnormalities, the diagnosis requiring routine histological examination.

P71

The Frequency and Significance of Post-Mortem Identification of Haemosiderin-Laden Macrophages in Infant Lungs

{P} MA Weber, MT Ashworth, RA Risdon, M Malone, NJ Sebire
UCL Institute of Child Health and Great Ormond Street Hospital for Children, London, United Kingdom

Introduction: The presence of haemosiderin-laden macrophages (HLMs) in lung sections represents evidence of previous pulmonary haemorrhage. It has been suggested that the presence of such HLMs in infant lungs at post-mortem examination may be an indicator of asphyxia.
Methods: A search was carried out of a database of anonymised paediatric post-mortems to identify all cases in whom HLMs were identified on routine histopathological examination of Perls' stained lung sections, and the basic clinical details and other post-mortem findings of these cases were reviewed.
Results: During the study period (1996 to 2005 inclusive), there were 965 infant autopsies (<1 year of age). Of these, 50 (5%) demonstrated the presence of HLMs. The age distribution of this group was 1 day to 12 months (median 3.4 months). In 12 infants (24%), there was evidence of either fatal non-accidental injury (NAI) or of previous NAI, some showing healed or healing rib fractures. In a further 28 infants (56%), there were features in the clinical history or on pathological examination to explain the presence of HLMs; these included prematurity with hyaline membrane disease or chronic lung disease, evidence of pneumonia or other severe infection, or congenital heart disease. In 10 infants (20%), there were no significant findings of note, and there were no suspicious circumstances; 4 of these deaths were co-sleeping associated.
Conclusion: Pulmonary HLMs are histologically identified in approximately 5% of infant post-mortems, the majority of which are associated with no suspicious circumstances, although in up to a quarter of cases HLMs may represent a marker of non-accidental injury.

P72

Histological Examination of the Macroscopically Normal Brain is of Limited Value in Determining the Cause of Death in SUDI

{P} MA Weber, TS Jacques, B Harding, M Malone, NJ Sebire
UCL Institute of Child Health and Great Ormond Street Hospital for Children, London, United Kingdom

Introduction: Current autopsy protocols for the investigation of sudden unexpected death in infancy (SUDI) recommend detailed neuropathological examination. This study aims to establish whether positive findings on histological examination of the brain determine the cause of death in SUDI post-mortem examinations.
Methods: Retrospective analysis of >1,500 consecutively performed paediatric post-mortem examinations in a single specialist centre, from 1996 to 2005. SUDI was defined as death of an infant aged 7 to 365 days that was sudden and unexpected.
Results: The brain was examined in 96% of the 546 infants that presented as SUDI (including formal neuropathological examination by a paediatric neuropathologist in 266 infants). One third of SUDI deaths were explained after completion of the autopsy. 37 of these were due to neuropathological causes, including head injury, meningitis and intracranial haemorrhage; in 33 (89%) the diagnostic abnormality was suspected on macroscopic examination. In four the diagnosis relied solely on histological examination, but in three of these the clinical features were suggestive of a possible underlying neurological condition, which elicited formal neuropathological examination. One case of meningitis was unsuspected until microscopic examination.
Discussion: The majority of SUDI in which neuropathological examination determined the cause of death were identified on history or on macroscopic examination. Whilst thorough neuropathological examination may provide important information about possible mechanisms of SUDI, such examinations rarely provide the cause of death in this age group in the presence of a macroscopically normal brain.

P73

The Contribution of Formal Neuropathological Examination in Paediatric Autopsies

{P} MA Weber, TS Jacques, B Harding, M Malone, NJ Sebire
UCL Institute of Child Health and Great Ormond Street Hospital for Children, London, United Kingdom

Introduction: In the UK there are only a small number of paediatric institutions that offer a specialist paediatric neuropathological autopsy service. This is a review of the role of formal neuropathology in paediatric post-mortem examinations.
Methods: Retrospective analysis of >1,500 post-mortem examinations performed over a 10-year period, from 1996 to 2005, in a single paediatric specialist centre; those cases referred for formal specialist neuropathological examination of the brain were included in this study.
Results: There were 1,516 paediatric post-mortem examinations, of which the majority included some form of examination of the brain. Of these, 651 (53%) were examined by a paediatric neuropathologist, either for specific neurological indications, or as part of the local autopsy protocol for sudden and unexpected deaths. Overall, there were positive findings in 55% of cases. Restricting cases to those that were performed for possible neurological indications, including forensic autopsies, abnormal findings were demonstrated in 87% of cases. Diagnoses ranged from complex congenital malformations to hypoxic-ischaemic encephalopathy, head injury and rare mitochondrial encephalopathies.
Discussion: Specialist paediatric neuropathological examination at autopsy yields positive findings in the majority of cases where there is a clinical history suggestive of possible neurological disease. Neuropathological services play an important role in the investigation of paediatric deaths.

P74

Challenges of the New Coroners (Amendment) Rules 2005: Experience at a Specialist Paediatric Pathology Centre

{P} MA Weber, N Baxter, MT Ashworth, M Malone, NJ Sebire
UCL Institute of Child Health and Great Ormond Street Hospital for Children, London, United Kingdom

Introduction: With the implementation of the Coroners (Amendment) Rules 2005 on 1 June 2005, relatives of the deceased must consent to one of three options concerning the handling of tissue taken during the post-mortem examination: 1) disposal of the tissue by the pathologist, 2) returning the material to the relatives, or 3) retention of the tissue for research or other purposes. It is the duty of the coroner to inform the pathologist of the relatives' wishes, usually by means of a signed coroner's consent form, within a specified time period.
Methods: Retrospective audit of the coroners' consent forms of all coronial paediatric autopsies performed in a single institution from 1 June 2005 to 31 May 2006.
Results: Of 209 coronial autopsies, only 38 (18%) had submitted a form in accordance with the new rules. The forms varied widely between different coroners, with up to a third of forms lacking an option for tissue disposal, and almost one quarter of forms without an option for tissue retention or returning tissue to the family. Of the 29 forms in which relatives were given an option for tissue retention, only 21 (72%) specifically addressed consent for research, and of these, relatives consented to research in only 14 (67%). Whilst some forms were confusing, even contradictory, the majority (82%) also failed to distinguish between blocks and slides, and other tissue samples or organs.
Discussion: The new Coroners (Amendment) Rules are variably interpreted by different coroners, resulting in substandard consent forms. We recommend that the coroners' consent forms are drawn up in consultation with the Royal College of Pathologists, that a single standardised form is used by all coroners, and that coroners' officers receive appropriate training in taking consent.

P75

Needle Core Biopsies for the Pathological Investigation of Paediatric Tumours: A Single Centre Experience

S Gibson, D Rampling, {P} MA Weber, M Malone, DJ Roebuck, NJ Sebire
Great Ormond Street Hospital for Children, London, United Kingdom

Introduction: The use of image guided, minimally invasive, needle core biopsies for the primary diagnostic investigation of paediatric tumours is becoming increasingly important. One potential argument against the use of such minimal sampling has been the assumption that insufficient tissue will be available for the full range of investigations required.
Methods: It has been our departmental policy to handle all tumour core biopsies according to a predefined protocol. We retrospectively report the results of such a protocol on 100 unselected consecutive needle core biopsies obtained during 2005-2006.
Results: Of 100 consecutive biopsies for the assessment of paediatric tumours, adequate tissue was obtained for histopathological assessment in 100%, imprint preparations for fluorescence in-situ hybridisation in 100%, snap frozen tissue for storage in 96%, tissue for immediate molecular analysis stored in RNA protection medium in 92%, sufficient tissue for tumour banking in 88%, and tissue was submitted for cytogenetic analysis in 76%.
Discussion: The use of image guided, needle core biopsies for the assessment of paediatric tumours, when performed by experienced interventional radiologists in conjunction with specialist pathology departments optimised for dealing with small fresh specimens, can allow a full range of diagnostic and prognostic histopathological and molecular assessments to be performed with minimal patient morbidity.

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Needle Core Biopsy Diagnosis of Neuroblastic Tumours in Childhood: A Single Centre Experience

DJ Roebuck, D Rampling, S Gibson, {P} MA Weber, J Anderson, NJ Sebire
Great Ormond Street Hospital for Children, London, United Kingdom

Introduction: Traditionally, histopathological diagnosis of paediatric tumours has been on the basis of open biopsies. However, increasingly, minimally invasive image-guided needle core biopsies are being performed for this indication.
Methods: We retrospectively reviewed the outcomes of consecutive unselected needle core biopsies carried out at our paediatric centre with regard to clinical and histopathological features.
Results: There were 110 separate needle biopsy procedures carried out for suspected neuroblastic tumours of 121 lesions in 105 children aged 0-12 years (median 2.6 years) from a range of anatomical sites, predominantly (50%) abdomen / retroperitoneum. Sufficient tissue was initially obtained for diagnostic pathological assessment in 118 (98%) cases. The final diagnosis from needle biopsy was neuroblastic tumour in 100 (83%), other malignant tumours in 13 (11%), other benign lesions in 5 (4%), and 3 (2%) were non-diagnostic; of these 3, 2 had a rebiopsy demonstrating neuroblastoma, and in one the presumed lesion has spontaneously resolved. In 4 cases, needle biopsy revealed ganglioneuromatous elements only, and the final resection diagnosis was nodular ganglioneuroblastoma. There were no significant clinical complications. The overall diagnostic accuracy rate, including the rebiopsied cases, was 99%.
Discussion: Minimally invasive needle core biopsy is a safe approach to the diagnosis of neuroblastic tumours in children and can provide sufficient material for pathological diagnosis. As suggested in current guidelines, ganglioneuroma and ganglioneuroblastoma cannot be reliably distinguished on needle biopsy alone.

