

Reflections on a Career in Liver Pathology

Stefan Hübscher

Emeritus Professor of Hepatic Pathology, University of Birmingham.

Early Influences

Autumn 1953 - A Passage to America



Agnes Treitz
20/01/1928 -



Georg Hübscher
12/07/1926 – 03/11/1970

25th November 1954, Madison, Wisconsin



January 1956

The Hübschers arrive in Birmingham

Georg has decided not to pursue a career as a clinician and is appointed to a research position in Biochemistry in the Medical School

Return to Germany intended

Queen Elizabeth Hospital, Birmingham - circa 1955



4 Underwood Road, Handsworth Wood



- Restaurants
- Hotels
- Attractions
- Transport
- Parking
- Chemists
- Cashpoints

Sign in

4 Underwood Rd,
Birmingham B20 1JH

Cherry Orchard Primary
School and Nursery

West Bromwich
Albion Football Club



April 1969

The family moves to Nottingham

Georg is appointed as Professor in Biochemistry
at the new Medical School

Nottingham High School





Nottingham High School – Notable Political Alumni



Kenneth Clarke



Ed Davey



Geoff Hoon



David Frost



Ed Balls



Nottingham High School – Other Notable Alumni



David Adams



Matt Armstrong

Summer 1970, Widemouth Bay, Cornwall



Why Medicine?

By default rather than by design.....



Paul Dawson
Biology Teacher, Nottingham High School

September 1974

Return to Birmingham

University of Birmingham Medical School

Graduation Day, July 1979



Why Pathology?



Douglas Brewer
05/08/1919 – 20/12/2016

Why Liver Pathology?

Department of Pathology, January 1981





Elwyn Elias
Consultant Physician, QEH, 1979-2008

Clin. exp. Immunol. (1983) **52**, 207–218.

**Dual role of the liver in regulating
circulating polymeric IgA in man:
studies on patients with liver disease**

K. G. CHANDY,* S. G. HÜBSCHER,† E. ELIAS,‡ J. BERG,§ M. KHAN* &
D. BURNETT* *Departments of *Immunology, †Pathology and ‡Medicine, University of
Birmingham and §Department of Clinical Chemistry, East Birmingham Hospital, Birmingham, UK*

(Accepted for publication 26 November 1982)

Table 1. Distribution of SC in liver biopsies

	Intensity of staining	Bile duct epithelium	Portal tract macrophages	Portal vessels	Biliary canaliculi	Hepatocyte cytoplasm	Hepatic sinusoids	Sinusoidal phagocytes
Controls	Neg	0	5	2	3	7	5	5
Surgical biopsies (n=7)	+	4	2	5	4	0	2	2
	++	3	0	0	0	0	0	0
Autopsies (n=6)	Neg	0	6	5	4	4	2	2
	+	1	0	2	1	0	2	2
	++	5	0	0	1	2	2	2
	Neg	2	15	13	7	19	7	11
Disease (n=28)*	+	2	10	8	12	7	18	15
	++	24	3	7	9	2	3	2

* Diseased group: chronic active hepatitis (3), alcoholic hepatitis (6), alcoholic cirrhosis (7), non-alcoholic cirrhosis (3), primary biliary cirrhosis (5), extrahepatic biliary obstruction (4).

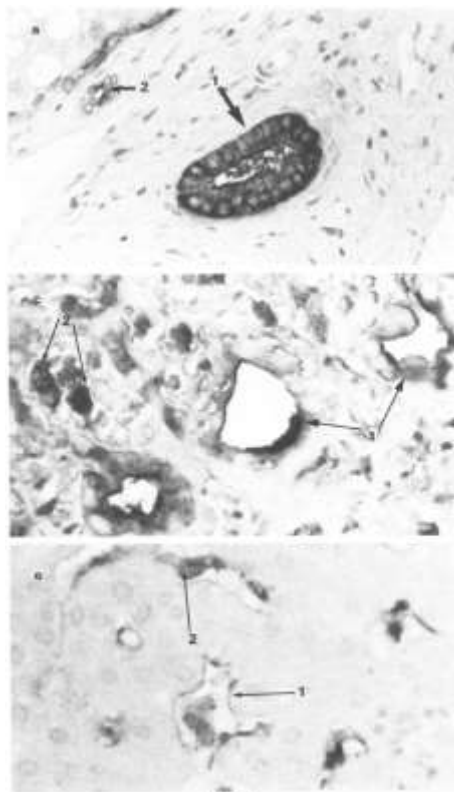


Fig. 3a, c, e.

