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Milestones

50 years of Hepatology: The Royal Free Hospital School of Hepatology

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ABSTRACT

Writing about the history of Hepatology would necessarily imply writing about the history of the Liver Unit and the School of Hepatology created by Dr. Sheila Scherlock at the Royal Free Hospital (London). On the 70th anniversary of the creation of the first liver unit (Hammersmith Hospital) this article presents a brief account of the history, organization, structure, educational program and contributions of perhaps the first and the most influential medical research models created for the study of liver diseases: the Royal Free Hospital Liver Unit.

1. Introduction

Hepatology as a modern discipline can trace its origins back to the "Liver rounds" by Hans Popper in Chicago in the 1940s and the creation of the American Association for the Study of Liver Diseases (AASLD) in 1948. The term *Hepatology* seems to have been born at the first International Association for the Study of the Liver (IASL) meeting in 1958 presided by Dr. Sheila Sherlock [1–3].

Coming up to the 70th anniversary of the creation of the first liver research unit in the world we present a brief account of the history of the Liver Unit at the Royal Free Hospital from its inception (1948) to the merger of the Royal Free Hospital School of Medicine (RFHSM) with University College London (1998).

2. Dame Sheila Sherlock

> "*A teacher to her students, a healer to her patients, a mentor to her colleagues, a perfect companion to her husband and a trusted friend to those who had the privilege to know her.*" (O.P. Sharma) [4].

Sheila Sherlock (1918–2001) has been considered by many as the world's most famous liver doctor [5,6]. Some of her first steps in liver medicine can be traced to the Hammersmith Hospital in London where she learnt the relatively new technique of liver biopsy resulting in an article published in The Lancet in 1943 [7]. When she first set up a "special unit for liver diseases" at the Hammersmith Hospital between 1948 and 1949 [4] her major interests then were hepatic handling of glucose, the patho-physiology of portal circulation, hepatic encephalopathy (she coined the term) [1] and the treatment of fluid retention in liver disease. Dr. Sherlock's unique personality and example stimulated those around her to achieve their best [8]. A former fellow wrote: "she taught us how to be a caring physician, a specialist physician, a clinical researcher, a teacher, and how to make this world a better place" [4]. Dame Sheila was an outstanding speaker in her typical concise, well-organized and thoroughly to the point style [8] and tried to transmit those abilities to her fellows. She received many honours including the royal appointment as Dame Commander of the British Empire (DBE) from which she became widely known as *Dame Sheila*. She started working at the old Royal Free Hospital site, which housed the Liver Unit, at Gray's Inn Road from 1959 and moved subsequently to the new Royal Free Hospital at Pond Street, in Hampstead [1], where she worked until 1983 when she retired at age 65.

3. Liver unit

One of the contributions of the Royal Free Hospital to Hepatology and to Medicine in general was a model of a clinical research unit. This was initiated in the Hammersmith Hospital where Dame Sheila initially formed a group with Henry Dible, Earl King, Barbara Billing, Alexander Bearn, Pete Reynolds, Jan de Groote and Frank Iber [1,9]. Soon, the 19-bed unit was full of clinicians and young researchers from the Commonwealth and North America [4]. In

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Fig. 1. Dame Sheila Sherlock (centre in white coat) with lecturers, consultants, scientists and a large number of national and international fellows and visitors at the Liver Unit in the Royal Free Hospital (Hampstead).

1959 Dr. Sherlock and a group of collaborators moved to the Royal Free Hospital at Gray's Inn Road. For 15 years the main unit was housed in what was called "the Hut" on the rooftop of the Hospital [1]. Despite the cramped condition excellent collaborative research was performed. Research workers and lecturers would be seen alike doing biochemistry or clinical work, plotting graphs, looking down microscopes all imbued with the enthusiasm characteristic of Dame Sheila's Liver unit [8].

The liver unit attracted leading clinicians and basic scientists from all continents, organizing research groups into different areas of liver disease which worked in specialized sections and laboratories housed under one roof. From the early years there were groups studying bilirubin metabolism, alcohol liver disease and hepatic encephalopathy, lipid metabolism, haemochromatosis and iron metabolism, cholestatic liver disease, portal hypertension and ascites, autoimmune liver disease, viral hepatitis, drug metabolism and hepatotoxicity, liver transplantation and more recently liver cancer and molecular biology. All of the above were complemented by excellent associated Departments such as Pathology and Radiology which also developed international reputations in liver disease. There Dr. Kenneth Hill (Pathology) had introduced the term "alcoholic hepatitis" [9]. He was followed by Dr. Peter Scheuer. The liver unit in Hampstead comprised 2 clinical wards and two wings for the research laboratories, offices, seminar rooms, clinical investigation rooms and the Ingram endoscopy and ERCP suite [1,9]. After the merge with University College it became the Sheila Sherlock Liver Centre.