P77

Solid Tumour Cytogenetic Analysis of Paediatric Tumours: Results of Resections versus Needle Core Biopsies

H Kempski, N Austin, S Chatters, J Chalker, {P} MA Weber, DJ Roebuck, NJ Sebire
Great Ormond Street Hospital for Children, London, United Kingdom

Introduction: Paediatric tumours are associated with a range of specific gene fusion transcripts which were initially identified using cytogenetic studies. Routine cytogenetic analysis is a major component of the evaluation of haematological malignancies in this age group but solid tumour cytogenetics is less commonly performed.
Methods: During the last 2+ years we have submitted all solid tumours received fresh in the laboratory and with sufficient material, for routine cytogenetic studies. This study retrospectively reviews the results of this policy.
Results: 223 specimens were submitted for cytogenetic analysis, including 117 resections (RS) and 106 needle biopsies (NB). The success rate for culture and karyotype was 85 (80%) for NB and 103 (88%) for RS. Of the 125 samples fully analysed to date, significant abnormal karyotypes were identified in 38 (30%), including 19 (32%) NB's and 19 (29%) RS's.
Discussion: This study has demonstrated that firstly, routine cytogenetic studies are feasible from paediatric solid tumour specimens with an overall culture success rate for cytogenetic analysis of around 80%. Secondly, the success rate and abnormality rate is similar for specimens derived from open biopsies or resections compared to needle core biopsies. Cytogenetic studies should be considered a routine component of the evaluation of paediatric solid tumours even in cases only sampled by needle core biopsies, since around one third will yield potentially important abnormal results.

P78

Histological Sampling to Determine the Cause of Death in SUDI Post-Mortem Examinations: A New Minimum Dataset?

{P} MA Weber, DJ Fowler, M Malone, NJ Sebire
UCL Institute of Child Health and Great Ormond Street Hospital for Children, London, United Kingdom

Introduction: The Kennedy protocol recommends the sampling of a minimum number of tissue blocks in the autopsy investigation of sudden unexpected death in infancy (SUDI), which, in addition to neuropathological examination of the brain, also include lungs, heart, thymus, pancreas, liver, spleen, lymph node, adrenal glands, kidneys, bone marrow and muscle, as well as any macroscopic lesion. The aim of this study is to determine the frequency with which histological examination alone determines the final cause of death.
Methods: Retrospective analysis of >1,500 consecutively performed post-mortem examinations from a single centre, carried out by specialist paediatric pathologists. SUDI was defined as death of an infant aged 7 to 365 days that was sudden and unexpected. The neuropathological causes of death were excluded from this analysis.
Results: Of the 546 SUDI, 180 (33%) were explained by the autopsy findings, of which 143 died from a non-neuropathological cause of death. Of these, histological examination directly determined the final cause of death in 91 (64%) cases, viz. of the lungs in 73 (51%), the heart in 13 (9%), the liver in 4 (3%), and the kidneys in one infant. Microscopic examination of other organs did not directly determine the cause of death in any case in this series.
Discussion: Whilst comprehensive tissue sampling for histological investigation may contribute to our understanding of the pathophysiology of SUDI, these findings suggest that extensive routine sampling of all organs may not be justified by the available evidence for the purposes of determining a cause of death for HM Coroner.

P79

Gigantic recurrent abdominal desmoid tumour: A case report and review of literature

{P} E Rakha, M Kandil
Histopathology Department, Menoufia, Egypt

Deeply seated fibromatosis or desmoid tumour (DT) is a rare entity characterized by benign proliferation of fibroblasts. Although non-malignant, this tumour can be life-threatening due to its invasive property and high recurrence rate. We report a unique case of a huge recurrent abdominal DT (36 cm in diameter, 25 kg in weight) that caused pressure necrosis and sloughing of the overlying anterior abdominal wall and produced a large fungating mass protruding outside the abdomen (7 kg in weight). Surgical debulking of the tumour was performed to remove the fungating mass and part of the intra-abdominal tumour as a palliative measure. However, the remaining tumour tissues continued to grow rapidly irrespective of the postoperative adjuvant therapy. Radical surgical removal of the tumour, although hazardous, was considered as the only line of treatment to save her life. Surgical removal of the tumour was successful and the procedure was followed by an excellent clinical recovery. The patient is still alive with no evidence of recurrent disease after a 6-year follow-up. This case demonstrates the ability of DT to grow rapidly, achieving a huge size that may endanger patients' life. Surgical removal of DT is the treatment mainstay regardless of the size of the tumour.

P80

Metastatic Malignancy Mimicked by Subcutaneous Injection of Mistletoe Extract

{P} AI Finall[1], SA McIntosh[2], WD Thompson[2]
[1]University Hospital of Wales, Cardiff, United Kingdom, [2]Aberdeen Royal Infirmary, Aberdeen, United Kingdom

A case of a 61-year old woman with a five-year history of follicular lymphoma that underwent wide local excision of a well differentiated tubular breast carcinoma in mid 2005 is presented. She complained of a tender, anterior abdominal wall mass to her surgeon during follow-up. This was removed with the concern that it represented recurrence of her lymphoma or a metastatic deposit of breast carcinoma.
The histology showed a septal and lobular panniculitis with a heavy infiltrate of eosinophils. In addition, peri-vascular follicular lymphoid aggregates and vasculitis were seen. The features were similar to those seen in lupus panniculitits with no evidence of malignancy. Investigations for SLE were negative. However, after significant diagnostic deliberation, the patient volunteered a twelve month history of subcutaneous mistletoe injections in the region of excision.
A review of the literature revealed two reports of the histological features of mistletoe-induced inflammation, which we compare with our case.
Subcutaneous injection of aqueous extract of mistletoe is a commonly used adjunct in central European oncology practice, but is less often used in Britain. This case highlights the diagnostic difficulty that can arise when clinicians and pathologists are unaware of their patients' use of alternative therapies.

P81

UNUSUAL SITES TO GO FOR A LEIOMYOSARCOMA

{P} A Naveed, B Benatar, N Shaath
Tameside General Hospital, Ashton, Manchester, United Kingdom

Leiomyosarcoma is a malignant neoplasm of smooth muscle. It accounts for 10 to 20% of the soft tissue sarcoma. It occurs in adults in fifth to seventh decades affecting women more than men. Most common sites are extremities. Metastases are usually to lung, liver, brain, and bone. Fifty percent of the cases eventually metastasise and the 5 year survival rate is 60-50%

We present an interesting case of a 65 years old lady who was diagnosed with leiomyosarcoma of femur and was treated with surgery and chemotherapy. She remained disease free for several years when she developed metastatic disease in vertebrae and iliac crest. She latter on developed anaemia and was found to have nodules in stomach and the duodenum. These nodules on biopsy proved to be metastases from the primary leiomyosarcoma. She then developed changes in her voice and a solitary nodule in her thyroid, which again was the metastatic sarcoma on cytological examination.

We will present case history and literature review of this unusual case.

P82

EMP3 over-expression is associated with oligodendroglial tumours retaining chromosome arms 1; and 19q

{P} HK Ng, K Li, JCS Pang
The Chinese University of Hong Kong, Hong Kong, China

The epithelial membrane protein 3 (EMP3) gene, located on chromosome 19q13, has been implicated as a candidate tumor suppressor gene (TSG) in neuroblastomas and gliomas. The aim of this study was to investigate whether EMP3 is involved in oligodendroglial tumors (OTs), which frequently carry combined chromosomes 1p and 19q deletion. We first investigated the transcript level of EMP3 in a cohort of 57 OTs by quantitative real-time RT-PCR. Our results showed that 10 (18%) tumors had reduced EMP3 expression level compared to normal brains. Six of these tumors carried chromosome 19q13 deletion, but no statistical correlation was found between the two parameters. Intriguingly, a similar proportion (11 of 57, 19%) of tumors displayed EMP3 overexpression, with 8 of them having transcript level >10-fold higher than normal brain. All 11 OTs retained chromosomes 1p36 and 19q13 and a significant association was found between EMP3 overexpression and balanced chromosomes 1p36 and 19q13 ($p=0.004$). The methylation status of EMP3 was evaluated by bisulfite sequencing in 29 OTs with diverse expression levels. All tumors except 3 showed aberrant methylation of EMP3 and no correlation was observed between transcript level and methylation status, suggesting that methylation alone does not mediate transcriptional down-regulation of EMP3 in OTs. In conclusion, our study demonstrates that EMP3 overexpression is involved in OTs retaining chromosomes 1p and 19q and does not support EMP3 as the target TSG on chromosome 19q13 in OTs.

Abstracts

Oral

O1

$Apc^{+/1310T}$ Mice Develop Early-Onset, Severe Gastrointestinal Adenomas

{P} MG Deheragoda[1], P Pollard[2], E Nye[3], P Seedhar[1], NA Wright[1], I Tomlinson[1]
[1]Histopathology Unit, London Research Institute, Cancer Research UK, London, United Kingdom, [2]Molecular and Population Genetics Unit, London Research Institute, Cancer Research UK, London, United Kingdom, [3]Experimantal Pathology Unit, London Research Institute, Cancer Research UK, London, United Kingdom

Individuals with familial adenomatous polyposis (FAP) develop multiple colorectal adenomas, gastric and duodenal polyps and extra-intestinal manifestations. FAP occurs in patients with germline mutations in the adenomatous polyposis coli (*APC*) gene. The truncating APC-1309ΔAAAGA mutation is associated with a particuarly severe FAP phenotype Therefore, using embryonic stem (ES) cell targeting and homologous recombination, we have generated a novel murine model, $Apc^{+/1310T}$, that is analogous to the human APC-1309ΔAAAGA mutation. We report that $Apc^{+/1310T}$ mice express a truncated Apc protein, and present with early onset adenoma development in the stomach, large and small bowel. We present phenotypic and molecular analysis of Apc^{+1310T} which is more severe than the existing Apc mouse models, and will provide opportunity to study effects of specific germline *Apc* mutations on wnt signalling and gastrointestinal tumourigenesis.

O2

Expression of CK17, CK15, CA15.3, ER-α, ER-β1 and ER-β2 in cutaneous adnexal tumours

{P} Y Alizadeh, IH Chaudhry, A Shaaban
Department of Pathology, Leeds General Infirmary, Leeds., Leeds, United Kingdom

Cutaneous appendageal tumours (AT) can pose a diagnostic challenge even to experienced pathologists. Our aim was to investigate the expression of novel putative follicular differentiation markers and sex hormone receptors in ATs.
Methods and materials: Benign and malignant ATs (n=31) with classical histological features, diagnosed between 2000 and 2006, in the department of histopathology at Leeds General Infirmary, were selected, reviewed and labelled by a standard immunohistochemistry using specific antibodies. A series of basal cell carcinomas (n=5) and squamous cell carcinomas (n=6) were included for comparison. The sections were reviewed and scored independently by 2 pathologists.
Results: All AT subtypes expressed ER-β1 and ER-β2; the proportion and intensity of staining greater in the former. ER-α expression was negative in all cases. All follicular tumours expressed CK17 strongly (10/10). The staining in eccrine tumours (5/15) and sebaceous tumours (3/5) was weak and patchy. Expression of CK15 and CA15.3 proved inconclusive.
Conclusion: We show for the first time that ER-β1 and ER-β2 are expressed in a range of skin Ats, which may relate to tumour pathogenesis. CK17 has greater specificity and sensitivity for follicular tumours over eccrine/sebaceous neoplasms and thus may play an important role in the routine diagnostic setting.