Table 2. Distribution of IgA in liver biopsies

		Bile duct epithelium	Portal inflammatory cells	Portal vessels	Biliary canaliculi	Hepatocyte cytoplasm	Hepatic sinusoids	Sinusoidal phagocytes
Controls	Neg	1	2	0	5	0	0	0
Surgical biopsies (n=7)	+	6	5	4	2	1	1	1
	++	0	0	3	0	6	6	6
	Neg	0	4	0	6	0	0	0
Autopsies (n=6)	+	5	3	6	0	2	6	6
	++	1	0	0	0	4	0	0
Disease (n=28)	Neg	7	5	2	17	0	0	0
	+	19	20	13	7	5	8	8
	++	2	3	13	4	23	20	20

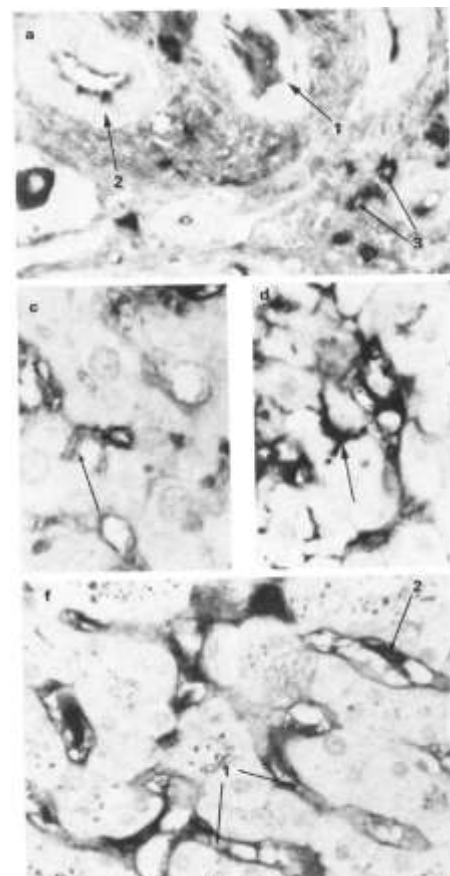


Fig. 4a, c, d, f.

Why Liver Transplant Pathology?



Paul McMaster
Consultant Surgeon, QEH, 1980 -2003

Occasional Review

Improved survival after orthotopic liver grafting

R Y CALNE, ROGER WILLIAMS, M LINDOP, J V FARMAN, M E TOLLEY, K ROLLES,
B MACDOUGALL, J NEUBERGER, R J WYKE, A T RAFTERY, T J DUFFY, D G D WIGHT,
D J G WHITE

BRITISH MEDICAL JOURNAL VOLUME 283 11 JULY 1981

- 108 liver transplants (Cambridge/Kings), 1968 -1981
- 20 survivors
- Recent 1 year survival 24% (versus 13% for first 46 patients transplanted)

Liver Transplantation in Birmingham (1982-1983)

OL Number	Date of Transplant	Indication for Transplant	Outcome
1	January 1982	Cirrhosis + Hepatocellular carcinoma	Died at 6 weeks, technical complications
2	May 1982	Hepatocellular carcinoma	Died 21 years later
3	June 1982	Primary biliary cirrhosis	Died 27 years later
4	Jan 1983	Primary biliary cirrhosis	Died 28 years later

Birmingham Liver Unit

The First 5000 Liver Transplants

Liver Transplant Number	Date
1	January 1982
1000	November 1994
2000	April 2001
3000	June 2007
4000	April 2013
5000	July 2017

International Symposium: Liver Transplantation & Liver Research in Birmingham

Celebrating 5000 Liver Transplants & 30 years of Liver Research

Birmingham, 5th - 6th September 2017

Programme of Events



Tuesday 5th September

10.30 *Registration & Refreshments*

Session 1:

Chairs; Mr John Isaac, Clinical Service Lead, Queen Elizabeth Hospital Birmingham & Dr Scott Russell, Consultant Anaesthetist, Queen Elizabeth Hospital Birmingham

11.30 **Welcome**

Mr Thamara Perera, Consultant Transplant Surgeon,
Queen Elizabeth Hospital Birmingham & Birmingham Children's Hospital

11.35 **Introduction on behalf of Queen Elizabeth Hospital Birmingham**

Dame Julie Moore DBE, Chief Executive, University Hospitals Birmingham NHSFT

11.40 **Introduction of behalf of Birmingham Children's Hospital**

Sarah-Jane Marsh, Chief Executive, Birmingham Women's and Children's NHSFT

11.45 **The Birmingham Liver Unit**

Professor Stefan Hübscher, Leith Professor and Professor of Hepatic Pathology, University of Birmingham

12.05 **KEYNOTE LECTURE: How Liver Surgery entered into the field of liver Transplantation**

Professor Henri Bismuth, Paul Brousse Hospital, Paris

A Review of Liver Transplant Pathology – With Focus on Rejection (Liver Unit Meeting circa September 1983)

Most pathological studies incorporated into clinical reviews

Liver biopsies not used in routine clinical assessment

- Samples taken often showed complex changes, difficult to interpret
- Many observations based on study of failed liver allografts