The proximity of clinicians, academics, basic scientists, research laboratories, imaging services and hospitalized patients provided the opportunity for optimal clinical care and facilitated clinical and translational research. It was a model later reproduced by many former fellows in many parts of the world [10] (see below). Members of the Unit usually had a lectureship at the medical school and a National Health Service post which ensured their full-time involvement with the unit's programs. Research groups formed around particular lines of research and most frequently a research laboratory, each having a leader and technicians, research fellows, PhD students, visiting scholars and visiting fellows [6]. At one time 28 different nationalities were counted among the fellows, lecturers and academics (Fig. 1).

4. Educational program

As in the traditional English system, fellows were allocated to a particular area of study of the liver under the supervision of the Professor or Senior Lecturer. There would always be an expert scientist to oversee the laboratory work. When the Professor judged that the research fellow, registrar or PhD student had worked enough, he or she would be called to her or his office for review and analysis of the results [9]. Fellows were expected to submit abstracts of their work to national and international scientific meetings [6,11]. Before presenting their work to conferences, exhaustive rehearsals were required. These were serious occasions and Professor Sherlock demanded clear, concise, confident and informative presentations. Trainees would frequently be told to improve delivery, restructure complicated slides, rearrange the presentations or to improve diagrams and illustrations [4,11]. Sharp and sometimes fierce criticisms would be followed by warm expressions of support and camaraderie which would add to that feeling that the liver unit was the centre of things and that everything new in liver disease was happening around there [11]. Basic science presentations would be no easier as most of the lecturers had a strong basic science background. It was through this and other presentations at the unit that fellows got their first understanding of how to construct and deliver a scientific paper [11]. When the presentations were transformed into written articles ready for publication the Professor would review them again and make new corrections. The edited versions emerged as examples of creative elegance with simple figures, clean tables and accessible line diagrams [4].

The high point of the week was the Professor's general ward round. Lecturers, fellows, registrars, students and often visiting dignitaries would attend. This was followed on Wednesday afternoons by a clinical meeting for case discussions. Typically the Professor would start the discussion directing questions to the students. Then she would question junior doctors preparing for the membership to the Royal College of Physicians (MRCP) and finally the lecturers and Professors. Visiting dignitaries were not spared and could expect to be subjected to a certain amount of questioning. No prisoners were taken during these discussions and individuals new to the unit could find it a little intimidating. Nevertheless the meeting was always conducted in the spirit of honest academic inquiry with zest and good humour and for the majority it was a most refreshing and enjoyable experience. No doubt, the one best prepared for the meeting and for all meetings was the Professor, armed with the most recent scientific articles and medical literature and having previously discussed the case with several specialists.

The unit had a weekly liver pathology meeting presided over by Professor Peter Scheuer who was a quietly spoken gentleman who was very confident of his art. There was also a weekly radiology meeting with Dr. Robert (Bob) Dick. The radiology conference room was small and crowded and Dr. Dick was a larger than life character that made the Royal Free a major centre for liver imaging and interventional radiology. The scientific program included a journal club meeting (bibliography review) every other week and there was also a "research in progress" meeting where 1 or 2 fellows would present their on-going research. There was also an annual liver update meeting with international faculty that would be attended by an international crowd joined for three days that ended in a small tennis tournament. At a time when there was no internet or digital libraries a good library was an essential complement to the research work and the Royal Free Hospital had one.

5. Scientific contributions

The contributions of the Royal Free Liver Unit to the Hepatology field over the years are numerous, varied and, in many cases,

transcendental but difficult to list in a limited space. Some examples include: the introduction of new techniques such as hepatic vein catheterization, intrasplenic pressure measurement and venography into the assessment of portal hypertension; the description of different patterns of portal hypertension, the understanding of the pathophysiology of ascites and the role of new diuretics; the role of the hepatitis B virus (when it was still known as the "Australia antigen") in the development of cirrhosis and liver cancer, autoimmunity as the cause of primary biliary cirrhosis including the description of the mitochondrial antibody; use of corticosteroid therapy for autoimmune hepatitis; in hepatic encephalopathy, the first descriptions of the neuropathological syndromes and their relationship to collateral shunting as well as the introduction of the term "portal systemic encephalopathy" [12]; alcoholic cirrhosis, complex lipoprotein changes in liver disease [2]. Classic articles were produced on the circulatory changes in the lungs, kidneys and peripheries, on unconjugated hyperbilirubinaemias, on Wilson's disease, haemochromatosis, the Budd–Chiari syndrome, extrahepatic portal vein block, partial nodular transformation of the liver, and primary sclerosing cholangitis [13]. Another major area was liver transplantation which started in 1984–1985. New contributions continue to be produced and many more are expected to be developed in the coming years [5].

6. Publications

Many articles and publications came out from the Royal Free Liver Unit; 718 were written or co-authored by Dame Sheila [2,10] and a recent citation search showed 26,769 citations.