O3

Clinical Diagnosis of Melanoma – Sensitivity and Specificity

{P} BT Eden-Green, J Chow
St George's, University of London, London, United Kingdom

Background. The incidence of malignant melanoma is increasing in the UK, with significant increases in mortality. The clinical diagnosis can be difficult, and delays in diagnosis result in poorer patient prognosis. Recent national guidelines have suggested that audits of clinical diagnosis should be carried out, comparing the clinical against the histopathological diagnosis.
Method. The records for all histopathologically identified primary melanomas and naevi excised during 2005 at the Trust were analysed. The clinical diagnosis for each lesion was recorded, alongside information on the microstage of the melanoma, the specialty that carried out the diagnosis, and information about the patient.
Results. 106 primary malignant melanomas were identified at the Trust in 2005. Sensitivity of the clinical diagnosis was 73%, specificity 93% and positive predictive value 72%. Comparisons between specialties revealed that there was no significant difference in the sensitivity of diagnosis between plastic surgeons and dermatologists for the earliest (microstage pT1s and pT1a) lesions.
Conclusions. Sensitivity and specificity of diagnosis is in line with other centres. There are currently no national targets for sensitivity and specificity of clinical diagnosis, however audits like this are useful to monitor diagnostic accuracy at the Trust over time, and to compare with other centres.

O4

IgG4 Immunostaining of Pancreatic and Extrapancreatic Tissue in the Diagnosis of Autoimmune Pancreatitis

{P} MG Deheragoda[1], NI Church[2], M Rodriguez-Justo[1], P Munson[1], N Sandanayake[2], EW Seward[2], K Miller[1], M Novelli[1], S Pereira[2], ARW Hatfield[2], GJM Webster[2]
[1]Department of Pathology, University College Hospital, London, United Kingdom, [2]Department of Gastroenterology, University College Hospital, London, United Kingdom

Autoimmune pancreatitis (AIP) often presents with a pancreatic mass, biliary and pancreatic strictures, an appearance that mimics pancreatic malignancy. Diagnosis of this disease entity is crucial to allow effective therapy with steroids and avoid unnecessary surgery.
This disease is multisystemic. However, all current diagnostic criteria rely on clinical, radiological and pathological appearances in the pancreatic system for a definitive diagnosis. Percutaneous pancreatic biopsy carries a 4% adverse risk, so finding a means of diagnosing this entity without resort to pancreatic biopsy is desirable.
We present a series of 11 patients in whom a diagnosis of autoimmune pancreatitis was suspected on clinical and radiological grounds. 17 biopsies (13 extrapancreatic biopsies) and 3 gallbladder resections were assessed. All tissue was assessed with H and E staining and use of IgG4 immunostaining. >10 IgG4 positive plasma cells/HPF was considered positive for a diagnosis of AIP. Organ specific negative control tissue contained <3 IgG4 positive plasma cells/HPF.
The use of IgG4 immunostaining enabled a diagnosis of AIP in 10/11 patients, 7/11 patients were definitively diagnosed with AIP using extrapancreatic tissue. This study demonstrates the potential use of IgG4 immunostaining of pancreatic and extrapancreatic biopsy tissue in the diagnosis of AIP.

O5

Immunohistochemical Study of Plasmacytoid Dendritic Cells in Lymph Nodes Draining Breast Cancer by BDCA2 and CD123 Antibodies

{P} R Ahmad[1], H El-Hassi[1], M Burke[2], H Singhal[2], SC Knight[1], NM Aqel[2]

[1]Antigen Presentation Research Group, Faculty of Medicine, Imperial College London, Northwick Park and St Marks Campus, London, United Kingdom, [2]Northwick Park Hospital, London, United Kingdom

Background. Plasmacytoid dendritic cells (PDC) are a distinct subset of antigen presenting cells which are major producers of Interferon type-1 and contribute to development of immune response. These cells are known as "plasmacytoid monocytes, PM" in tissue sections. They are found in groups in paracoretex of reactive lymph nodes (LN), close to high endothelial venules (HEV). PM are characterised by their bright expression of CD123 (IL-3 alpha-chain receptor); an important cytokine for PM survival, proliferation and differentiation) and by their specific expression, in frozen section, of an antibody reactive with blood dendritic cells (BDCA2).
Methods. We examined PM in frozen sections of 40 axillary LN draining breast carcinoma by using two antibodies, namely BDCA2 and CD123. The antigen localisation was performed using biotinylated detection system.
Results. PM stained strongly for BDCA-2 and CD123 in frozen sections of all LN; they were found scattered discretely in LN paracortex and in groups, close to HEV. A few PM were found in subcapsular LN sinus.
Conclusions. **1.** Identification of PM in LN paracortex, discretely and in groups close to HEV, confirms previous data on the localisation of these cells in reactive lymph nodes. **2.** PM were observed in LN subcapsular sinus; this may suggest that some PM migrate to LNs through the afferent lymphatics. **3.** Consistent demonstration of PM in LN draining breast cancer suggests a possible role for PM in mounting an immune response towards cancer cells **4.** BDCA-2 was found to be highly specific to PM; this can facilitate the use of this antibody to isolate a pure population of PM in flowcytometric studies.

O6

Richter's Transformation of Chronic Lymphocytic Leukaemia

{P} MA Catherwood[1], L Venkatraman[2], M El-Agnaf[3], TCM Morris[1]

[1]Belfast City Hospital, Belfast Northern Ireland, United Kingdom, [2]Royal Victoria Hospital, Belfast Northern Ireland, United Kingdom, [3]Ulster Hospital, Dundonald Northern Ireland, United Kingdom

Background: Richter's transformation of CLL into high grade lymphoma occurs in up to 10% of cases. In CLL, unmutated IgVH status implies a poor prognosis in comparison to mutated IgVH genes. The mutational status and cytogenetic aberrations of CLL's that transform to Richter's syndrome are not well understood.
Purpose: To determine the mutational status and cytogenetic abnormalities in CLL patients with Richter's transformation.
Methods: BIOMED-2 protocol and primers were employed for determining IgVH mutational status and gene usage. Mutations were identified by comparison with the germline sequence using IMGT and Ig Blast databases. Chromosomal abnormalities were determined using interphase fluorescent in situ hybridisation (FISH) and commercial CLL set FISH probes.
Results: Of the 270 CLL patients studied, 6 patients transformed to high grade B-cell lymphoma (3 diffuse large B-cell lymphoma, 2 prolymphocytic leukaemia and 1 classical Hodgkin's lymphoma). Two of these patients had mutated VH genes, while the remaining 4 possessed unmutated IgVH genes. On FISH analysis the 2 mutated cases showed no detectable abnormality (n=2). The unmutated sub-group consisted of: biallelic del 13q14 (n=1), del 11q23 (n=1), trisomy 12 (n=1) and del 17p13 (n=1).
Conclusions: These results suggest that Richter's transformation may occur irrespective of mutational status and chromosomal aberrations and may be due to other factors including treatment related immunosupression.

O7

Expression and Regulation of Hypoxia-Inducible Factor (HIF) in Osteoclasts and GCTB

{P} HJ Knowles, NA Athanasou

University of Oxford, Oxford, United Kingdom

The alpha subunit of the transcription factor Hypoxia-Inducible Factor (HIF) is over-expressed in many human cancers where it is commonly associated with poor prognosis and resistance to therapy. Giant cell tumour of bone (GCTB) contains numerous osteoclast-like multinucleated giant cells and a mononuclear component predominantly comprising macrophages and stromal osteoblast-like cells. We have analysed expression of HIF-1α, HIF-2α and the HIF downstream target gene BNIP3 by immunohistochemistry in 12 GCTB. Giant cells were immunoreactive for HIF-2 > HIF-1 with cytoplasmic > nuclear staining. BNIP3 expression generally correlated with that of HIF-1α. A variable proportion of mononuclear stromal cells and macrophages were also positive for all factors. HIF expression was further analysed by Western blot in normal human monocyte-derived osteoclasts and the osteoblastic cell line MG-63. In both cell types the osteoclastogenic factors M-CSF and HGF induced HIF-1α and HIF-2α expression for the period 2-16h post-stimulation. This is the first demonstration of HIF expression in either GCTB or human osteoclasts. Induction of HIF by growth factors that promote osteoclast differentiation / activity and its expression in osteoclasts, osteoblasts and macrophages in vivo suggests a potentially important role for the HIF pathway in osteoclast differentiation and the pathogenesis of GCTB.

O8

Ossification During Distraction Osteogenesis in Patients Fitted with Ilizarov Frames

{P} E Byrne, C Evans, C Hutchinson

University of Manchester, Manchester, United Kingdom

This study aims to find a pattern of ossification in the fracture gap of patients fitted with tibial Ilizarov frames and assess how this pattern varies with time from the operation.
A series of 55 digitised anterior-posterior plain x-ray films from 17 tibias fitted with Ilizarov frames were analysed. The pixel densities from set sections of each fracture gap were obtained using Image J. An increase in pixel density was assumed to be ossification. The results were standardised using a section of tibial cortical bone distant from the fracture gap.
The results show pixel density is greater at the proximal and distal ends of the fracture gap than the centre, this becomes less apparent with time. Pixel density is greater at the medial aspect of the fracture gap than the lateral aspect, this becomes more apparent with time.
We conclude that ossification starts at the proximal and distal ends of the fracture gap progressing toward the centre with time. The medial aspect of the fracture gap ossifies more readily than the lateral aspect, this is seen throughout the process. These findings correlate well with previous animal studies, validating this method as a potentially useful tool in research and clinical practice.

