Interview

The following interview takes a deep dive into the experiences of Gideon Hirschfield, a leading hepatologist currently based in Toronto, Canada. He spoke to EMJ about patient-centred treatment across several sub-specialties, with a focus on autoimmune liver disease and transplantation.

Gideon Hirschfield

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Q1 With your many years' experience as a consultant hepatologist, what initially sparked your interest in liver disease and has motivated you to continue researching?

I was lucky. I first did my undergraduate training in Oxford, UK, and then Cambridge, UK. When I was doing my clinical training in Cambridge, I was very fortunate to be exposed as a medical student to a professorial medical surgical firm with academic physician and surgeon scientists, with a clear focus on liver disease. This included experience with Sir Roy Calne, who was, as many people know, a pioneer of liver transplantation. That combination in Cambridge meant that my very first exposure in medicine was in advanced hepatology and transplantation, and that really sparked my interest and enjoyment of looking after patients with complex liver diseases.

Q2 Before your current spell in Toronto, Canada, you studied at both Oxford and Cambridge, and educated as a professor at the University of Birmingham, UK. Where do you feel you gained your most valuable experience?

That is a very hard question to answer. Each stage of my career has been positive and has facilitated the next stage. I was very lucky to go to Oxford and learn how to write. I was then very lucky to go to Cambridge, and learn how to think critically about clinical medicine. I also gained junior doctor experience in central London, UK, particularly at the Hammersmith Hospital, which is a phenomenal academic health science centre. This led to a PhD at University College London, UK, on the Royal Free Hospital, London, UK campus, providing significant critical appraisal skills in basic science. After this, I returned to Cambridge to complete my advanced training in liver disease. Then, fortunately for me, I spent some time in Toronto, Canada, and was faculty here, before returning to faculty in Birmingham. Currently, I am back in Toronto.

I do not think that I can claim that one place has been, you know, the place. I think that what I have learned is that if you put yourself in exciting environments, with colleagues who are interested in being physician scientists and academic medics, you can bring together really high-quality clinical medicine and clinical science, often spanning laboratory work. I am now working more predominantly in clinical translational work and clinical trials.

You cannot plan everything. It could have worked out that I became something else. It depends on who you are lucky enough to meet, who you are lucky enough to be mentored by, and where opportunities arise at different times. So, for anyone moving through a similar career, it is impossible to plan everything. I fundamentally enjoy looking after patients with complex liver disease, and I anchor everything around being an active clinician.

Q3 A couple of your recent publications have focused on optimising liver transplantation. Could you summarise the key points from the topical article you co-authored, called 'Availability of living donor optimizes timing of liver transplant in high-risk waitlisted cirrhosis patients', considering the long waiting lists many hospitals are currently experiencing?

I think that is an important question, and it does have relevance both in the UK and in Canada, and also beyond.

We look after patients with primary sclerosing cholangitis (PSC), a rare disease, as one of our academic and clinical interests. Unfortunately, it has a very high need for liver transplantation. More than 50% of patients will need a transplant and often these are young patients. Currently, the way liver transplants are allocated is based on something called the model for end-stage liver disease (MELD) score and derivatives of this score measure synthetic liver failure. What that means is that not everybody who needs a liver transplant, based on their blood tests or symptoms, is prioritised in the same way. Currently, prioritisation is driven by how serious your liver failure is. But this does not necessarily work for young people with PSC, whose MELD scores do not accurately reflect how sick they are. What we were interested to see is what was happening in our programme in Toronto and comparing that with the USA.

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In Toronto, we have access to live donor transplantation. This is not something that has taken off as much in the UK, but it is available elsewhere in the world. What we have noticed is that our patients with PSC were using disproportionate amounts of live donor transplantation to get the organ that they needed to prolong their life and improve their quality of life. We used this as a marker to say that the current system is not allocating livers to these patients in an equitable way, at least not in an equitable way that measures what they need. So, whilst the MELD score may be quite good for picking up 30-day or 3-month mortality, there are many reasons for liver transplantation, including PSC, where the MELD score does not reflect what is going on in your patient. In our programme, live donor transplantation is the reason why our patients are not dying on the waiting list, which reflects that the system is not perfect.

Therefore, the point of the paper was to highlight this inequity, recognising that there are not enough livers and that is always going to be a challenge. But we need to think about how we allocate who gets the next liver, and this cannot only be based on who is the sickest as defined by who has the highest short-term mortality through a MELD score. It needs to look at other ways of measuring this morbidity and potential mortality.

There are many people around the world thinking about how we allocate livers. This is an ongoing problem, as more and more people will need liver transplantation for other diseases. Therefore, we have a commitment, as a community of transplanters, to find ways to measure who goes next that do not only look at death, which may be skewed by patient age. This should take into account lots of factors, particularly relevant for diseases like biliary diseases, primary biliary cholangitis (PBC), and PSC. Females will often have a lower MELD score because of their body mass, and the biology of the disease means that the MELD score may be lower, and it does not always capture risk of cancer.

Q4 As a widely recognised thought leader in liver medicine and patient-centred treatment, how have you seen this field change over the course of your career?

I think our patients are much more at the centre of healthcare, particularly in the clinic. There is also much better access to their medical information. Our patients can see every blood result, every letter, every scan, every appointment, and they have live access. There is literally no difference between what I can see and what they can see in the ambulatory setting. So, I think that is a major step forward for patients.