Rejection not thought to be a major problem

No clear consensus regarding pathological features of rejection

From late 1983, liver biopsies obtained routinely in Birmingham :

- **End of first week**
- **To investigate graft dysfunction**

A Study of Early Post-Transplant Biopsies in Birmingham (late 1983 – early 1985)

21 biopsies from seven patients, 6-102 days post transplant

Exclusion of other causes of graft dysfunction (infection, ischaemia, biliary obstruction)

Histological features of acute rejection:

- Portal inflammation
- Bile duct inflammation
- Venous endothelial inflammation

5/7 cases resolved with increased immunosuppression

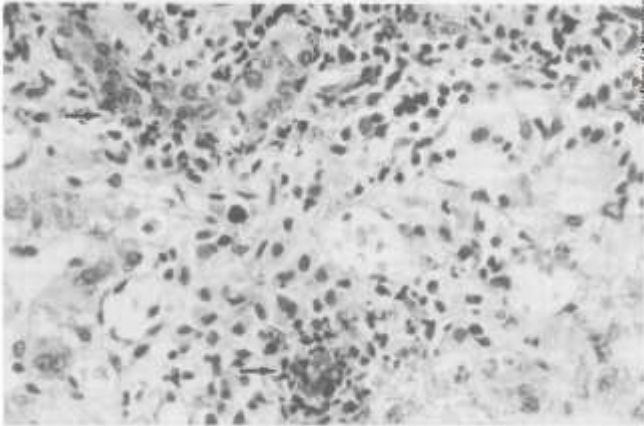
2/7 developed graft failure (chronic rejection)

- Bile duct loss
- Foam cell arteriopathy

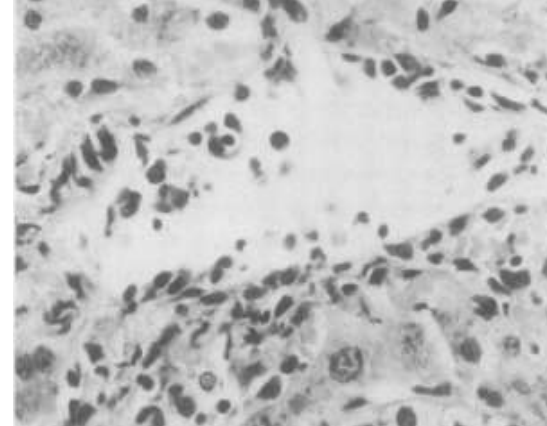
Biopsy findings in cases of rejection of liver allograft

SG HUBSCHER, D CLEMENTS,* E ELIAS,* P McMASTER†

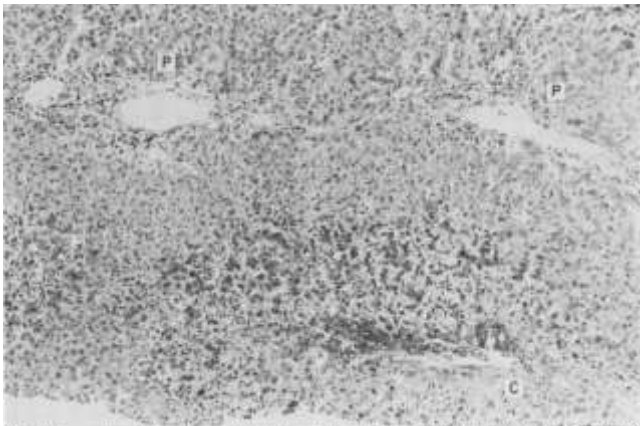
*From the Department of Pathology, The Medical School, University of Birmingham, and the Departments of *Medicine and †Surgery, Queen Elizabeth Hospital, Edgbaston, Birmingham*



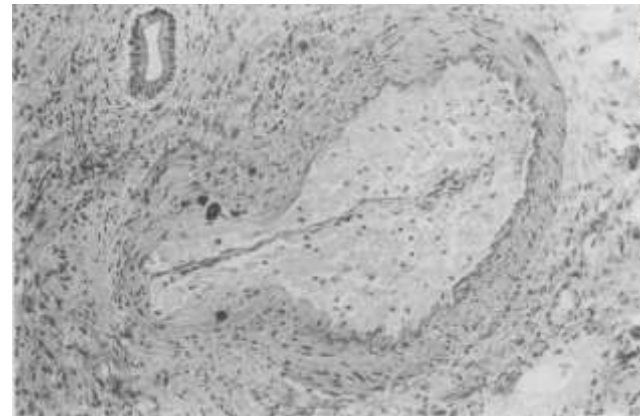
Liver biopsy, day 15 post-transplant. Mixed portal inflammatory infiltrate. Neutrophils infiltrating bile duct epithelium



Liver biopsy, day 7 post-transplant. Hepatic venous endothelial inflammation



Liver Biopsy, day 28 post-transplant. Severe centrilobular cholestasis. Portal tracts contain no bile ducts



Post mortem liver, 5 months post-transplant. Hepatic artery contains subendothelial foam cells

Liver Transplantation in Birmingham

Three (of many) legacies bequeathed by Elias & McMaster



Bridget Gunson

1. Multidisciplinary working

2. Data collection

- By September 2017, Liver Transplant Database had information from >11,000 patients
- Also databases for Liver Medicine and Hepatobiliary Surgery

3. Establishing a research centre



**Centre for Liver & Gastrointestinal Research
University of Birmingham**



David Adams



Phil Newsome

Department of Pathology and Birmingham Liver Unit

Other colleagues who I have enjoyed working with and who have influenced my career during the past 40 years.

