



Milestones

Andrew K. Burroughs: a research hepatologist extraordinaire

P. Aiden McCormick^a, Octavio Campollo^{b,*}^a Liver Unit, St Vincent's University Hospital, Dublin, Ireland^b Center of Studies on Alcoholism and Addictions, University Health Sciences Center, University of Guadalajara, Antiguo Hospital Civil de Guadalajara, Guadalajara, Mexico

ARTICLE INFO

Article history:

Available online 17 June 2021

Keywords:

Clinical
Portal hypertension
Transplantation, Royal Free Hospital

ABSTRACT

Andrew K (Andy) Burroughs passed away in March 2014 at the early age of 60 years. Andy was one of the last of the great all round giants of hepatology. He was a consummate physician, clinical investigator and educator. Over a period of 35 years at the Royal Free Hospital Liver Unit he produced a prodigious quantity of original research and made major contributions in many areas of hepatology including portal hypertension, liver transplantation and chronic liver disease. His work on the methodology of clinical trials is carried on by the Baveno consensus meetings. From bedside clinical mastery to early molecular biology applications to diagnosis and pathology, his contributions left a mark in liver science and advanced medical science in general. He also was praised by his work in medical education particularly in post-graduate mentorship and, an admirable human touch with patients. We will not see his like again.

© 2021 Fundación Clínica Médica Sur, A.C. Published by Elsevier España, S.L.U. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

"A physician, a scientist, a mentor and a teacher that contributed enormously to evidence-based medicine especially in portal hypertension and liver transplantation."

European Association for the Study of Liver Diseases.2020

Professor Andrew Kenneth Burroughs has been described as a giant of hepatology. That is an apt description. Andy, as he was known to his friends and colleagues, bestrode the world of hepatology for almost four decades. He was a consummate clinician, a thoughtful academic, a tireless worker and a generous mentor. He is remembered fondly by the many hundreds of hepatologists worldwide he taught or influenced. To many of those who first met him it was difficult to sort out his true origins. Andy was born in England to an Italian mother and an English father. A blend with roots on both sides of the English channel resulting in a "mix of British gentleman and a light-hearted Italian" [1]. Soon after, the family moved to Rome where Andy spent his childhood and early school years. He subsequently attended boarding school in England and then studied medicine at the University of Liverpool. Andy excelled at his medical studies, winning the gold medal and finishing first in his year in 1976. Three years after that he moved to London to work with the legendary Prof. Dame Sheila Sherlock and Prof. Neil McIntyre in the Academic Department of Medicine (Liver unit) in

Table 1

Breakdown of Prof. Andy Burroughs publications on liver diseases.

Description	Number
Pubmed publications	631
First author	60
Senior author	352
Portal hypertension	147
Liver transplantation	176
Chronic liver disease	168
Primary biliary cholangitis (PBC)	48
Hepatocellular carcinoma	34
Randomized controlled trials	48
Meta-analyses	36

the Royal Free Hospital (RFH). It was there that Andy discovered his love for hepatology and he went on to make the unit his home for the rest of his professional life.

Andy's appetite for work, both clinical and academic, was legendary and his scientific output prodigious. There are 631 of his publications listed on Pubmed. The exceptionally high quality is demonstrated by a h-index of 88 with more than 33,000 citations. Table 1 provides a breakdown. Andy was first author on 60 and senior author on 352 publications. There were 48 randomised controlled trials and 36 meta-analyses. Portal hypertension and liver transplantation were Andy's main focus. However, he was interested in all areas of hepatology and had 48 publications on primary biliary cholangitis (PBC), 34 on hepatocellular carcinoma and 15

* Corresponding author:

E-mail addresses: a.mccormick@ucd.ie (P.A. McCormick), calcohol@hotmail.com (O. Campollo).