O9

IDIOPATHIC INFANTILE CORONARY ARTERY CALCIFICATION

{P} MN Sheppard[1], N Sabire[2], Y Ho[3]
[1]Dept. of Histopathology, Royal Brompton and Harefield NHS Trust, Imperial College, London, United Kingdom, [2]Dept. of Histopathology, Hospital for Sick Children,Great Ormond Street, London, United Kingdom, [3]Dept of Cardiac Morphology, National Heart and Lung Institute, Imperial College, London, United Kingdom

Idiopathic calcification of coronary arteries is a rare hereditary condition of infancy. Complications include cardiac ischaemia, cardiac failure and systemic hypertension. We present three cases who masqueraded as other cardiac diseases with no indication of the real diagnosis prior to autopsy.
5 month old girl presented with respiratory failure and hypertension who died within 24 hours of admission. All the coronary arteries were thick walled with narrow lumen. The aorta, great vessels and renal arteries also showed thickening of the wall. Histology confirmed calcium in the internal elastic lamina of all vessels.
Female aged 2 months who was diagnosed with a large VSD. She died suddenly prior to surgery and at autopsy the right coronary artery orifice was reduced to a pin hole. The coronary arteries had white patches which were calcified with associated ventricular infarction.
11 year old female presented with cardiac failure and was diagnosed as dilated cardiomyopathy. Two weeks late she died suddenly. Coronary arteries were patent but were firm with calcification and there was ventricular infarction.
This rare condition should always be considered in infants and children resenting with hypertension, cardiac failure or sudden death.

O10

Case report: An unusual case of a primary neuroendocrine tumour of the lung with divergent differentiation presenting with recurrent pneumonia

{P} M Haris[1], S Osborne[2], S Edward[2], L Davidson[2], W Merchant[2], IH Chaudhry[2]
[1]Department of Respiratory Medicine, North Cheshire Hospitals NHS Trust, Warrington, United Kingdom, [2]Department of Pathology, Leeds General Infirmary, Leeds, United Kingdom

We report a case of a 36-year-old man, who presented with 6-month history of recurrent chest infections. Flexible Fibreoptic Bronchoscopy and Positron Emission Tomography (PET) / Computed Tomography (CT) confirmed a soft tissue mass at the inferior aspect of the right hilum, with marked ^{18}F Fluorodeoxyglucose (FDG) uptake in keeping with malignant etiology. The patient underwent resection of the right middle and lower lobe.
Histopathology revealed a lobulated multi-nodular endobronchial tumour composed of aggregates and single ganglion-like cells set in a neural stroma with a fascicular growth pattern. No immature elements were seen. Immunohistochemistry revealed the stromal component to be positive for S100 protein, Neurofilament, and CD56, whilst the ganglion-like cells were positive for Synatophysin, N52 and chromogranin. GFAP, SMA, TTF-1 and desmin were all negative.
The features raise the possibility of a gangliocytic paraganglioma, a ganglioneuroma or composite paraganglioma of the lung. The terminology in the literature is confusing and opens up the debate on how best to classify such lesions.

O11

Co-Ordinate Expression and Prognostic Significance of Nuclear Receptor Co-Regulators and Interleukins in Human Breast Cancer

{P} AR Green, S El-Sheikh, EC Paish, IO Ellis, E Stylianou
University of Nottingham, Nottingham, United Kingdom

We investigated associations between cytokines and steroid receptor co-regulators in breast cancer to identify possible prognostic indicators. Interleukin (IL)-1α, IL-1β, IL-8 and SRC-1/NCOA1, AIB1/NCOA3, SMRT/NCOR2, CBP/p300 expression was assessed using immunohistochemistry in breast carcinomas (n=130) prepared as tissue microarrays. The targets were correlated with each other, clinicopathological variables and patients' outcome.
Associations between the co-ordinate expression of IL-1α, IL-1β, IL-8 and co-regulators in breast cancer were found, particularly with AIB1/NCOA3. Expression of IL-8 was inversely correlated with oestrogen receptor and progesterone receptor. Co-regulators CBP/p300 and SMRT/NCOR2 were positively associated with oestrogen receptor α, β and androgen receptor whilst expression of AIB1/NCOA3 and SRC-1/NCOA1 were associated with estrogen receptor β alone. Both IL-8 and SRC-1/NCOA1 showed a significant positive correlation with a good prognosis whilst SRC-1/NCOA1, SMRT/NCOR2 and CBP/p300 were associated with lower histological grade. There was no association between expression of interleukins 1 or 8 nor co-regulators with patients' outcome or response to endocrine therapy. This study has demonstrated associations between cytokine and nuclear receptor co-regulator expression suggesting a possible molecular cross-talk between these pathways. Interleukins 1 and 8 may compete for the same co-regulators essential to the regulation of transcription of target genes which may be an important molecular mechanism by which breast cancer tumorigenesis is regulated.

O12

ALTERED DNA REPAIR AND RESPONSE PROTEIN EXPRESSION IN NON-INVOLVED CANCER-CONTAINING BREASTS.

{P} AJ Batchelder, RA Walker
University of Leicester, Leicester, United Kingdom

We have previously identified differences in growth regulation and myoepithelial cell function of normal breast from cancer-containing breasts. This study investigated expression of proteins implicated in DNA damage response and repair in histologically normal tissue from cancerous breasts (NTCCB) and age-matched controls, to determine whether there are any differences that could promote breast carcinogenesis.
Expression of ATM, BARD1, BRCA1, HSP27 and HSP70 was determined by immunohistochemistry in 58 NTCCB (cases) and 62 normal tissues from women without cancer (controls). HSP27 expression was significantly greater in the case group ($p=0.001$). Extent of immunostaining for ATM and HSP70 was similar for both groups. BRCA1 staining was greater in NTCCB from women $\leq$39 years but was not statistically significantly different. BARD1 staining in the case group was lower, but also was not statistically significant. Quantitative RT-PCR was used to compare BRCA1 gene and protein expression. Higher gene expression was found in NTCCB, correlating with immunohistochemical studies.
The greater expression of HSP27 may confer a survival advantage to altered cells due to its anti-apoptotic functions, and is further evidence, along with our previous studies, of altered apoptotic regulation in cancer-containing breasts. This may result in an underlying susceptibility to breast tumourigenesis.

O13

Abstract withdrawn

O14

CISH, a simple, robust and cost-efficient test for HER2 status

{P} S Di Palma, N Collins, M Kissin, M Cook
Royal Surrey County Hospital, Guildford, Surrey, United Kingdom

Human epidermal growth factor receptor 2 (HER2) is important in signal transduction in both normal and abnormal cells. HER2 protein overexpression and/or gene amplification is detected in approximately 20% breast tumours, is associated with an aggressive phenotype and is predictive of response to trastuzumab therapy. Here we evaluate the robustness, utility and cost-effectiveness of a chromogenic in situ hybridisation (CISH)-based assay for analysing HER2 status routinely. Formalin fixed paraffin embedded samples were examined using a CISH assay, analysed by light microscopy and scored according to the manufacturers protocol. The results from 161 of the samples were compared to results obtained using the immunohistochemistry (IHC) DAKO HercepTest and FISH PathVysion analyses that had been performed in external reference laboratories. 20.8% samples were found to have amplification of the *HER2* gene. There was 100% concordance between CISH and FISH but only 95% concordance between CISH and IHC. 1 IHC1+ sample was found by CISH to have a high level amplification and 7 IHC 3+ samples were found to be HER2 non-amplified. Using CISH in place of IHC and FISH was approximately 25% more cost effective per sample. It is concluded that CISH is as accurate as FISH. It is a simple but robust assay for HER2 evaluation that can be easily and cost-effectively integrated into the routine workload of a pathology laboratory, the level of amplification can be reported and it involves the pathologist in the diagnosis.

O15

Low level or loss of detection of acetylated Lys16 and trimethylated Lys20 of Histone H4 and its Effect on the Malignant Phenotype and Patient Outcome in Breast Carcinoma

{P} SE El Sheikh[1], AR Green[1], DM Heery[2], IO Ellis[1]
[1]*Department of Pathology ,Nottingham University Hospital, Nottingham, United Kingdom,* [2]*School of Pharmacy, Nottingham University, Nottingham, United Kingdom*

Histone modification is recognised to play a key role in control of gene expression and chromatin structure in normal cells, but whether or how these modifications are altered in cancer are unclear. Monoacytelated lys16 and trimethylated lys20 at H4 have been found to be lost in breast cancer cells. However the clinical significance of this aberration is unknown. In this study we assessed post-transitional modification of H4 at these two residues in a well-characterised series of breast carcinomas (n=880) with long term follow-up using immunohistochemistry and tissue microarray technology and the result was correlated with the clinicopathological variable and patient outcome.
Low level or loss of detection of acetylated/trimethylated H4 was observed in medullary type carcinoma and was associated with high grade, poor Nottingham prognostic index, larger tumour size, development of distant metastasis, negative (oestrogen receptor, luminal cytokeratines) and positive basal cytokeratines. Survival analyses showed low/loss of detection of these modifications is associated with shorter overall survival and shorter disease free interval.
This work demonstrates that, low level or loss of detection of Monoacytelated lys16 and trimethylated lys20 at histone H4 may play a role in breast cancer development and is associated with an aggressive phenotype and poor patient outcome.

O16

Expression of BRCA1 protein in breast and ovarian cancers and its prognostic significance

{P} E Rakha[1], M Kandil[2], S El-Shaikh1[1], I Ellis[1]
[1]*Nottingham University, Nottingham, United Kingdom,* [2]*Histopathology Department, Menoufia, Egypt*

The purpose of the current study was to examine the expression and localization of BRCA1 protein, and to assess its prognostic value, in a well-characterized series of unselected breast and ovarian carcinomas. Methods: We have examined BRCA1 in series of invasive breast carcinoma (1600 cases, using tissue microarray), and ovarian tumours (whole tissue sections) immunohistochemically, to evaluate its expression pattern and to correlate this with clinicopathologic variables and patients outcome. Results: In the breast, altered nuclear expression (absent or reduced) was observed in 801 cases (54%) and cytoplasmic expression was detected in 541 breast cancers (36.6 %). Altered nuclear BRCA1 expression was more frequent in duct/no special type and medullary-like carcinomas and less frequent in lobular and tubular mixed carcinomas. It showed an associated with high tumour grade, advanced LN stage, larger size, vascular invasion, negative ER, PgR and androgen and positive p53, P-cadherin and basal CKs expression. Reduced or absent nuclear BRCA1 was associated with shorter disease free survival. Cytoplasmic expression was associated with high grade, larger size, development of recurrence, positive p53, P-cadherin, EGFR, HER2 and basal CKs expression. It also showed an inverse association with survival particularly in low grade, small size and ER positive subgroups. In ovarian tumours, altered BRCA1 expression was associated with LN disease and high grade tumours. Cytoplasmic and absent nuclear BRCA1 was associated with shorter survival. Conclusion: BRCA1 may play a significant role in the development and progression of breast and ovarian cancer. IHC assessment of BRCA1 expression could provide additional prognostic value that may affect patient management particularly in the well-differentiated breast cancer.

