Michael Charles Kew: A chronicle of his career

J H Hoofnagle, MD
Director, Liver Disease Research Branch, National Institutes of Health, Bethesda, Maryland, USA

Michael Charles Kew was born in 1939 in Johannesburg, South Africa. His parents, Max and Dorothy Kew, were South African citizens, his father a businessman. At an early age, Michael was recognised as a brilliant student. He graduated with first class honours from Jeppe High School at 15 years of age in 1955. From there, he enrolled at the University of the Witwatersrand (Wits) in 1956, the beginning of a more than 50-year career in association with the university. He received his MB BCh in 1961 (graduating *cum honoribus primus*), followed by an FCP (SA) in 1965, a medical doctorate (MD) in 1968, a PhD in 1974 and Doctor of Science (DSc) in 1982. His success in academic medicine was recognised with his induction as a member of the Royal College of Physicians of London (MRCP) in 1971, followed by his election as a fellow of the Royal College (FRCP) in 1979. This rapid acquisition of professional degrees and recognition is a testament to his academic and research performance at the Johannesburg Teaching Hospital Complex and University of the Witwatersrand. Here he began work as a physician in the Department of Medicine in 1967, later becoming a principal physician and senior lecturer (1971), a consultant hepatologist (1972), professor of medicine (1978) and senior physician and physician in charge of the Liver Unit (1972), as well as a member of the SA Medical Research Council (1997).

Professor Kew's initial academic and research studies were on a broad spectrum of liver diseases including viral hepatitis, drug-induced liver disease, portal hypertension, haemosiderosis, heatstroke and hepatocellular carcinoma (HCC). These were the clinical conditions and challenges that he faced on the wards of the Johannesburg Teaching Hospital, and particularly at Baragwanath Hospital that serves the sprawling Soweto township. A very special and dramatic challenge was HCC, which in Johannesburg, unlike other places in the world, was an extremely aggressive, rapidly fatal cancer affecting young adults in their 20s and 30s, rather than the middle-aged or elderly, as seen in the rest of the world.

In 1970, Dr Kew was awarded a Wellcome Research Fellowship to work in the Liver Unit at the Royal Free Hospital, London, with the world-renowned Dame Sheila Sherlock. There he pursued investigational studies on portal hypertension, but also carried out a clinical study on the spectrum of HCC, co-authoring with Dame Sheila what is now recognised as a classic clinical description of this little-understood cancer.

Returning to South Africa, Dr Kew began what became a life-long commitment to the study of HCC. His initial studies were largely descriptive and clinical, but he rapidly initiated analyses of pathogenesis based upon epidemiology and application of the serology, virology and molecular assays for the newly discovered hepatitis B virus (HBV). He and others showed that chronic infection with HBV was closely linked to liver cancer, and probably nowhere more strikingly than in sub-Saharan Africa. In a series of epidemiological, clinical, histological, virological and molecular studies, Professor Kew mapped out the close association of HCC with chronic HBV infection, the integration of HBV DNA into the tumour cells, the contributing factors of age, sex, iron status and environmental factors in the progression and expression of HCC, thereby establishing himself as the foremost authority on this significant tumour.

I first met Professor Kew in 1978, at the 2nd International Symposium on Viral Hepatitis, held in San Francisco. I had just finished training in gastroenterology-hepatology with Leonard Seeff (another South African) at the Washington DC VA Hospital, and started in the Liver Diseases Section of the National Institutes of Health. Mike gave the plenary overview presentation on hepatitis B and liver cancer. The talk was clear, concise and convincing, and given in that crisp, distinctive South African accent. It was immediately apparent to me and to all in the audience that this was someone who knew what he was talking about, a speaker who had seen and taken care of patients with liver cancer. It was immediately evident that he was a scholar, a careful thinker and, importantly, a clinical and basic scientist. Until that time, epidemiologists, pathologists, cell biologists and clinicians were the experts on HCC. Michael was all of these. He brought a freshness and excitement to the topic, proving a thoughtful and complete approach to understanding liver cancer and the role of hepatitis viruses, viral genes, host genes and environmental factors in its aetiology and pathogenesis. He also provided insights into what might ultimately be done for the prevention, early detection and treatment of HCC.