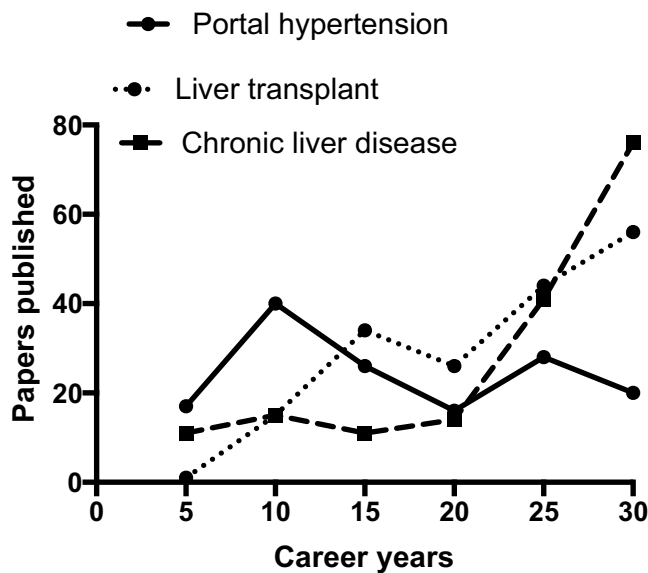


Fig. 1. Prof Andrew K Burroughs publications over time. Initial focus on portal hypertension followed by increasing interest in liver transplantation and chronic liver disease.

on viral hepatitis. Early in his career Andy became interested in the idea that PBC was triggered by bacterial infection. He was the first to draw attention to the increased incidence of significant bacteriuria in patients with PBC in 1984 [2]. This interest resulted in a publication in *Nature* in 1992 linking anti-mitochondrial antibodies, urinary tract infections and molecular mimicry [3]. Twenty eight years later this hypothesis is still a leading contender in the pathogenesis of PBC [4].

Over the years Andy's research interests varied. A review of his work illustrates many of the hot topics in hepatology over the past 4 decades. A graphic description of his publications on portal hypertension, liver transplantation and chronic liver disease over time is shown in Fig. 1. His initial interest and abiding passion was portal hypertension [5]. This was a time when there were rapid advances in the management of variceal haemorrhage. In 1980 Didier Lebrech had reported that propranolol lowered portal venous pressure and represented a possible medical treatment for portal hypertension [6]. Andy was initially a sceptic, publishing a negative controlled trial in the *New England Journal of Medicine* [7]. He subsequently became a convert to pharmacological therapy and in particular the prognostic benefits of measuring portal venous pressure. Andy had a major interest in clinical trials and in particular methodology and statistical analysis [8]. During this period there were a large number of clinical trials investigating the use of beta-blockers, vasoconstrictors, endoscopic sclerotherapy and surgical approaches to the prevention and treatment of variceal haemorrhage [9]. At International meetings there was vigorous debate on the relative merits of the various techniques and trials. Andy was usually to be found in the thick of these controversies with friends and colleagues including Jaime Bosch, Roberto Grossmann, Didier Lebrech, Roberto de Franchis, Shiv Sarin and many others. Very high standards were expected of these clinical trials and they were rigorously reviewed. Regular meetings were held to standardise the methodology underpinning clinical trials in portal hypertension culminating in the *Baveno consensus* meetings [10]. Interestingly most of these trials were initiated by enthusiasts, performed on shoestring budgets and would be very difficult to replicate in the current regulatory climate.

Surprisingly Andy published more on liver transplantation than on any other subject. In 1983 liver transplantation transitioned from an experimental procedure to accepted treatment for

patients with end stage liver disease. Andy brought his clinical trial experience to this new field. Along with John O'Grady, from King's College Hospital, he co-led the pivotal TMC trial comparing tacrolimus and emulsified cyclosporin which helped to definitively establish tacrolimus as the primary immunosuppressive drug for liver transplantation [11]. Andy published on all aspects of liver transplantation and was an advocate of tailoring long term immunosuppression to reduce the risks of recurrent disease, particularly due to hepatitis C [12].