Too numerous to mention!

Liver Pathology in the United Kingdom

Illustrious Predecessors



Peter Scheuer
(15/11/1928 – 01/03/2006)



Bernard Portmann
(06/02/1940 – 22/04/2018)



Roddy MacSween
(02/02/1935 – 11/12/2015)

International Liver Study Group (Gnomes) Meeting - Washington DC, May 1997
Chief Gnome – Kamal Ishak



Liver Pathology in the UK

- 1. National Liver Histopathology EQA Scheme (1994 -)**
- 2. Annual Liver Update Meetings (2005 -)**
- 3. Establishing liver pathology as a distinct entity**
 - Liver Pathology Subcommittee of BSG Pathology Section (2007-2016)
 - UK Liver Pathology Group (2016-)

National Liver Pathology External Quality Assurance (EQA) Scheme

Scheme Organisers

- Alastair Burt (1994 – 2004)
- Judy Wyatt (2004 – present)

Deputy scheme organisers: Stefan Hübscher (2004 - 2018), Rachel Brown (2018 – present)

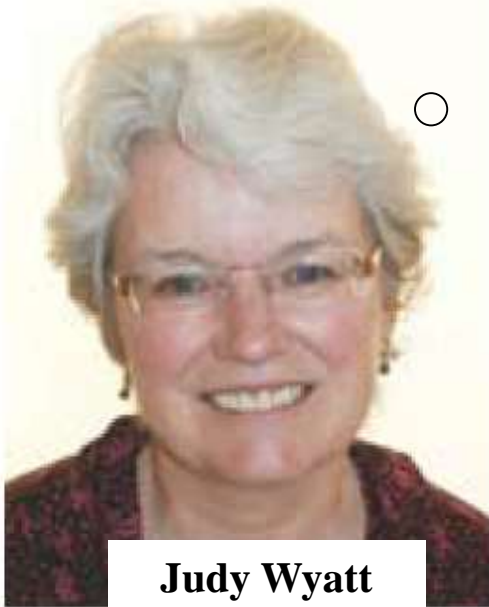
Format of Slide Circulations / Scoring / Discussion:

- Glass slides only / glass slides + digital (including special stains) /digital only
- Meetings initially “stand alone” or alongside other national meetings (BSG, Path Soc)
- Since 2011, EQA discussions incorporated into annual liver update meetings
- Methods of scoring evolved to reflect complexity of medical liver biopsy interpretation
- Opportunity to learn from different people’s perspectives and from complex cases where consensus cannot be reached (“not for scoring”)
- Introduction of “masterclass” discussions for complex/contentious cases.

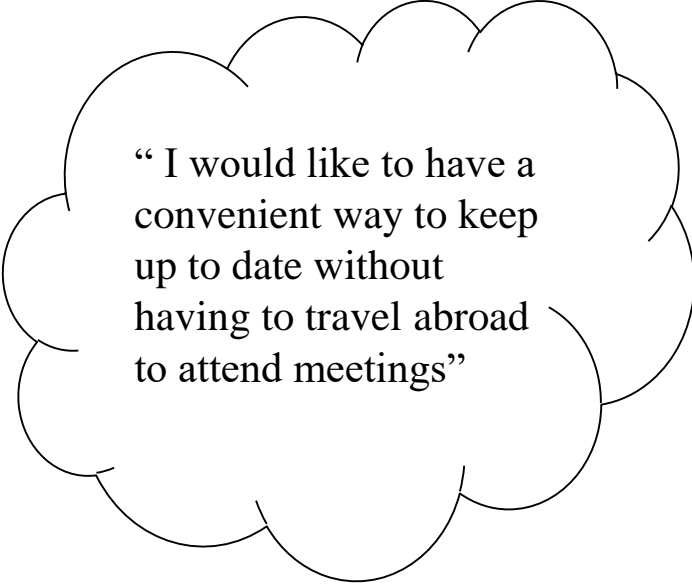
Liver Pathology in the UK

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Annual Liver Update Meetings



Judy Wyatt

A large, cloud-shaped thought bubble with a scalloped border. It is connected to the portrait of Judy Wyatt by three small circles of increasing size. The text inside the bubble is: "I would like to have a convenient way to keep up to date without having to travel abroad to attend meetings".