6.1. Diseases of the liver and biliary system

Professor Sherlock wrote, edited and collaborated in many books but one of the most famous liver text books in the world is her *Diseases of the Liver and Biliary System* [2,13] which reached its 13th edition now co-edited with former Royal Free fellows [14].

7. The Royal Free Liver Unit Alumni: an academic family

Dr. Sherlock always cared for all the members of the Liver Unit to participate in social, cultural and sporting activities apart from the educational and research program.

Both young and renowned clinicians and basic scientists from many countries visited regularly and participated in the academic and research program. They were coming from around the world including a large number of fellows from Latin America including: Matías Burmicky (Venezuela), Octavio Campollo (Guadalajara, Mex.), René Cárdenas (Mexico city), Martha Fillipi (Brazil), Joao Galizzi (Brazil), Miguel Garassini (Venezuela), Luis C. Gayotto (Brazil), Luis Guevara (Mexico city), David Kershenobich (Mexico), Juan Lagarriga (Mexico), Vera L. Lima (Brazil), Alfredo Marten (Costa Rica), Linda Muñoz (Mexico), Silvano Raia (Brazil), Edna Strauss (Brazil), Rosangela Texeira (Brazil) and Marta Velasco (Chile). Several of those founded liver units in their homecountries like in the case of Dr. Luis Guevara who founded with David Kershenobich and Misael Uribe the Liver Unit at the National institute of Nutrition (INNSZ) in Mexico [10] (Fig. 2).

Several members remained after Dr. Sherlock's retirement to continue the tradition of the school of Hepatology: Prof. Neil McIntyre, Dr. James Dooley, Prof. Andy K. Burroughs and Marsha Morgan, to be joined by Geff Dusheiko, Pat Moore, David Patch and Humphrey Hodgson and most recently Prof. Massimo Pinzani.

The history of Hepatology cannot be written without including the history of the Liver Unit at the Royal Free Hospital in London, founded by Dame Sheila Scherlock. The notable contributions and teachings of the Royal Free Hospital's School of Hepatology – "a centre for the investigation and treatment of liver disease" [5] – are milestones in the history of Hepatology [15].

Fig. 2. Dame Sheila Sherlock with Prof. Luis Guevara (R) and Prof. Octavio Campollo (L).

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Conflict of interest

The authors have no conflicts of interest to declare.

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References

[1] McIntyre N. Sheila. Hepatology 2002;35:507–9, http://dx.doi.org/10.1053/jhep.2002.0350507.
[2] Popper H. Sheila Sherlock. In: A career in Medicine. London: Smith Kline & French Laboratories Ltd.; 1983.
[3] Guevara L. Professor Dame Sheila Sherlock (1918–2001). Ann Hepatol 2002;1(1):5, http://dx.doi.org/10.1016/S1665-2681(19)32185-4.
[4] Sharma OP. The life of Sheila Sherlock "The Liver Queen". London: Royal College of Physicians; 2007.
[5] Hodgson H. Sheila Sherlock's legacy. Lancet 2002;359:460, http://dx.doi.org/10.1016/S0140-6736(02)07673-0.
[6] Heathcote J. Personal reminiscences: Sheila Sherlock. Hepatology 2002;35:1536–7, http://dx.doi.org/10.1053/jhep.2002.34132.
[7] Dible JH, McMichael J, Sherlock S. Pathology of acute hepatitis. Aspiration biopsy studies of epidemic, arsenotherapy and serum hepatitis. Lancet 1943;2:402, http://dx.doi.org/10.1016/S0140-6736(00)87419-X.
[8] Pepys M. Dame Sheila Patricia Violet Sherlock 31 March 1918. Biogr Mem Fellows R Soc 2003;49:475–93, http://dx.doi.org/10.1098/rsbm.2003.0028.
[9] Dooley J. Dame Sheila Sherlock (1918–2001). Life and work. Freiburg: Falk Foundation; 2003.
[10] Campollo O.Presentation. Proceedings of the international symposium on liver diseases. Guadalajara, Mex: Sociedad de Gastroenterología de Jalisco; 2003.

[11] Smallwood R. A fellow at the Free. Gut 1978;19:465–7, http://dx.doi.org/10.1136/gut.19.6.465.
[12] Sherlock S, Summerskill WHJ, White LP, Phear EA. Portal-systemic encephalopathy: neurological complications of liver disease. Lancet 1954;2:453–7, http://dx.doi.org/10.1016/S0140-6736(54)91874-7.
[13] Sherlock S, Dooley J. Diseases of the liver and biliary system. 11th ed. Oxford: Blackwell Science; 2002.
[14] Dooley JS, Lok ASF, Garcia G, Pinzani M. Sherlock's diseases of the liverand biliary system. 13th ed. Chichester, UK: Wiley-Blackwell; 2011, http://dx.doi.org/10.1002/9781444341294.
[15] Panduro A. Regeneration of Annals of Hepatology: renewed, active and growing stronger. Ann Hepatol 2019;18:279–80, http://dx.doi.org/10.1016/j.aohep.2019.04.002.