Andy had a method for learning that used the best of both worlds. Very often you would see him going or coming from the Biochemistry department, surgery, clinical epidemiology or some of the basic science laboratories where he would go to learn from or to discuss a new research project with some of those scholars. He would come back to his tiny office to read and study further on a particular subject. As he developed a very good understanding on statistical analysis we once asked him where had he learned it from and he said "I learnt it from the British Medical journal (BMJ) they have a good section on statistical analysis and I have read them all". For a sustained period hepatology was dominated by advances in liver transplantation and in the treatment of hepatitis C. The study of chronic liver disease became somewhat unfashionable and appeared to be neglected or under-represented at international meetings. Andy, as usual, was ahead of the curve in identifying this trend. He published extensively on chronic liver disease. From Table 1 it can be seen that in later years Andy's publications on chronic liver disease increased significantly. Three areas of interest stood out. Andy was always interested in issues of coagulation, one of those areas. He published extensively on the measurement of coagulation in liver disease and its impact on prognosis [13]. Measurement of renal function was another area of interest. With collaborators he established a new technique for assessment of glomerular filtration rate in patients with liver disease [14]. In addition to its role in the pathogenesis of PBC Andy was also interested in the role of infection in chronic liver disease. This was particularly in relation to precipitating decompensation or variceal bleeding. He published a highly cited meta-analysis in 2010 showing that bacterial infections increased in-hospital mortality four-fold in patients with hepatic cirrhosis [15].

Andy was a dedicated internationalist. He had an abiding love for all things Italian and spoke the language fluently. Every August was spent with his wife and family in his holiday home in Abruzzo. Over the years 22 Italian fellows came to work with Andy in the Royal Free. He was held in such high regard in his second homeland that he was honoured by the award of *Cavaliere Ufficiale dell'Ordine al Merito della Repubblica Italiana* in 1989. Moreover, the European Association for the Study of Liver Diseases (EASL) has established a fellowship award on his name for young fellows. Forty five fellows from 15 other countries also came to study under Andy's guidance including a large cohort of 13 from Greece and 9 post-graduate students, nurturing that famous international flavour of the RFH liver unit. All were attracted by Andy's vision, energy, enthusiasm and good humour. Andy established strong and long lasting collaborations with colleagues in many other countries, particularly Spain, the United States and Italy. He was very much a citizen of the world, a European, while also being very English in many admirable ways. At international meetings you would see him socializing with many different groups of hepatologists either English, American, French, Spanish, Italian and so, either commenting on the latest article on a particular liver problem or having a laugh with his fellows over a glass of wine. His academic legacy lies in his large corpus of published work, his original insights regarding diseases of the liver and their treatment, and the hundreds of hepatologists he inspired and mentored.

Last but not least, there is still a large group of over 1600 liver transplant patients that are grateful for Andy being an “engaging, charming, smiling and caring consultant” [1].