“ I would like to have a convenient way to keep up to date without having to travel abroad to attend meetings”

Regular Features at Liver Update Meetings

- Update from this year’s AASLD Meeting - Rob Goldin
- Update from this year’s Gnomes Meeting - Alastair Burt, Stefan Hübscher
- Occasional updates from other meetings (EASL, ECP)
- “What’s hot” topics
- Since 2011 – Liver EQA discussions

Liver Update Meetings 2005-2019 - Presentations by Stefan Hübscher

Year	Venue	Subject of talk
2005	Southampton	Role of liver biopsy in acute and chronic hepatitis
2006	Nottingham	Pathology of autoimmune overlap syndromes
2007	Lancaster	Histological assessment of late post-transplant liver biopsies
2008	London	Histological assessment of inflammatory liver diseases
2009	London	Post-liver transplant infections
2010	Dundee	Non-cirrhotic portal hypertension
2011	Southampton	Role of liver biopsy in AIH, PBC and PSC
2012	Leeds	Update on NAFLD
2013	London	Update on HCC
2014	Stratford *	Well differentiated hepatocellular lesions
2015	Harrogate *	Acute hepatitis and acute liver failure
2016	Gloucester*	Patterns of acute liver injury
2017	Oxford*	Non-tumoral vascular diseases
2018	London*	Drug-induced liver injury
2019	Cambridge*	Primary malignant epithelial neoplasms of the liver

* 2014-2019 = Updates from this year's Gnomes meeting

Liver Pathology in the UK

1. National Liver Histopathology EQA Scheme (1994 -)
2. Annual Liver Update Meetings (2005 -)
3. **Establishing liver pathology as a distinct entity**
 - **Liver Pathology Subcommittee of BSG Pathology Section (2007-2016)**
 - Chair - Stefan Hübscher
 - Secretary – Judy Wyatt
 - **UK Liver Pathology Group (2016-)**
 - Chair - Stefan Hübscher (until September 2020), then Rachel Brown
 - Secretary – Judy Wyatt

UK Liver Pathology Group

The UK Liver Pathology Group (UKLPG)
was formed in 2016 with the purpose:

To promote excellence in liver histopathology services in
the UK and Ireland, across all levels of specialisation,
through professional collaboration in education, quality
assurance and research.



International Liver Pathology Collaborations

International Liver Pathology Collaborations

1. International Liver Study Group (aka “Gnomes”)

- First meeting attended by SGH in June 1995, Loch Lomond (Chief Gnome – Roddy MacSween)

2. Banff Working Group on Liver Allograft Pathology

- First Banff liver sessions held in July 1995, Banff Centre, Alberta, Canada

Annual Meetings of the International Liver Study Group

- First meeting, July 1968, University of Zürich (Martin Schmid)
- Approximately 15 circulating members - current members based in Europe (8), North America (4) , Australia (1) , Asia (1)
- Also non-circulating members (including non-pathologists)

- Cases circulated prior to meeting (2/person) to cover particular theme
- Suggested diagnoses submitted prior to meeting and collated by local organiser

- Cases presented and discussed further at meeting (2 days)
- Aim to reach consensus and provide summary/guidelines

A CLASSIFICATION OF CHRONIC HEPATITIS

J. DE GROOTE
M.D., A.H.O. Leuven

PROFESSOR OF MEDICINE

ACADEMISCH ZIEKENHUIS ST. RAFAËL, LEUVEN, BELGIUM

P. GEDIGK
Dr.med. Innsbruck

PROFESSOR OF PATHOLOGY,
UNIVERSITY OF BONN, GERMANY

H. POPPER
M.D. Vienna, Ph.D. Illinois
PROFESSOR OF PATHOLOGY,
MOUNT SINAI SCHOOL OF
MEDICINE, NEW YORK, U.S.A.

P. J. SCHEUER
M.D. Lond., M.C.Path.
SENIOR LECTURER
IN MORBID ANATOMY,
ROYAL FREE HOSPITAL SCHOOL
OF MEDICINE, LONDON W.C.1

H. THALER
M.D. Vienna
UNIVERSITY LECTURER,
WILHELMINENSPITAL,
VIENNA, AUSTRIA

V. J. DESMET
M.D., A.H.O. Leuven

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M.D. Basle
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OF MEDICINE,
STADTSPITAL WAID,
ZÜRICH, SWITZERLAND