Following the meeting in 1978, Michael Kew was an invariable presence as a speaker at international symposia on viral hepatitis. In addition to contributing data from South Africa and the African continent, he succeeded in providing an overview and a balanced understanding of HCC, the most dreaded complication of viral hepatitis. He contributed to our knowledge of hepatitis B and liver cancer, documenting the abysmal results of conventional chemotherapy, and initiated trials of new therapies for chronic HBV infection, while documenting the changing epidemiology of hepatitis B and liver cancer.

Professor Kew was awarded a Fogarty Visiting Scientist position with Dr Robert Purcell in the Hepatitis Viruses section of the National Institutes of Health (NIH), and there he developed a working knowledge of the laboratory tools required to advance his research into the molecular virology of hepatitis B and liver cancer. I was at the NIH at the time, and asked Bob Purcell why we didn't see more of Mike Kew. Purcell answered that he was too busy, and added that Mike was the hardest-working, most dedicated Fogarty scholar who he had ever worked with. Following the 2-year sabbatical, Michael returned to Johannesburg, where he continued to make important contributions to our understanding of hepatitis B and HCC, using molecular tools to further elucidate the interaction of hepatitis B with the liver. He further explored co-factors that might alter viral carcinogenesis, defining the roles of genotypes and viral variants, the role of co-infection with hepatitis C and D viruses and viral host interactions. He also explored the potential role of chronic hepatitis B therapy as a means of decreasing the risk of HCC, and the changing epidemiology of hepatitis B and HCC in South Africa and worldwide.

I have personally benefitted greatly from my association with Professor Kew, and must pay tribute to his important role as a mentor of young physicians, attracting the best and brightest into the field of hepatology and viral hepatitis research. At the Liver Diseases Section of the NIH in the 1980s and 90s, Michael sent us three of his best trainees. All three were stars.

Geoff Dusheiko was the first hepatology fellow trained by Mike Kew. He came to our group a year after I joined the NIH. He got us started in hepatitis B immunology, and set up assays for HBV DNA

polymerase that were the bedrock of much that we did clinically on hepatitis B in ensuing years. Geoff returned to South Africa, where he worked with Michael Kew starting trials for the therapy of hepatitis B in South Africa, and 5 years later moved to London to become Professor of Medicine and chief of the Hepatology Section at the Royal Free Hospital.

Adrian di Bisceglie was our second Kew trainee. Adrian quickly showed his expertise, sound judgment and maturity, and was appointed a senior staff physician within 2 years of arriving, and subsequently was made chief of the Hepatitis Section. In the lab, he developed assays for HBV DNA in serum and liver, and helped us embark on studies for the therapy of chronic hepatitis B and what was then known as 'non-A, non-B' hepatitis using recombinant human interferon alpha. Adrian later went on to become Chief of Hepatology and Chairman of Medicine at St Louis University, and president of the American Association for the Study of Liver Diseases (AASLD).

The third Kew trainee was Chris Kassianides, who developed the duck HBV model in our lab and participated in our early trials of therapy for hepatitis B, C and D. Chris became a close friend, and a frequent visitor even after he left to finish specialty gastroenterology training and later returned to South Africa. Chris has become a champion for advanced hepatology and gastroenterology training in South Africa and the African subcontinent and is founder and chairman of the Gastroenterology Foundation of South Africa. Chris conceptualised and organised a truly magnificent festschrift symposium in 2016 to honour Michael Kew, which led to the compilation of this festschrift.

I write of many things that occurred 20, 30 and even 40 years ago. I have achieved the age where I realise that one's contribution to biomedical science is not only in the number of papers you publish, or how often you are invited to speak, or what honorary degrees and awards you can claim. Perhaps more importantly, one's contribution is also measured in what you leave behind, those you have mentored, your trainees, your scientific children in whom you foster a love and commitment of science and medicine, and who then pass on this enthusiasm and commitment to future generations. Professor Kew has been successful in all of these respects, and a leading source in the growing light that has surrounded the darkness of viral hepatitis and the disease burden that it causes. I am proud to have been asked to contribute to this festschrift for this most deserving physician, scholar, researcher, teacher and mentor. Mike, congratulations on a sterling and successful career.