O17

Receptor Status In DCIS is Variably and Inconsistently Reported: A Study of 1684 Cases from The Sloane Project

{P} JStJ Thomas[1], A Hanby[2], SE Pinder[3], JC Macartney[4], IO Ellis[5], K Clements[6], H Bishop[7]
[1]Pathology Dept, Western General Hospital, Edinburgh, [2]Pathology Dept, St James's University Hospital, Leeds, [3]Histopathology Dept, Addenbrookes Hospital, Cambridge, [4]Pathology Dept, University Hospital, Coventry, [5]Pathology Dept, City Hospital, Nottingham, [6]West Midlands Cancer Intelligence Unit, University of Birmingham, [7]Breast Unit, Royal Bolton Hospital, Bolton, United Kingdom

The Sloane Project is an anonymised UK-wide audit of screen-detected atypical hyperplasia and in situ carcinoma of the breast. Full pathology data are available on 1684 of 2615 cases entered. These include oestrogen (ER), progesterone (PGR) and Her2 receptor status and the scoring/cut-off criteria for positivity used.
Results: For hormone receptors, a majority of respondents used the Allred scoring system, or a percentage of positive cells and a small number the "histoscore". ER status & grade are given below:

Grade	High (%)	Intermediate (%)	Low (%)	Unknown	Totals (%)
	994 (59)	491 (29)	180 (11)	19	1684
ER pos	325 (69)	198 (94)	79 (99)		602 (79)
ER neg	148 (31)	12 (6)	1 (1)		161 (21)
Unknown	521	281	100		

ER positivity in low and intermediate grade DCIS was significantly more frequent than in high grade DCIS ($p<0.001$). Cut-off criteria were provided for 78% of the ER positive cases and 48% of ER negative cases. There was a wide range of cut-off values with Allred scores of 2 – 8, percentages of 0 – 50% and histoscores of 10 – 90 all apparently utilised. PGR status was known in 463 cases and Her2 status in 110 (44 positive (40%) and 66 negative). For Her2 status reporting, 31 cases had no stated cut-off for positivity given; in the remaining cases the cut off varied between 2+ and 3+.
Conclusion: At the present time, hormone receptor and Her2 status are not generally used to influence the clinical management of DCIS, but there is considerable variation in cut-off criteria used. There is a need to standardise reporting protocols and clear guidance is required on scoring methodologies and recommended cut-off points.

O18

RISK FACTORS FOR LOCAL RECURRENCE IN YOUNGER WOMEN WITH BREAST CANCER

{P} SE Laird[1], RA Walker[1], A Stotter[2]
[1]University of Leicester, Leicester, United Kingdom, [2]University Hospitals of Leicester, Leicester, United Kingdom

Younger women have higher rates of local recurrence (LR) following breast conserving therapy (BCT). This study examined whether this relates to pathological features and/or smaller surgical excisions.
Clinical and pathological characteristics were assessed for 483 women with early stage breast cancer who had BCT between 1997 and 2001, and were related to margin size, age (≤40 >40 years) and local recurrence. There were 48 women ≤40 years of age. On univariate analysis grade 3, lymph node status and age ≤40 years related to radial margin of excision < 3mm, and grade 3, presence of high grade DCIS and age ≤40 years with small all margins. Logistic regression analysis showed that age ≤40 years, grade 3 and Infiltrating Lobular Carcinoma were associated with radial margin < 3mm. Grade 3 and presence of vascular invasion (VI) were associated with age ≤40 years on univariate analysis but on multivariate analysis only breast volume and excision volume were associated with younger age. Actuarial survival curves showed presence of VI, high grade DCIS and grade 3 to decrease LR free survival.
More aggressive pathological features are associated with LR and could increase this in women ≤40 years of age, but smaller breasts and excision volumes are also important factors.

O19

Pathological Features of Primary Breast Cancer in the Elderly – A Large Series from a Single Centre

{P} KL Cheung[1], AWS Wong[1], H Parker[1], VWY Li[1], L Winterbottom[2], DAL Morgan[2], IO Ellis[1]
[1]University of Nottingham, Nottingham, United Kingdom, [2]Nottingham University Hospitals, Nottingham, United Kingdom

Majority of breast cancer are diagnosed at >65 years though research efforts are spent mainly on younger patients. Knowledge on elderly breast cancer is urgently needed.

Patients >70 years who had early operable primary breast cancer (<5cm) were included. Pathological features of diagnostic needle core biopsies taken from 2,078 tumours from 2,061 consecutive patients diagnosed in 1987 – 2006 were reviewed.

There were 1,996 invasive carcinoma of mammary type (96%) with (N=200) or without associated ductal carcinoma in-situ (DCIS); 81 were DCIS only (3.9%). One malignant adenomyoepithelioma was seen. Among the invasive carcinoma, no special features were seen in 87.1% while lobular and mucinous features were noted in 6.9% and 3.1% respectively. Vascular invasion was found in 11 cases of invasive carcinoma. Histological grades and oestrogen receptor (ER) status were assessed:

Grade	N	%		ER status (H-score)	N	%
1	167	20.2		0	284	18.2
2	518	62.7		>0 – 50	26	1.7
3	141	17.1		>50 – 100	63	4
Total	826	100		>100 – 200	493	31.7
				>200 – 300	691	44.4
				Total	1,557	100

Among 44 DCIS which were graded, most (52.3%) were high grade.

We believe that this is the largest dataset of pathological features of primary breast cancer in the elderly from one single centre. Further work is underway to correlate them with the long-term clinical outcome.

O20

Her2 expression: Correlation of Chromogenic In-situ Hybridization with Immunohistochemistry and Fluorescent In-situ Hybridization

{P} M Sohail[1], N Banu[1], CJ Calder[2], S Mungwana[2], S Florio[2], F Lewis[3], M Moorghen[2], M Pignatelli[1], A Hanby[3]
[1]University of Bristol, Bristol, United Kingdom, [2]Bristol Royal Infirmary, Bristol, United Kingdom, [3]University of Leeds, Leeds, United Kingdom

Her2 gene is located on chromosome 17 and encodes a growth factor receptor. Her2 amplification is a prognostic marker and its assessment is also required to plan the treatment of breast cancer with Herceptin. Immunohistochemistry (IHC) is used in the first instance to determine Her2 status of the breast cancer. Equivocal (2+) cases are further tested for gene amplification by fluorescent in-situ hybridization (FISH). In this study we compared the recently described chromogenic in-situ hybridization (CISH) method for Her2 assessment with FISH and IHC.
Methods: 94 cases of breast cancer were selected from the archives of Department of Histopathology of the Bristol Royal Infirmary. IHC was carried out by indirect immunoperoxidase using anti-HER2 monoclonal antibody (Dako A0485) FISH and CISH were performed using specific probes from Q-BIOgene (PONCHER2) and Zymed Lab (84-0146) respectively.
Results: IHC score was 0 in 28, 1+ in 29, 2+ in 20, and 3+ in 17 cases. Her2 gene was amplified in all 3+ cases and not amplified in 0 and 1+ cases on FISH and CISH tests. There was no discrepancy between FISH and CISH results in 2+ cases.
Conclusion: CISH is a reliable, alternative and quick method for the Her2 assessment in breast cancer.

O21

Malignant Phyllodes Tumour of the Breast with In-situ, Invasive and Metaplastic Epithelial Malignancy

{P} SA Melmore, TR Helliwell
The Royal Liverpool and Broadgreen University Hospitals NHS Trust, Liverpool, United Kingdom

Phyllodes tumours arise from proliferation of mammary stroma and epithelium and demonstrate a morphological continuum from fibroadenoma to pure stromal sarcoma. Epithelial malignancy in phyllodes tumour is rare.
We report the case of an 80 year lady who presented with a 7cm breast lump. FNA smears contained plentiful pleomorphic malignant cells consistent with a high nuclear grade breast primary. A core biopsy suggested malignant phyllodes tumour. CT scan excluded metastases. She had a wide local excision and histology confirmed a malignant phyllodes tumour with sarcomatous stroma and small areas of benign phyllodes tumour. Unusually, the epithelium also showed malignant features with in-situ carcinoma and foci of invasion into the stroma. Immunohistochemical staining of the spindle cells was positive for p53, CD117 and smooth muscle actin and negative for AE1/AE3, similar to previous reports of malignant phyllodes tumour, but positive for CAM5.2 and S-100 and negative for CD34 and Bcl-2, suggestive of metaplastic carcinoma. We discuss the spectrum of histological appearances including stromal cellularity, atypia, mitotic rate and stroma-to-epithelium ratio and the challenges in distinction between malignant phyllodes and metaplastic carcinoma arising in a benign phyllodes tumour.

O22

EXFOLIATIVE CYTOLOGY -A NOVEL RAPID DIAGNOSTIC TOOL USING BREAST MAMMOTOME CORE BIOPSIES

N Dutt, {P} C Kaur
Kings College Hospital, London, United Kingdom

Objective: The aim of this study is to evaluate the role of breast exfoliative cytology in rapid diagnosis of mammotome targeted lesions.
Method: Prospectively, 86 mammotome breast core biopsy samples were collected from the screening unit over a period of 5 months. All the biopsies were obtained in tissue culture fluid and manually agitated to encourage cell exfoliation. The cores were then fixed in formalin and processed routinely. At least 4 cytospin preparations were obtained from each fluid sample, which were stained (diff quick and PAP), assessed blindly and allocated C1 - C5 categories. Cytology results were correlated with the mammotome biopsy results.
Results: Absolute sensitivity: 82.75%, Complete sensitivity: 96.55%, Specificity: 78.37%, PPV (C5): 100%, F – 0%, F+0%, INAD: 11.62% These are in accordance with NHBSP QA guidelines.
Conclusion: We have established that using this technique, a rapid cytology diagnosis can be obtained from the mammotome core biopsies done routinely, without significantly altering the practice protocols within a busy breast screening service. To the best of our knowledge this is the first attempt at obtaining exfoliated cells from mammotome cores to establish a rapid diagnosis.