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PROFESSOR OF PATHOLOGY,
UNIVERSITY OF ZÜRICH,
SWITZERLAND

W. WEPLER
Dr.med.

DIRECTOR, INSTITUTE OF PATHOLOGY, STADTKRANKENHAUS,
KASSEL, GERMANY

Special Article

Histological grading and staging of chronic hepatitis

Kamal Ishak¹, Amelia Baptista², Leonardo Bianchi³, Francesco Callea⁴, Jan De Groote⁵, Fred Gudat⁶, Helmut Denk⁷, Valeer Desmet⁸, Gerhard Korb⁹, Roderick N. M. MacSween¹⁰, M. James Phillips¹¹, Bernard G. Portmann¹², Hemming Poulsen¹³, Peter J. Scheuer¹⁴, Martin Schmid¹⁵ and Heribert Thaler¹⁶

¹*Armed Forces Institute of Pathology, Washington, USA,* ²*University of Lisbon, Lisbon, Portugal,* ³*Hofstetten, Switzerland,* ⁴*Servizio di Anatomia e Istologia Patologica, Spedali Civili, Brescia, Italy,* ⁵*Department of Medicine, University of Leuven, Leuven, Belgium,* ⁶*Institute for Pathology, University of Basel, Basel, Switzerland,* ⁷*Department of Pathology, University of Graz, Graz, Austria,* ⁸*Department of Pathology, University of Leuven, Leuven, Belgium,* ⁹*Weiden, Germany,* ¹⁰*Department of Pathology, Western Infirmary, University of Glasgow, Glasgow, UK,* ¹¹*Department of Pathology, Hospital for Sick Children, University of Toronto, Toronto, Canada,* ¹²*Institute of Liver Studies, King's College Hospital, London, UK,* ¹³*Frederiksberg, Denmark,* ¹⁵*Watt, Switzerland,* ¹⁶*Vienna, Austria*



Gnomes Meeting, Birmingham, May 2015

Gnomes Meeting , Athens, May 2018 - Group Photograph by the Parthenon



The Ceremonial Transfer of the Gnomes Hat



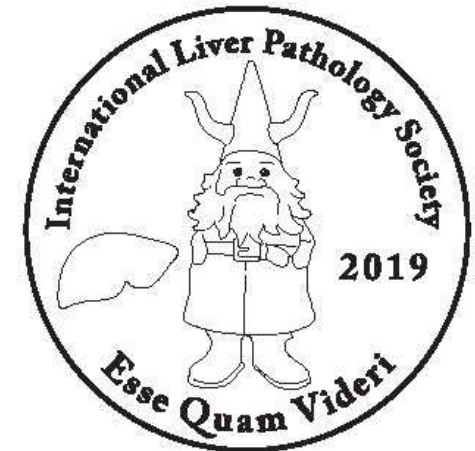
Ravello, Italy – June 2014
Receiving hat from Luigi Terracciano



Birmingham – May 2015
Transferring hat to Alastair Burt

Gnomes Meeting - Rochester, Minnesota June 19-22 2019

Primary Malignant Epithelial Neoplasms of the Liver Chief Gnome – Michael Torbenson



(To be rather than to seem)



Gnomes Meeting, Washington, May 4th – 6th 2022

The Banff Conferences on Allograft Pathology

The Banff Conferences on Allograft Pathology



The Banff Conferences on Allograft Pathology



Kim Solez

Professor and Chairman, Department of Pathology, University of Alberta (1987–92)
Director of Experimental Pathology, Department of Laboratory Medicine and Pathology,
University of Alberta (1992-)

The Banff Conferences on Allograft Pathology

- First meeting held in 1991 in Banff, Canada
- Meetings held every 2 years since then
- First liver sessions held at 3rd Banff Conference, July 1995
- Multidisciplinary meetings attended by pathologists, physicians, surgeons, basic scientists + others with an interest in organ transplantation
- Working groups aim to reach consensus concerning the classification and diagnosis of rejection (and other allograft complications)
- Produce guidelines documents
 - 5 documents produced by Banff Working Group on Liver Allograft Pathology

First Banff Liver Session, Banff Centre, Banff, Canada – July 1995





Jake Demetris

Starzl Professor of Transplant Pathology and Director, Division of Liver and Transplantation Pathology.
University of Pittsburgh, PA



Chris Bellamy



Desley Neil

Banff Working Group on Liver Allograft Pathology – Guidelines Documents

**Banff Schema for Grading Liver Allograft Rejection:
An International Consensus Document**

Hepatology 1997;25:658-663

**Update of the International Banff Schema for Liver Allograft
Rejection: Working Recommendations for the Histopathologic
Staging and Reporting of Chronic Rejection**

Hepatology 2000; 31: 792-799

**Liver Biopsy Interpretation for Causes of Late Liver
Allograft Dysfunction**

Hepatology 2006; 44: 489-501

**Importance of Liver Biopsy Findings in
Immunosuppression Management: Biopsy
Monitoring and Working Criteria for Patients
With Operational Tolerance**

Liver Transplantation 2012; 18: 1154-1170

**2016 Comprehensive Update of the Banff Working
Group on Liver Allograft Pathology: Introduction of
Antibody-Mediated Rejection**

