Interviews

Stephen Ryder and Kieron Lim spoke to EMJ about the influences and inspirations that led them to work in the field of hepatology and the effects the COVID-19 pandemic has had on liver disease.

Featuring: Stephen Ryder and Kieron Lim.

Stephen Ryder

Clinical Director of Research and Innovation, Nottingham University Hospitals NHS Trust; Chair of the Clinical Advisory Board, British Liver Trust; hepatology Vice President of the British Society of Gastroenterology

Q1

What inspired you to study medicine? Was there a particular aspect of your medical education that influenced your career path?

A lot of it is serendipity: you happen to be in a particular place at a particular time. And an awful lot of it is down to the people that you meet. While I was a trainee in medicine, there were two or three very influential people who shaped my future. One of them was a gastroenterologist in in the West Midlands, Hugh Bradby, who persuaded me down the path of gastroenterology rather than cardiology, which is where I had started looking. After that, it was the coming together of a few things: the practical aspects of gastroenterology and the machines to work with, as well as the people. And then finally, it was working with two eminent hepatologists, Howard Thomas at St Mary's and Roger Williams at King's, that really sparked a major interest in the liver for me. From an academic viewpoint, it was working with Jon Rhodes in Liverpool, who was my MD supervisor for a research project surrounding cancer and the gastrointestinal tract; working with John was a very pivotal moment for me in terms of research, and he has been a very close friend ever since.

Q2

The hepatitis C virus was isolated for the first time in 1988, just a few years after you qualified as a doctor. Could you please tell me about this time in your career and how hepatitis C virus became your major clinical focus?

"A whole new disease was discovered in that early phase of my gastroenterology career; just being there at the start of something and seeing it build was very impressive"

Hepatitis C virus (HCV) was discovered when I was a trainee and was a huge scientific breakthrough. A whole new disease was discovered in that early phase of my gastroenterology career; just being there at the start of something and seeing it build was very impressive. I remember the first studies published following the discovery of HCV and the discovery that a significant number of people around the world were infected with the virus. At that stage nobody knew what it meant to have HCV. Previous studies had all suggested HCV to be a fairly benign disease, a chronic persistent hepatitis. But over the first few years, the magnitude of the disease became very obvious and set the scene for me when I arrived in Nottingham in 1994; here, I was very fortunate to have a colleague, Will Irving, working in virology and who has been very instrumental in HCV research. When I arrived, I received a call from Will asking me if I was interested in working with HCV and my answer was yes, and that is how it all started.

Q3 You have played a large role in co-ordinating clinical trials for HCV treatment and ensuring patient access to these trials. What are the main barriers to clinical trial access in the UK? And what is your opinion on the future of decentralised clinical trials?

We are very fortunate in the UK to have very good clinical trial infrastructure. We have seen it with the COVID-19, for example: the UK led the world in introducing therapies for a new disease. I think that the UK is a very good place to be a patient in terms of trial access. The main challenge we have is that there are still inequalities with access to trials. Individuals still rely on their local hospital and team, where there needs to be an interest for having the right infrastructure in place to make trials work. There are areas of the country that have relatively little trial activity in particular specialties.

There is no doubt that the way in which trials are being conducted is changing and, due to digital, the way in which they are delivered is also changing. I think we will see a lot more trials being delivered in primary and community care. This was seen with the COVID-19 trials, which were performed in nursing homes and community settings. There will also be more use of real-world data, data that has been collected for other reasons, as part of clinical trial outcomes; this will make trials much more accessible and deal with some of the access inequalities. I can see the trials from the hospital setting, where I am based, becoming more interventional and being performed earlier. We conduct more trials in sick inpatients and there are more trials of new drugs being administered to the very first human subjects. That is going to be the biggest change, I believe: seeing those trials developing and concentrating in big hospitals and seeing a lot more trials developing out of primary and community care.

Q4 The highest rates of HCV are in developing and resource-limited countries, where the path towards HCV management and

eradication may be different to high-income countries. What measures need to be in place to ensure patients access to treatment and progress toward the management or eradication of HCV?