O23

Amyloidosis of the Submandibular Salivary Glands

{P} M Tripathi, VM Reddy, TE Giles, TR Helliwell
The Royal Liverpool and Broadgreen University Hospitals, Liverpool, United Kingdom

Symptomatic involvement of major salivary glands by either primary or secondary forms of amyloidosis is very rare.
We describe a case of primary submandibular gland amyloidosis diagnosed on aspiration cytology and confirmed by histology.

A 39 year old man presented with bilaterally enlarged submandibular glands and not other significant history. Fine needle aspiration cytology showed a duct surrounded by smudged eosinophilic connective tissue confirmed as amyloid on Congo red stain. On histology the gland was replaced by deposits of amorphous eosinophilic material, strongly positive for congo red stain. Residual glandular tissue was associated with predominantly B lymphocytic infiltration and lambda light chain expression in the few plasma cells present. Electron microscopy revealed the typical fibrillar structure of amyloid protein.

His bone marrow aspirate showed approximately 10% plasma cells with polyclonal light chain expression. A CT scan of his chest, abdomen and pelvis was normal. Liver enzymes, renal function, calcium and blood count were normal and the urinary Bence Jones protein was negative. Serum immunoglobulin has revealed a slightly raised polyclonal IgA. Patient is still under the follow-up.
In the absence of systemic disease or evidence of myeloma, this patient appears to have a primary amyloidosis of submandibular salivary gland.

O24

A clinicopathologic study on microvessel density determined by CD34 or CD105 in benign and malignant gastric lesions

{P} C Li, H Denley, RFT McMahon, V Arora, S Kumar
[1]*Department of Histopathology, Manchester Royal Infirmary, Manchester, United Kingdom,* [2]*Department of Pathology, The University of Manchester, Manchester, United Kingdom*

Microvessel density (MVD) is regarded as a surrogate marker for angiogenesis and has been used for predicting tumour prognosis. In this study, MVD was identified immunohistochemically by two monoclonal antibodies against CD105 and CD34 in tissue sections of gastric carcinoma (51 cases), chronic gastritis (30 cases) and hyperplastic polyps (10 cases), and the results were correlated with clinicopathologic features. The expression of CD105 in the microvessels within benign lesions was weak, and MVD identified by CD105 was markedly lower than that determined by CD34. CD34 was strongly expressed in microvessels of hyperplastic polyps and chronic gastritis. In contrast to benign lesions, CD105 expression was significantly increased in microvessels of gastric carcinoma. CD105 stained well-formed mature as well as newly formed immature vessels within the cancer tissue. Correlation analysis showed that MVD determined by CD105 correlated well with vascular invasion, distant metastases, and formation of ascites. Survival analysis demonstrated an inverse correlation between MVD and overall survival: patients with MVD of 32 or beyond survived for a much shorter time than those with MVD below 32. Multivariate analysis confirmed that MVD determined by CD105 was an independent prognostic factor for survival. MVD identified by CD34 inversely correlated with overall survival, but it did not correlate with other clinicopathologic parameters except formation of ascites. In conclusion, CD34 was universally expressed in blood vessels within benign and malignant tissues, whereas CD105 expression was weaker in benign tissues but considerably stronger in gastric carcinoma. These data suggest that both CD105 and CD34 can be used for quantification of angiogenesis, but preference should be given to CD105 in predicting prognosis in gastric carcinoma.

O25

Desmoplasia is accompanied by enhanced vascular maturation in colon cancer

{P} A Gaumann[1], S Schmid[1], S Schulte[2], F Hofstädter[1], L Kunz-Schughart[3]
[1]Institute of Pathology, Regensburg, Germany, [2]Harvard Medical School, Boston, United States, [3]OncoRay ZIK Dresden, Dresden, Germany

Introduction: The heterologous cellular microenvironment actively affects tumour pathogenesis, progression and therapy. Recent reports emphasize the role of pericytes in vessel maturation. Since vascular targeting is a promising therapeutic approach but the role of pericytes recruited from peritumoral fibroblasts to contribute to tumour vascularisation is still ambiguous, we analyzed vessel density and maturation relative to stroma formation in sporadic colon cancer. **Design:** 55 consecutive colon carcinomas were retrieved and classified for stroma formation (grade 1-3). Vascularisation was quantified in sections stained for CD31 and podoplanin and vessel maturation was assessed by counting pericyte coverage following double labelling of PDGFR-β or α-smooth muscle actin combined with CD31 or podoplanin. The expression pattern of various angiogenesis and fibrogenesis-modulating growth factors and their receptors is under investigation. **Results:** High grade desmoplastic tumours show a significantly lower microvessel density at the periphery, invasion front and in desmoplasic areas than tumours with low grade desmoplasia. Lymphatic vessel density is unaltered. In contrast, pericyte coverage is significantly enhanced in desmoplastic high vs. low grade tumours. **Conclusions:** The desmoplastic reaction in colon carcinomas is accompanied by reduced vessel density and enhanced vascular maturation supporting the hypothesis that tumour vascularisation is essentially modified by the fibrous stromal reaction. Thus, tumour desmoplasia may critically impact anti-angiogenic therapy.

O26

Sessile Serrated Polyps in Proximal Colon: Our Experience

{P} N Bhatt, HW Chong
St Georges Hospital, London, United Kingdom

Introduction: Sessile Serrated Polyp is a recently described entity with important prognostic implications because of a high associated risk of MSI-high proximal colon cancers. Hence it is important to recognise and watch them closely.
Aim: (1) To identify the true incidence of SSP in proximal colon (2) To identify areas of improvement
Method: All the right-sided colonic polyps (n=72) diagnosed as hyperplastic polyps (HPP) on biopsies were retrieved from APEX during 01/01/2004 to 31/12/2005. Size of polyps was noted. They were classified as i) true SSP, ii) true HPP, iii) indeterminate and iv) not serrated polyps.
Results: 48 were true HPP, 9 were true SSP, 10 were indeterminate and a change in diagnosis was considered in 5 polyps- 1 inflammatory polyp, 2 tubular adenomas and 2 mucosal prolapses. Indeterminate cases were either poorly orientated or had a crush artefact.
Conclusion: SSPs form a significant proportion of serrated polyps in proximal colon. Their detection rate is poor because of lack of evidence-based guidelines. Reproducibility is doubtful because of overlapping entities, limited by the quality of biopsy and confusing & controversial terminology.
Recommendations: Consistent terminology should be used in reports, with advice on surveillance. Comment on excision should be made, where possible.

O27

Eosinophilic oesophagitis in adults.

{P} R Ramakrishnan, H Chong
St George's Hospital, London, United Kingdom

Introduction: Eosinophilic oesophagitis (EE) is a clinicopathologic entity characterised histologically by eosinophilic infiltration of the oesophageal squamous epithelium. Although well described in children, EE has only fairly recently been recognised in adults, especially young adults, in whom EE usually presents as dysphagia. Histologically, EE may be mistaken for reflux oesophagitis (GORD). However, unlike GORD, EE is unresponsive to standard acid blockade measures.
Material and methods: We reviewed oesophageal biopsies reported as inflammation and/or GORD in patients between 18 and 50yrs of age, between January 2004 and December 2005. Cases showing dysplasia and/or Barrett's oesophagus were eliminated from the study. The biopsies were reviewed for the presence of (1) greater than or equal to 20 eosinophils/hpf and (2) eosinophilic microabscesses.
Results: 55 biopsies were reviewed from 52 cases. The mean age was 40.5 years. The male to female ratio was1.6:1 (55/34). 3 biopsies with markedly increased eosinophil count (>=20/hpf) were reclassified as EE. The histological features were correlated with the clinical and radiological appearances.
Conclusion: It is important to identify EE due to different therapeutic implications & its association with other allergic conditions. We are extending this current study to include mainly adult cases from years 2001 to 2006.

O28

Rapamycin inhibits the spontaneous formation of de novo cancer in p53 knockout mice

{P} A Gaumann[1], G Koehl[2], A Hoehn[2], M Kovacs[2], F Hofstädter[1], HJ Schlitt[2], EK Geissler[2]
[1]Pathology, Regensburg, Germany, [2]Surgery, Regensburg, Germany

Introduction: Cancer is a major problem in transplant recipients. Recent data suggest that rapamycin (RAPA), or mycophenolate mofetil (MMF), may reduce tumor growth. However, little experimental data exists regarding cancer prevention. Here we tested the effects of long-term RAPA, MMF or cyclosporine (CsA) use on spontaneous tumor formation in p53 knock-out mice. **Methods:** p53 knockout mice received either placebo, RAPA, MMF or CsA at immunosuppressive doses starting on week 10 after birth. Drugs were fed at typical immunosuppressive doses. Mice were monitored daily and sacrificed when clinical signs of disease occurred. The experimental endpoint was week 28. Tissues from major organs were taken for further analysis.
Results: All untreated mice developed clinically evident tumors by week 28 as confirmed by histology. All CsA-treated mice developed clinical tumors by week 28. With MMF treatment, 7/10 mice showed clinical evidence of tumor by week 28. However, histology revealed that the remaining 3 mice had subclinical cancer. In contrast, RAPA treatment resulted in only 3 clinically evident tumors before the experimental endpoint, with histology revealing subclinical tumor in 3 additional mice, but no evidence of tumor in 4 animals. Log-rank analysis shows a significant decrease in cancer occurrence in the RAPA group (P=0.02 vs. controls); but not in either the CsA or MMF group.
Conclusions: Our results show that de novo development of cancer is reduced in p53 KO mice under RAPA immunosuppression, but MMF and CsA treatment does not affect de novo tumor development in this model.