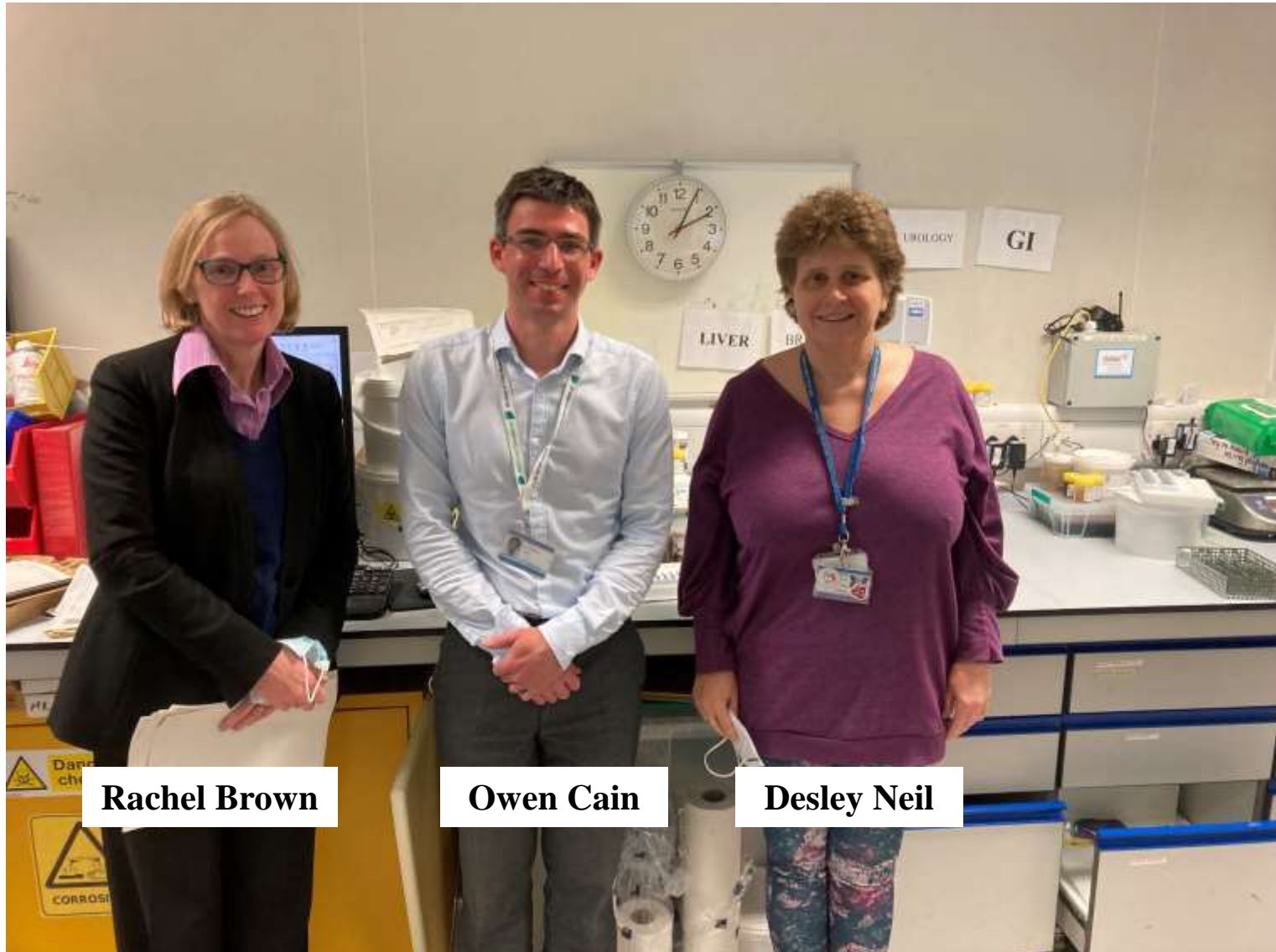
Am J Transpl. 2016; 16: 2816-2835

What Next?

1. For liver pathology in Birmingham?

2. For me?

The Liver Pathology Team at UHB in 2022



Rachel Brown

Owen Cain

Desley Neil

What Next?