There are a set of things that would need to be in place in any country to make it work: you have to be able to find people who have the disease, you have to be able to afford to get treatment to those people, and the people have to want to take the treatment. At its most basic, those are the three areas and if you look at each of them in turn, some resource-poor countries actually have really good public health infrastructures because they recognise that the best way, economically speaking, of improving the health of the population is to know what the local public health problems are, and to manage it locally. Using the infrastructures already in place is absolutely critical and we have seen a number of low- to middle-income countries do really well in terms of HCV treatment and access; however, I think that good public health infrastructure is one of the defining factors of the countries that do. In terms of access to medicines at an affordable price, this is clearly still an issue. Although, I think the manufacturers have been significantly altruistic in their approach in terms of allowing manufacturing at much lower costs in various parts of the world. This needs to continue to make sure that people have access to affordable treatment. There is still a large need globally to educate and for people to recognise HCV as a problem because unless most people want treatment, we are not going to get there. There is still an ongoing role for the World Health Organization (WHO) and governments to keep pressure on the elimination target so that governments sit up and take it seriously and use the resources they have to sensibly reach that target for their population.

Q5

The COVID-19 pandemic has seen innovation in vaccine development and technologies and has influenced the development of other vaccines (e.g., mRNA vaccines against HIV from both Moderna and Oxford University's Jenner Institute). Has the pandemic innovated or advanced the possibility for an HCV vaccine?

The technology changes that happened with the development of COVID-19 vaccines were very rapid; we saw RNA vaccines really appear for the first time and I think that there will be many new technologies applied to other vaccines now. It is a very exciting time to see how everything will progress. Something else that the pandemic has done is made governments realise how important vaccines are and that there needs to be an infrastructure in place that can both develop and deliver vaccines, while being robust. I think we will see a lot more investment in that capacity. It is an incredible opportunity: both the new technologies and the political drive that will come out of seeing the impact an infectious

disease can have and what vaccines can achieve. I am very optimistic that it will translate.

Q6 You recently raised your concerns about the effect the COVID-19 pandemic has had on the incidence of liver disease in the UK. What measures or initiatives are needed to support those individuals at risk?

It has certainly been one of the major downsides of lockdown, particularly because people are less active and drink more, which is unquestionably not good for the liver. Certainly, from a local perspective in Nottingham, I have seen more people admitted and more people who are dependent on alcohol and have more mental health problems related to alcohol. There is a big agenda here and a big need for public health messages and more support for these individuals. The government needs to take action to destigmatise issues surrounding alcohol. It is a very common problem and alcohol support services and treatment services must be invested in, so that people can get the help they need when they need it.

This is also an opportunity for the Chancellor. This is perhaps not so popular to say, but the supermarkets, although they did a very good job at keeping us supplied during lockdown, made a lot of money and sold an awful lot of alcohol. There is an opportunity here to increase alcohol prices and tax in the supermarket and to reduce the cost and tax of pub and restaurant meal and beverages. As we come out of lockdown, encouraging people to be more active and watch their weight will be really important. The same applies to food and weight as it does with alcohol; unless people have access to weight management services, weight is difficult to control because food is cheap and all around us. If you combine that with inactivity, then you are going to end up with health problems, including problems for your liver later on in life. It needs to be a concerted approach, which focuses on including behaviour change as part of the infrastructure for individuals as we come out of lockdown.

Q7 Could you discuss the impact your work as Chair of the Clinical Advisory Board, British Liver Trust, has for research and society?

I have been involved with the British Liver Trust (BLT) for a long time now, and it is partly due to the fact that the patient voice has needed strengthening because of all those issues I mentioned around stigmatisation. Individuals have found it difficult to come forward and talk about their problems and to publicise them. Therefore, I was very keen to support the BLT, prior to becoming their medical adviser. The Clinical Advisory Board is to ensure that everything is connected: to bring together clinicians who are interested in liver disorders and connect them with patient groups to ensure a single voice and access to patient views both locally and nationally, and help push the whole agenda for patients forward. I have been hugely impressed with people's willingness and dedication of time to support the themes of the BLT.

From a research perspective it has also had a benefit; when designing a clinical trial, you have to find someone to fund that trial and having patient involvement is absolutely critical. It is not simply a group of doctors dictating what is important; you need patients to tell you what is important. The BLT having links with many patient groups around the country has been very helpful in pushing that agenda forward too.

Q8 Finally, if you could write a letter to yourself in 1985 when you had just qualified, what advice would you give to yourself?

It is an interesting thought to look back to a time and situation that is so very different from now. One of the most striking reflections is how different healthcare is now. HCV had not even been discovered and now we are near a stage of eliminating it as a human disease, which is extraordinary. I think firstly it would be about medicine as a career. It is still hugely rewarding, and I still love coming to work every day. Secondly, I would say that you can make a difference and be there for patients at an individual level and have that one-on-one interaction with someone and try to solve a problem. And then you are able to scale the impact you can make at the level of a clinical trial, which will change the future of medical practice and certain health policies. Looking back to 1985, I would never have thought any of what I mentioned was achievable; but looking back over the course of my career, they absolutely have been. ■