Abstracts

Speakers

S1

Pathology in a PBL Curriculum

{P} RFT McMahon
University of Manchester, Manchester, United Kingdom

Undergraduate programmes in UK medical schools have changed considerably over the last 2 decades, with many moving to an integrated system with reduced emphasis on individual disciplines, such as pathology. A popular method has been the problem based learning (PBL) approach, pioneered by the University of Maastricht and used in several UK schools including Manchester. There is a spiral approach with each of the 4 semesters in phase 1 (years 1-2) providing the biomedical science basis while the equivalent semesters in phase 2 (years 3-4) revisit the same themes in clinical practice. Phase 3 (year 5) is designated as preparation for practice. Each of the semesters is based around 8-12 clinical scenarios, within which aspects of general pathology (inflammation, vascular pathology and neoplasia in phase 1), and systemic pathology (cardiorespiratory, gastrointestinal or urological in phase 2). Pathologists participate by being members of semester design teams, group facilitators, suppliers of resource material, deliverers of theatre events, giving access to sign up sessions such as autopsies, providers of questions for assessment, and examiners. Students wishing to develop a deeper understanding of pathology have an opportunity to undertake Student Selected Components (SSCs, giving blocks of exposure to pathology practice), Research Project Options (11 weeks) or an intercalated BSc/MRes. PBL is a time and labour intensive method of delivery and with dwindling numbers of academic pathologists is very difficult to sustain. Nonetheless, with the aid of NHS colleagues and trainees, it is possible to maintain the profile of pathology within a curriculum and ensure that graduates will have had sufficient exposure to pathology to make an informed career choice after Foundation Programmes.

S2

Assessment in Pathology

{P} JWM Chow
St George's, University of London, London, United Kingdom

There has been a radical change in medical education in the United Kingdom since the first publication of 'Tomorrow's doctors' by the General Medical Council in 1993, and more recently revised in 2003. These define a core curriculum of essential knowledge, skills and attitudes that medical students are expected to acquire, and recommend schemes of assessment to ensure that curricular outcomes are attained. The advent of an integrated curriculum and integrated methods of assessment has led to loss of identity of pathology as a distinct discipline in many British medical schools. Nevertheless, it is a recommendation that the scientific basis of medical practice is a key component of the curriculum. As such, the teaching, learning and assessment of pathology has the same importance in medical education today, as before 1993. The place of pathology in medical assessment can be instituted with appropriate blue-printing. Special attainment in pathology can be recognised by prizes in pathology.

S3

Medical students don't need to be learn pathology – against

{P} AD Burt
School of Clinical and Laboratory Sciences, Faculty of Medical Sciences, Newcastle University, Newcastle upon Tyne, United Kingdom

The essence of pathology is encapsulated in the current strap line of the Society – understanding disease. As such it provides the fundamental evidence base which underpins all medical practice. It not only informs the 21st century medical practitioner, guiding appropriate clinical investigation and interventions but also informs the 21st century patient. Patients are increasingly well versed on their own disease from abundant information available on the web; physicians and surgeons are having to adapt to this and now need to be able to facilitate clearer understanding of the processes that are occurring in their patients. This requires a good grasp themselves of basic mechanisms of disease. There is anecdotal evidence that the knowledge and skills base in this regard is lacking in many of today's medical graduates in a similar way to that highlighted recently with therapeutics. Many modern curricula in the United Kingdom have (very reasonably) concentrated on developing good communication skills in our undergraduates and junior doctors with an emphasis on holistic medicine. All too often however the key role of understanding the basic mechanisms of disease is excluded from this holistic vision.

Training the doctors of the future without this foundation is untenable. It would be akin to saying that one could train a car mechanic without reference to what can go wrong under the bonnet as long as they can talk clearly and listen to their customers. We should certainly debate how pathology is taught; it must be contextualised and integrated but not lost within pedagogic systems such as problem based learning. We should not on the other hand have to debate whether pathology is taught. It is the scientific study of disease. As others have said, without it medicine is little more than witchcraft and sorcery!

S4

Training Routes in Academic Pathology

{P} KE Robertson[1], M Deheragoda[2]
[1]University of Dundee, Dundee, United Kingdom, [2]CRUK London Research Institute and University College London, London, United Kingdom

An understanding of pathology is a prerequisite to understanding disease. Only through continuing research can we improve our current knowledge. For the trainee pathologist interested in research, teaching and diagnostic pathology, a career in academic pathology is the perfect solution. With the ever advancing field of molecular pathology and its integration into our everyday practice, the importance of academic pathology to our specialty and ultimately our patients and the public has been reaffirmed. As a consequence, the future of academic pathology in the UK has been significantly strengthened by the ongoing support of our Royal College, the Pathological Society, individual Universities and Research Council Fellowship schemes. As in life, there is always more than one way to achieve our goals and thus there is more than one training route in Academic Pathology.

Dr Deheragoda and Dr Robertson co-chair the Trainee Sub-committee of the Pathological Society. They are both academic trainees in histopathology but are undertaking different training routes. Dr Robertson is a Clinical Lecturer and honorary SpR in Dundee, whilst Dr Deheragoda is a Cancer Research UK Clinical Fellow at the CRUK London Research Institute and an honorary SpR at University College Hospital. In this talk they will talk briefly about their own experiences as academic trainees and discuss the possible benefits and drawbacks of their particular chosen route in academic pathology training.

S5

HOW TO BE A GOOD TEACHER

{P} P Domizio
Professor of Pathology Education, Barts and the London, Queen Mary's School of Medicine, London, United Kingdom

Good teachers are role models as well as educators and there is no doubt that they can inspire their students to go along certain career paths. There has been much debate in the educational literature about what makes a good teacher, but a widely accepted definition is still lacking. Most students describe a good teacher as accessible, enthusiastic, passionate, humorous, caring and non-judgmental. Good teachers are learner-orientated – they take into account how much their students already know, they put learning into context and they actively engage their students in the learning process. Good teachers provide a supportive, trusting and non-threatening environment in which the student positively enjoys learning. Giving a good lecture is an art, akin to a stage performance in which the lecturer is protagonist and holds the audience's attention to the end. Some of the skills involved in giving a good lecture stem from the lecturer's personality, but others can be practiced and learnt. Good lectures are well-planned, well-structured, well-delivered and properly timed. The personal rewards for being considered a good teacher are high. At professional level, the climate is slowly changing with increasing recognition and promotion of good teachers.

S6

How to Write a Scientific Paper and Get it Published

{P} CS Herrington
University of St Andrews, Fife, United Kingdom

There are numerous issues that influence whether a paper gets published, but many of these relate to the central underlying principle that it should address a specific hypothesis, and do so in a concise, informative way. The first impressions of editors and reviewers are key to the success of a submission and are often determined by the title, abstract and figures: these components are therefore worthy of particular attention. There is an increasing trend for authors to 'aim high' (by which they usually mean submission to journals with a high impact factor) and the probability of success with the major international journals is increased significantly if the basic principles above are adhered to, and attention is paid to the instructions for authors for that particular journal. There are, however, no guarantees and failure to persuade one journal to publish your work should not deter you from trying others.

S7

Proteomics and Prostate Carcinoma

{P} L Egevad
International Agency for Research on Cancer (IARC), Lyon, France

As a result of earlier detection of prostate cancer, a majority of patients now have non-palpable tumors (T1c) of low grade (Gleason score 6). Consequently, some of the prognostic discrimination obtained by staging and grading is lost and there is a need for adjunctive prognostic indicators. In the search for such tumor markers an exploration of the human proteome may be fruitful.

Two-dimensional gel electrophoresis (2-DE) is presently the most powerful method for analysis of cellular protein phenotype. Proteins are separated according to their size and charge, gels are compared by image analysis, protein spots of interest are excised and proteins identified by mass spectrometry. On prostate samples, 2-DE has been used for mapping of differential protein expression of the anatomical zones, benign tissue vs. prostate cancer and correlations with tumor grade. Disadvantages with 2-DE are that the technique is time-consuming, expensive and requires large tissue samples.

Non 2-DE methods, such as SELDI, ICAT and array based technologies, generally require smaller sample sizes and are more automated than 2-DE. However, with some of these methods only a limited set of proteins are detected in each assay and concerns have been raised about protein identification and data validation.

S8

The Value of Tissue Microarrays in Urological Pathology.

{P} DM Berney
Barts and The London, Queen Mary School of Medicine and Dentistry, London, UK, United Kingdom

Tissue microarrays are a technique for high throughput analysis of tissues. Urological pathology offers many opportunities for TMA construction of large series for biomarker analysis. Prerequisites for analysis are the identification of areas suitable for array and sampling multiple areas to allow for heterogeneity. Uses of TMA include the retrospective investigation of prognostic markers and the potential of prospectively correlating markers with chemo and radiosensitivity to allow individualised tumour therapy in the future.

This review will outline uropathological project undertaken in The Orchid Tissue laboratory in a range of malignancies including germ cell neoplasms, renal tumours, squamous cell carcinoma of the penis and prostate cancer. Technical problems will be discussed.

The Trans-Atlantic Prostate Group has produced an array of over 900 prostate cancer patients who had TURPs between 1991 and 1996, and treated by watchful waiting. TMA has allowed a vast number of potential biomarkers to be investigated. Recent advances in technology have allowed biopsy material to be arrayed successfully. This vastly increases the power of TMAs in urological pathology, particularly in the prostate where retrospective biopsy series can be analysed.

Immunochemistry is not the only technique that can be used successfully in TMAs. Fluorescence ISH has shown specific chromosomal translocations in prostate TMAs, and chromogenic ISH can better correlate abnormalities with light microscopic appearances.

S9

Evolving a 21st Century Uropathology EQA Scheme: From Slides to Images

{P} P Harnden
Leeds Teaching Hospitals, Leeds, West Yorkshire, United Kingdom

The NICE Improving Outcomes Guidance in Urological Cancer recommended the development of a national uropathology EQA scheme using the format of the breast pathology EQA scheme. The use of a fixed text proforma for participants' responses facilitates the collection of consistent data, which are analysed with Kappa statistics to measure agreement, identifying improvements in diagnostic consistency over time and areas of persistent difficulty. The first phase of the EQA scheme development, in collaboration with the Cancer Screening Evaluation Unit, focussed on prostatic core biopsies. Results showed good agreement for the major diagnostic categories of benign and invasive, but only after excluding almost 20% of circulated cases for failure to reach 75% agreement among the expert group. Areas of difficulty included interpretation of prostatic intraepithelial neoplasia, small foci of cancer, perineural invasion, tumour extent and Gleason grading. Moving to an image based system was the only practical way of opening the scheme to all. Comparison of readings of images versus slides showed intraobserver variation in difficult cases, but partly because of a shift towards the original slide-based consensus diagnosis. Overall, interobserver variation remained good for easy cases and improved slightly for difficult ones, making image based circulations a viable option with many advantages.