1. For liver pathology in Birmingham?

2. For me?

ORIGINAL ARTICLE

Standardizing the histological assessment of late posttransplantation biopsies from pediatric liver allograft recipients

1 Stefan G. Hübscher^{1,2} | Sandy Feng³ | Annette S. H. Gouw⁴ | Hironori Haga⁵ |
2 Hyo Jeong Kang⁶ | Deirdre A. Kelly⁷ | Mina Komuta⁸ | Andrew Lesniak⁹ |
Benjamin A. Popp⁹ | Henkjan J. Verkade^{10,11} | Eunsil Yu⁶ | Anthony J. Demetris⁹

¹Institute of Immunology and Immunotherapy, University of Birmingham, Birmingham, UK

²Department of Cellular Pathology, University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK

³Division of Transplantation, Department of Surgery, University of California, San Francisco, California, USA

⁴Department of Pathology and Medical Biology, University Medical Center Groningen, Groningen, the Netherlands

⁵Department of Diagnostic Pathology, Graduate School of Medicine, Kyoto University, Kyoto, Japan

⁶Department of Pathology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea

⁷Liver Unit, Birmingham Women's & Children's NHS Trust and University of Birmingham, Birmingham, UK

⁸Department of Pathology, Keio University, Tokyo, Japan

⁹Division of Liver and Transplantation Pathology, Department of Pathology, University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania, USA

¹⁰Pediatric Gastroenterology/Hepatology, Department of Pediatrics, University of Groningen, University Medical Center Groningen, Groningen, the Netherlands

3 ¹¹European Reference Network on Hepatological Diseases (ERN RARE-LIVER)

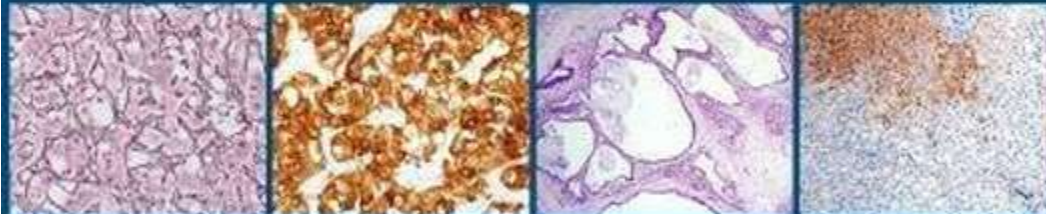
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MacSween's
Pathology
of the Liver



Alastair D. Burt
Linda D. Ferrell
Stefan G. Hübscher

ELSEVIER



Eighth Edition

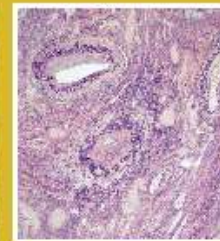
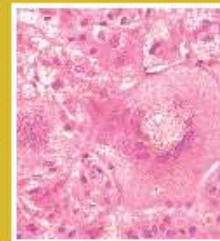


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DIGITAL
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Burt
Ferrell
Hübscher

MacSween's
PATHOLOGY of the LIVER

MacSween's **PATHOLOGY** *of the* **LIVER**



Eighth
Edition



Alastair D. Burt
Linda D. Ferrell
Stefan G. Hübscher





www.westbrom.com

English Football League Championship Table, 7th May 2022

	Team	Played	Won	Drawn	Lost	For	Against	GD	Points
1	— Fulham	46	27	9	10	106	43	63	90
2	— AFC Bournemouth	46	25	13	8	74	39	35	88
3	— Huddersfield Town	46	23	13	10	64	47	17	82
4	— Nottingham Forest	46	23	11	12	73	40	33	80
5	— Sheffield United	46	21	12	13	63	45	18	75
6	— Luton Town	46	21	12	13	63	55	8	75
7	— Middlesbrough	46	20	10	16	59	50	9	70
8	— Blackburn Rovers	46	19	12	15	59	50	9	69
9	— Millwall	46	18	15	13	53	45	8	69
10	— West Bromwich Albion	46	18	13	15	52	45	7	67
11	— Queens Park Rangers	46	19	9	18	60	59	1	66
12	— Coventry City	46	17	13	16	60	59	1	64
13	— Preston North End	46	16	16	14	52	56	-4	64
14	— Stoke City	46	17	11	18	57	52	5	62
15	— Swansea City	46	16	13	17	58	68	-10	61
16	— Blackpool	46	16	12	18	54	58	-4	60
17	— Bristol City	46	15	10	21	62	77	-15	55
18	— Cardiff City	46	15	8	23	50	68	-18	53
19	— Hull City	46	14	9	23	41	54	-13	51
20	— Birmingham City	46	11	14	21	50	75	-25	47
21	— Reading	46	13	8	25	54	87	-33	41
22	— Peterborough United	46	9	10	27	43	87	-44	37
23	— Derby County	46	14	13	19	45	53	-8	34
24	— Barnsley	46	6	12	28	33	73	-40	30



April 2007



**THE UNIVERSITY
OF BIRMINGHAM**

Inaugural Lecture

**Liver Transplantation through the Eyes of a
Pathologist**

**Professor Stefan Hübscher
Professor of Hepatic Pathology
Division of Cancer Studies**

at 5.15 pm on Wednesday 4th April 2007

in the Leonard Deacon Lecture Theatre
Medical School

SCHOOL OF MEDICINE



Brewdog Beer School, Birmingham, 5th May 2022



James and Sophie's Engagement Party, November 2021



Tom & Anne's Wedding, October 2019



And, finally.....

Thank you!