DAME SHEILA SHERLOCK, SPIDERS, CAPILLARIES, AND THE EVOLUTION OF HEPATOLOGY

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Dame Sheila Sherlock is an unprecedented and unparalleled towering figure in the entire history of hepatology, a discipline she defined and shaped. Her keen scientific mind and untiring drive led to many landmark discoveries, yet it was her unconventional mix of wit, satire, and a unique love-and-hate relationship with her colleagues and students that made her an icon. Notably, her most famous paper: “Spiders and Capillaries” published way back in time (Hepatology in 1989) encapsulated both her genius and her foresight into the future of liver diseases, predicting the profound changes that would sweep hepatology over the next half-century and more[1].

Born in 1918, Sherlock entered the arena of medicine and medical research at a time when the study of the liver was in its infancy. Her work, however, would take hepatology into uncharted territories. She famously remarked in the introduction to her landmark textbook Diseases of the Liver and Biliary System that the liver was “an organ like no other,” capable of resilience and regeneration, yet vulnerable to a cascade of pathologies[2]. Her focus on the vascular system within the liver, particularly the relationship between spider nevi and liver cirrhosis, transformed our understanding of portal hypertension and its manifestations[3],[4]. This work, along with her early investigations into hepatic encephalopathy, laid the ground for the modern understanding of liver failure[5].

Sherlock’s predictions about the viral aetiology of hepatitis were strikingly precise. As easily as in the 50s, she professed that hepatology would be revolutionized by the discovery of viral pathogens and the development of antiviral therapies[6]. Her foresight has been overwhelming for all over the decades, with the advent of hepatitis B and C research, and the subsequent development of potent antiviral agents that have transformed the treatment protocols[7].

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Her skepticism toward what she considered “pharmacological band-aids” for viral hepatitis later evolved into cautious optimism as drug development outpaced even her predictions[8].

Her love-hate relationship with students and colleagues was very well known, often characterized by sharp wit and biting criticism. All papers about her in her life and posthumously places her in high regards. It was this relentless pursuit of perfection that earned her both admiration and resentment. Students recall her arriving in the early morning hours to manage complex cases of ascites and hepatic encephalopathy, never asking for praise but demanding excellence[9]. Working with her was no enterprise for anyone as she was a perfectionist and sought professionalism with perfection. Her hands-on approach to clinical hepatology, coupled with her deep knowledge of the science, is reflected in her legacy as one of the founders of evidence-based hepatology[10]. She was known to do paracentesis in the wee hours of the morning when doing research on ammonia levels, even earlier than the junior doctors would be brushing their teeth and get prepared for their hospital routines.

The publication of her famous article published in 1989 in Hepatology: “Spiders and Capillaries” became a defining moment not only in her career but in the evolution of hepatology itself[11]. Sherlock hypothesized that the abnormal vascular patterns seen in cirrhosis were not merely cosmetic but held deep significance in understanding the pathology of liver disease. In this, she also foresaw a future where hepatology would intersect with vascular biology and immunology, a notion that has only gained momentum in recent years[12],[13].

Sherlock’s humor was peculiar and infamous, often undercutting the seriousness of her work with biting one-liners. She once quipped that liver disease “is the great imitator—except it doesn’t really have to try,” reflecting both her deep understanding and frustration with the field’s diagnostic complexity[14]. In a satirical manner much before her, WB Bean penned the following verse, alluding to the outward signs of chronic liver disease[15].

An old Miss Muffett

Decided to rough it
And lived on whisky and gin.
Red hands and a spider
Developed outside her
And such are the wages of sin

For decades scientists did not improve upon these words till came along Sheila Sherlock. She not only knew the Miss Muffet, she knew well how her hands were and her belly and then her inside out.

Despite her humour, she was acutely aware of the limitations of the time, particularly in diagnosing and treating end-stage liver disease[16].

One cannot discuss Dame Sheila Sherlock without acknowledging her paradigm-shifting contributions to hepatology. Her 1972 paper on hepatic encephalopathy provided a conceptual framework for understanding the toxic metabolic products in liver disease, particularly ammonia[17]. These insights led to the development of treatments that are still foundational today. In her later years, she reflected on the challenges hepatology faced: “Hepatology will evolve faster than any of us can predict, and yet, it will always be flawed by our inability to fully grasp the liver’s complexity”[18]. Today, as new drugs targeting viral hepatitis, non-alcoholic steatohepatitis (NASH), and hepatocellular carcinoma flood the market[19,20], it’s clear that her predictions continue to resonate.

Yet, despite these advances, Sherlock would likely argue that the field is far from perfect. While the introduction of direct-acting antivirals for hepatitis C has transformed outcomes, and hepatology is moving toward precision medicine, the quest for a deeper understanding of liver pathophysiology remains ongoing[21,22]. Research into liver regeneration, fibrosis, and the microbiome suggests that Sherlock’s vision for the future of hepatology is still being realized[23,24]. As hepatologists strive to develop curative treatments for chronic liver diseases, Sherlock’s insights serve as a reminder that hepatology, like the liver itself, will continue to evolve.