Our patients are also engaged in the design of clinical services and the design of clinical research. A major change is the amount of time we now spend with patients and patient organisations discussing their needs. Does a transplant service allocate organs in a way that is fair to them? How is their quality of life addressed? How do we widen access? How do we ensure that all patients get access to high quality healthcare? I would say that we are much better at doing that than ever, even though we are not perfect (we never will be perfect) and have a publicly funded health system where there are significant strains on resources. Many of the things we would like to do are not necessarily in our control. But, without doubt, since I began training, our patient engagement and patient participation has never been higher.

Q5 Where do you see the gaps in research at current in the field of autoimmune liver disease, and what are the next steps for implementing personalised therapy for patients with immune and inflammatory mediated liver diseases?

Fundamentally, we would like to know the cause of the disease. If we knew the cause of the disease, we would be at a point where we can move beyond controlling the disease to curing the disease. In diseases like PBC, we have made enormous headways into controlling the disease. We have new and emerging therapies that are highly effective at stopping disease progression and improving symptoms. That said, they do not yet cure the patient. For PSC, we have not made as much progress. We hope that we will learn from some of the drugs that have been developed and from related diseases, but we really need to understand why someone gets PSC. Why do they get it at an early stage? Why is it associated with colitis? Understanding this means we may be able to use transformational therapies to really stop the disease and the inflammation. That would really, ultimately, improve quality and quantity of life.

We would love to be at the forefront of treatments, but we are limited by the fact that we do not fully understand what we should target. We sort of target what we see, but what we see is a reflection of many, many different factors, such as environmental and genetic, that led to the patient presenting. What we see in the clinic are patients with a heterogeneous disease presentation, so some people have mild disease, some have severe disease, some have symptomatic disease, and others are asymptomatic. We cannot yet make it personalised. We are getting more personalised and goal driven in our therapies, and we aim for normal tests, but we use biomarkers that are incredibly crude, as well as simple liver tests. These are great, and they are very immediately applicable, but they are not very sophisticated. To really personalise care, we need better biomarkers in the clinic, not just in the research setting. We need these biomarkers to link to why someone gets the disease.

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This is a journey, and the barrier to that going as fast as we would like is that, fortunately, or unfortunately, depending on how you look at it, these are rare diseases. Working together takes time to bring all the samples and all the patients to get our science up to scratch. We are pleased that the burden of disease is limited by how rare the diseases are, but at the same time, we are frustrated by the fact that because it is rare, the pace of change is inevitably a bit slower.

Q6 How does practising and researching in Canada differ to the UK? Are there any large similarities and/or differences?

Medicine has a lot of similarities in Canada and the UK. I always think of Canada as nesting between Europe and the USA, in terms of how we practice. We are a publicly funded health service. We have absolutely no private health care for anything that is reimbursed by the government. That is actually quite distinct to the UK, where there is a dual model of healthcare.

We have the same opportunities to provide healthcare to everyone, and the same challenges. Healthcare needs are growing at a rate that funding cannot keep up with, due to reasons such as ageing populations. Medicine is more complex than it ever has been, but there are opportunities for new and emerging therapies.

We live many of the similar problems that the UK has, particularly in terms of waiting times and access to care. But, equally, we focus on delivering healthcare for everyone who needs it, just based on residency requirements. There are lots of similarities, and lots of similarities in practice; however, Canada is very close geographically to the USA, so naturally some of our approaches start to look more like the medicine in the USA, in terms of patient choice, physician independence, and hospitals.

Q7 Where can we expect to see your research focus lie in the near future?

I hope that over the next five years we'll be continuing our work to understand what happens to patients living with autoimmune liver disease, particularly PBC, PSC, and autoimmune hepatitis. By that I mean better cohort studies, and using those cohort studies to understand biomarkers that we can use in clinical trials to predict outcomes early, so that our patients can have effective trial interventions without waiting a long time for clinical trial results.

I hope that we will be able to work alongside the development of new therapies that improve quantity and quality of life, and that we will be able to prove that those therapies are really helping our patients. Finally, I hope that if we educate our colleagues, and also educate other stakeholders in hospital and primary care, about the importance of rare liver diseases, particularly autoimmune, this will raise awareness. This would mean we get earlier diagnoses, patients are referred to specialist centres earlier, and are more likely to get early and effective treatment, both targeting quantity and quality of life. In 5–10 years' time, I hope to see a field where the diseases are being chipped away at, and we need liver transplantation less than less. We are already doing this for PBC (there are some very exciting new therapies coming soon), and we already have reasonable approaches, notably for autoimmune hepatitis, but we would like to improve them. Our real high priority is to make a difference now in PSC.

Q8 What advice would you give to a young hepatologist/gastroenterologist making their way into practice and research?

Always choose good mentors, show curiosity in your patients, and be compassionate. Always think: why did your patient get the illness they have? Think about this whatever illness you choose to study or find interesting.

If you understand the basic science and the unmet needs, you will be at the cutting edge of getting your patients the best care. Wherever you practise, if you set your goal as providing the best care for your patients, your patients will appreciate that, and you will have a more satisfying career.

Ultimately, if you are delivering state-of-the-art treatments that are effective and novel, you can be part of great quality of care. Everyone can take part in clinical research. It does not matter where you find yourself or what sector of medicine you are in, everyone can contribute to understanding what happens to our patients, and how to treat them better. So, being an active clinician and being involved in research is not restricted to academics. It is beholden on everyone who practises medicine to aspire to practise at the highest level. It is a lot more interesting and a lot of fun.