S10

Advances in B-cell lymphomas since the advent of the WHO classification

{P} ES Jaffe, E Campo, S Pittaluga, M Raffeld, L Staudt
National Cancer Inst, Bethesda, MD, United States

Since publication of the WHO classification in 2001, we have seen improvements in the understanding of the biology of many B-cell lymphomas, and new prognostic markers have been identified. Most progress has been achieved in the field of aggressive B-cell lymphomas, an area in which genetic and immunophenotypic tools are especially critical for deciphering disease entities.
The following topics will be covered:
Diagnosis and classification of grey zone lymphomas: implications for the understanding of mediastinal large B-cell lymphomas and nodular sclerosis Hodgkin's lymphoma.
Molecular profiling in the classification of diffuse large B-cell lymphomas: are surrogate markers useful for the distinction of the germinal center B-cell and activated B-cell lymphomas?
The morphological and biological spectrum of B-cell malignancies with a plasmablastic immunophenotype – How many separate entities?
T-cell/ histiocyte rich large B-cell lymphoma and the interface with nodular lymphocyte predominant Hodgkin's lymphoma – a biological spectrum or distinct disease entities?

S11

An Update on T-cell lymphomas

{P} A Dogan
Mayo Clinic, Rochester, MN, United States

Since the advent of the World Health Organization lymphoma classification, there have been important developments in the understanding of biology of T-cell lymphomas (TCL). These include insights into the relationship between normal T-cell physiology and TCL, insights into molecular pathogenesis and the discovery of novel markers for diagnosis. There is now good evidence that angioimmunoblastic T-cell lymphoma (AITL) is a neoplasm of germinal center T-cells, adult T-cell lymphoma/leukemia (ATLL) is closely related CD4+, CD25+ regulatory T-cells and most cases of blastic NK-cell lymphoma/leukemia (recently referred as CD4+/CD56+ hematodermic neoplasm-HDN) are of plasmacytoid dendritic cell origin rather than NK cell origin. First recurrent genetic abnormality in peripheral TCL (PTCL) has been described. The abnormality involves t(5;9)(q33;q22) and leads to fusion of ITK and SYK genes creating a novel oncogene. Studies of NK cell receptors (NKR) have lead to insights into pathogenesis of T and NK cell large granular lymphocyte leukemia (LGL) and hepatosplenic TCL (HSTCL). Investigators have utilized the biological discoveries to develop markers for better diagnosis and classification. These include immunophenotypic markers for diagnosis of AITL (CD10, CXCL13, PD-1), ATLL (FoxP3), HDN (TCL1, CD123) and LGL (NKR typing) and cytogenetic tests for diagnosis of PTCL (ITK/SYK), HSTCL (TCL1) and precursor T lymphoblastic lymphoma. It is hoped that these biological discoveries will lead to therapeutic advances in the near future.

S12

Hodgkin's lymphoma

{P} H Stein
Institute for Pathology, Campus Benjamin Franklin, Charité Universitätsmedizin Berlin, Berlin, Germany

Since the advent of the WHO classification most research in Hodgkin's lymphomas focussed on the extent and the underlying mechanisms of the extinction of the B-cell expression program and the expression of B-cell inappropriate molecules like CD30, CD15, GATA3, TARC, T-bet and many others by the Hodgkin- and Reed-Sternberg cells. The extinction of the B-cell program is due to a defect in the transcription machinery. The reason for this is manifold: crippling mutations, non-expression of transcription factors, epigenetic alterations of promoters and intrinsic inhibition of transcription factors which physiologically initiate and maintain the B-cell differentiation program. All these findings in conjunction with the numerous genetic alterations observed in cHL favour the view that the transformation event leading to cHL affects only one or few master regulators which cause(s) the dramatic change of the transcriptom and the remarkable genetic instability of Hodgkin/Reed-Sternberg cells. In support of this view is the observation of patients in whom cHL and follicular lymphoma simultaneously or subsequently occur. Although both lymphoma entities originate from the same mature precursor B cell as demonstrated by the same immunoglobulin gene rearrangement and by identical somatic hypermutations, their expression profiles differ completely. Whereas the follicular lymphoma fully maintains its germinal centre B-cell phenotype, the co-existing cHL has completely lost the germinal centre B-cell identity . This scenario suggests that the transforming event is composed not of many but only few steps which probably occur in a relative short time frame.

S13

Immunohistochemical Markers of Lymphoma

{P} DY Mason
University of Oxford, Oxford, United Kingdom

By the early 1990s the advent of "paraffin-reactive" anti-white cell monoclonal antibodies had transformed routine haematopathology and opened the way to the REAL classification (and to its direct successor, the WHO-sponsored scheme). As a result most lymphomas can be diagnosed today without great difficulty by morphology and immunohistology. However, a few entities remain "diagnoses of exclusion" (e.g. lymphoplasmacytoid lymphoma and marginal zone lymphomas), partly defined by the absence of specific immunohistological features. New markers are likely to prove valuable in such settings, and they may also allow subdivision of existing lymphoma categories. For example, the immunohistological recognition of subtypes of diffuse lymphoma and of T cell lymphomas is an obvious area for future progress. There is also much interest in predicting prognosis in lymphomas on the basis of immunohistology, but the scope of this approach can be overestimated: the most robust markers are likely to be among the minority that directly reflect an underlying genetic lesion. Finally, the number of immunohistological markers detectable in paraffin sections continues to grow steadily, both through commercial production and from initiatives such as the Human Protein Atlas. In consequence there is still substantial scope for new immunohistological insights into lymphoma.

S14

Molecular biology and molecular markers of lymphoma

{P} M-Q Du
University of Cambridge, Department of Pathology, Cambridge, United Kingdom

Molecular genetic features are one of the essential elements used in WHO classification of tumours of lymphoid tissues. Detection and characterisation of genetic abnormalities or molecular signatures valuable in lymphoma diagnosis, classification and prognosis have been continuously gaining attention in research since the introduction of WHO classification. Such research is particularly accomplished by the completion of the human genome project and the advent of high-throughput research tools such as genomic and expression microarray analysis. There are a number of important advances in our understanding of molecular genetics and pathobiology of several lymphoma subtypes. Notable examples include 1) the finding of the oncogenic products of t(11;18)/API2-MALT1, t(1;14)/IGH-BCL10 and t(14;18)/IGH-MALT1 in MALT lymphoma commonly targeting the pathway leading to NFκB activation, and demonstration of gastric MALT lymphoma with t(11;18) resistant to *H pylori* eradication; 2) identification of ZAP70 expression as a surrogate marker for CLLs that carry unmutated rearranged immunoglobulin gene and show poor clinical outcome; 3) sub-classification of diffuse large B cell lymphoma into germinal centre B cell-like (GCB) and activated B cell-like (ABC) subtypes with distinct molecular and clinical features by gene expression profiling, with the ABC subtype characterised by the enhanced NFκB activities and poor prognosis. These findings have direct implications in clinical management of patients with these diseases.

S15

Our changing view of the genome: implications for pathology

{P} PA Hall
Centre for Cancer Research & Cell Biology, Division of Pathology, Queen's University, Belfast, United Kingdom

The concept of the gene has evolved over the past century and the model of *'one gene one protein'* proposed by Beadle & Tatum has been radically altered in the molecular era. Furthermore the various genome sequencing projects demonstrated that the number of 'genes' is far less than had been anticipated: perhaps less than 30000 in man, whereas *Sacchoromyces cerevisiae* has ~6300 and *Drosophila melanogaster* ~12500. The massive increase in cellular complexity (tissues, organs, physiology etc) in metazoa, and in particular in vertebrates, thus seems out of proportion to the numeric increase in gene number and the informational content inherent in the encoded open reading frames. *How can this paradox be resolved?* Alternate splicing of RNA to give diverse mRNA species encoding numerous protein isoforms has a significant contribution to the resolution of this paradox. In man it may be that as much as 90% of the expressed genes are spliced so that the ~30000 genes may encode considerably more protein species. In addition, a range of potential post translational modifications also contributes to the increased complexity and diversity of protein species. In addition, the non-coding RNA has considerable informational content both in terms of *cis* and *trans* acting elements. By such routes the proteome is massively increased giving a much larger array of potential structural and regulatory protein species, thus creating the necessary building blocks for metazoan organisms. Central to the optimal functioning of these mechanisms is the correct levels of the correct elements of regulatory and other protein arrays. Controlling the stoichiometry of critical polypeptides then being central to normal cell function. Disease can then be a consequence of alterations not only in the coding sequence of open reading frames, but also in non coding regions. Moreover, no longer should we think of disease in terms of a gene-specific mutation but more widely accept that disease can be isoform specific. Furthermore genetic variation within the population provides a substrate for small differences in coding and non coding regions and hence in the subtle expression patterns of diverse proteins and hence subtly altering stoichiometry. Using examples from my previous studies in p53 and septin biology these ideas will be explored and their implications for pathology developed. It is essential that the discipline grasp the intellectual and technical challenges inherent in our changing view of the genome if pathology is to translate such developments into clinical practice.

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LBC in Non-Gynaecological Cytology

{P} JE McCarthy
St Marys NHS Trust, Paddington,London, United Kingdom

Liquid based preparation of non-gynaecological samples has many benefits and some limitations. The method discussed here is ThinPrep processing using the T2000. In our institution, we routinely process all bronchial samples including sputa by this method exclusively. ThinPrep processing has improved our pick up of primary lung carcinomas compared to direct spread technique and is quicker and easier to screen.
Thyroid FNAs are prepared using a combination of direct spread MGG stained slides together with a ThinPrep slide. This combination provides traditional smears coupled with a Pap stained method with the added benefit blood lysis.
We avoid using ThinPrep for other samples such as fluids and especially lymph nodes, notably for reasons of cost and as lymph node morphology is poorly presented in ThinPrep preparations.
This methodology is ideal for use in clinical situations such as the bronchoscopy suite where spreading of material may be suboptimal and to retain well preserved material for special stains and for immunocytochemistry. Its use should be tailored to the individual clinical situation and more importantly to the specimen type for maximum benefit and cost effectiveness.

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