References

- [1] Sudworth N. Professor Andrew K. Burroughs. Royal Free Charity. Liver patients' support group. Consulted 22/7/2020 at: <https://liversupportgrouproyalfreecharity.wordpress.com/2015/02/28/professor-andrew-k-burroughs/>.
- [2] Burroughs AK, Rosenstein IJ, Epstein O, Hamilton-Miller JM, Brumfitt W, Sherlock S. Bacteriuria and primary biliary cirrhosis. *Gut* 1984;25:133–7, <http://dx.doi.org/10.1136/gut.25.2.133>.
- [3] Burroughs AK, Butler P, Sternberg MJ, Baum H. Molecular mimicry in liver disease. *Nature* 1992;358:377–8, <http://dx.doi.org/10.1038/358377a0>.
- [4] Tanaka A, Leung PSC, Gershwin ME. Pathogen infections and primary biliary cholangitis. *Clin Exp Immunol* 2019;195:25–34, <http://dx.doi.org/10.1111/cei.13198>.
- [5] Burroughs AK, Walt R, Dunk A, Jenkins W, Sherlock S, Mackie S, et al. Effect of cimetidine on portal hypertension in cirrhotic patients. *Br Med J (Clin Res Ed)* 1982;284:1159–60, <http://dx.doi.org/10.1136/bmj.284.6323.1159-a>.
- [6] Lebrec D, Nouel O, Corbic M, Benhamou JP. Propranolol—a medical treatment for portal hypertension? *Lancet* 1980;2:180–2, [http://dx.doi.org/10.1016/S0140-6736\(80\)90063-X](http://dx.doi.org/10.1016/S0140-6736(80)90063-X).
- [7] Burroughs AK, Jenkins WJ, Sherlock S, Dunk A, Walt RP, Osuafor TO, et al. Controlled trial of propranolol for the prevention of recurrent variceal hemorrhage in patients with cirrhosis. *N Engl J Med* 1983;309:1539–42, <http://dx.doi.org/10.1056/NEJM198312223092502>.
- [8] Burroughs AK, Mezzanotte G, Phillips A, McCormick PA, McIntyre N. Cirrhotics with variceal hemorrhage: the importance of the time interval between admission and the start of analysis for survival and rebleeding rates. *Hepatology* 1989;9:801–7, <http://dx.doi.org/10.1002/hep.1840090602>.
- [9] Terblanche J, Burroughs AK, Hobbs KE. Controversies in the management of bleeding esophageal varices (1). *N Engl J Med* 1989;320:1393–8, <http://dx.doi.org/10.1056/NEJM198905253202107>.
- [10] de Franchis R, Pascal P, Ancona E, Burroughs AK, Henderson M, Fleig W, et al. Definitions, methodology and therapeutic strategies in portal hypertension. A Consensus Development Workshop, Baveno, Lake Maggiore, Italy, April 5 and 6, 1990. *J Hepatol* 1992;15:256–61, [http://dx.doi.org/10.1016/0168-8278\(92\)90044-P](http://dx.doi.org/10.1016/0168-8278(92)90044-P).
- [11] O'Grady JG, Burroughs A, Hardy P, Elbourne D, Truesdale A, UK and Republic of Ireland Liver Transplant Study Group. Tacrolimus versus microemulsified ciclosporin in liver transplantation: the TMC randomised controlled trial. *Lancet* 2002;360:1119–25, [http://dx.doi.org/10.1016/S0140-6736\(02\)11196-2](http://dx.doi.org/10.1016/S0140-6736(02)11196-2).
- [12] Manousou P, Cholongitas E, Samonakis D, Tsochatzis E, Corbani A, Dhillon AP, et al. Reduced fibrosis in recurrent HCV with tacrolimus, azathioprine and steroids versus tacrolimus: randomised trial long term outcomes. *Gut* 2014;63:1005–13, <http://dx.doi.org/10.1136/gutjnl-2013-305606>.
- [13] Thalheimer U, Triantos CK, Samonakis DN, Patch D, Burroughs AK. Infection, coagulation, and variceal bleeding in cirrhosis. *Gut* 2005;54:556–63, <http://dx.doi.org/10.1136/gut.2004.048181>.
- [14] Kalafateli M, Wickham F, Burniston M, Cholongitas E, Theocharidou E, Garovich M, et al. Development and validation of a mathematical equation to estimate glomerular filtration rate in cirrhosis: the royal free hospital cirrhosis glomerular filtration rate. *Hepatology* 2017;65:582–91, <http://dx.doi.org/10.1002/hep.28891>.
- [15] Arvaniti V, D'Amico G, Fede G, Manousou P, Tsochatzis E, Pleguezuelo M, et al. Infections in patients with cirrhosis increase mortality four-fold and should be used in determining prognosis. *Gastroenterology* 2010;139:1246–56, <http://dx.doi.org/10.1053/j.gastro.2010.06.019>, 56 e1–5.