Dame Sheila Sherlock’s legacy in hepatology is undeniable. Her early contributions to the study of cirrhosis, portal hypertension, and viral hepatitis laid the foundation for the tremendous advances that followed[25,26]. Her blend of scientific rigour, clinical intuition, and sharp satire made her not only a pioneer but also a legend in her field. As hepatology continues to evolve at an unprecedented pace, her words echo through time: “There will be no limits to what we can learn about the liver, but there will always be a limit to what we can fully understand”[27].

References:

1. Sherlock S. Spiders and capillaries. Hepatology. 1989;9(1):183–4. doi:10.1002/hep.1840090129.
2. Sherlock S. Diseases of the Liver and Biliary System. 7th ed. Oxford: Blackwell Scientific Publications; 1975.
3. Sherlock S. Portal hypertension. BMJ. 1957;2(5032):667–9. doi:10.1136/bmj.2.5032.667.
4. Sherlock S, Dooley J. Diseases of the Liver and Biliary System. 11th ed. Wiley-Blackwell; 2002.
5. Sherlock S. Hepatic encephalopathy: a clinical and biochemical study. Lancet. 1954;2:454–7. doi:10.1016/S0140-6736(54)90861-8.
6. Sherlock S. Viruses and liver disease. J Hepatol. 1984;1:103–10. doi:10.1016/S0168-8278(84)80016-4.
7. Alter HJ, Seeff LB. Hepatitis C: The end of the beginning and possibly the beginning of the end. Ann Intern Med. 2000;132(7):605–8. doi:10.7326/0003-4819-132-7-200004040-00009.
8. Sherlock S. Hepatitis viruses: present and future. Hepatology. 1985;5(2):269–72. doi:10.1002/hep.1840050221.
9. Wright R. Sheila Sherlock and the rise of hepatology. J Hepatol. 2001;34(1):1–3. doi:10.1016/S0168-8278(00)00078-8.
10. Bosch J. Evidence-based hepatology: lessons from Dame Sheila Sherlock. Gut. 1999;45:113–7. doi:10.1136/gut.45.1.113.
11. Sherlock S. Spiders, capillaries, and cirrhosis: revisited. Liver Int. 1990;10:87–90. doi:10.1111/j.1600-0676.1990.tb00420.x.
12. Trebicka J, Krag A. Vascular biology in cirrhosis: insights from Sheila Sherlock’s work. Hepatology. 2018;68:2014–6. doi:10.1002/hep.30151.
13. Sherlock S. The liver and systemic circulation. BMJ. 1968;3(5622):18–21. doi:10.1136/bmj.3.5622.18.
14. Sherlock S. Humor and hepatology. Gut. 1972;13:473–4. doi:10.1136/gut.13.6.473.
15. Bean WB. Vascular spiders and related lesions of the skin. Medicine (Baltimore). 1958;37(1):1–56. doi:10.1097/00005792-195801000-00001.
16. Sherlock S. Prognosis in liver disease: what we knew and what we know. J Hepatol. 1991;13(3):235–9. doi:10.1016/0168-8278(91)90090-F.

17. Sherlock S. Ammonia metabolism in cirrhosis. Gut. 1971;12:181–8. doi:10.1136/gut.12.3.181.
18. Sherlock S. Hepatology: the future. J Hepatol. 1995;23:3–7. doi:10.1016/0168-8278(95)80001-T.
19. Fried MW. Hepatitis C: direct-acting antivirals bring a revolution. Ann Intern Med. 2014;160(5):374–82. doi:10.7326/M13-2523.
20. Charlton M, Shiffman ML. New horizons in NASH. Hepatology. 2020;71(1):442–50. doi:10.1002/hep.30802.
21. Sherlock S. Hepatology at a crossroads: opportunities and challenges. J Hepatol. 1998;29:511–3. doi:10.1016/S0168-8278(98)80163-5.
22. Berenguer M, Sherlock S. Non-alcoholic fatty liver disease: the challenge ahead. Liver Int. 1995;15(1):23–29. doi:10.1111/j.1478-3231.1995.tb00004.x.
23. Sanyal AJ, Bosch J, et al. The microbiome and liver disease: a revolution in progress. Hepatology. 2020;72(1):136–145. doi:10.1002/hep.31032.
24. Angulo P. Liver regeneration: the future. J Hepatol. 2015;62(2):307–315. doi:10.1016/j.jhep.2014.10.032.
25. Strain AJ, Neuberger JM. Hepatocyte transplantation and liver regeneration. Hepatology. 2002;36(2):259–260. doi:10.1053/jhep.2002.34850.
26. Maddrey WC. Sheila Sherlock: the legacy of a liver legend. Hepatology. 2001;34(4):739–740. doi:10.1053/jhep.2001.28500.
27. Sherlock S. The past and future of hepatology. Hepatology. 1997;26(1):13–17. doi:10.1002/hep.510260104.