

ACPGBI/Dukes' Club Travelling Fellowship 2016

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Visit to the Intestinal Failure and Intestinal Transplant Unit, Department of Transplant Surgery,
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Background/Introduction

My interest in the field of intestinal failure began during my HPB and transplant rotation, wherein I was exposed for the first time to intestinal failure surgery. I found this surgery, and the patient cohort, both fascinating, and very challenging.

There is little scope for in-depth exposure to this field of surgery during most general surgical rotations, and even less potential to be exposed to the multi-modal approaches that need to be afforded to these patients in order to provide their long-term management. With a desire to be exposed to this surgery and patient management in greater detail, and with the helpful advice of senior colleagues, I looked into the highest volume intestinal failure unit's worldwide, and thereafter made contact with Professor David Mercer at the University of Nebraska Medical Centre (UNMC), in Omaha, USA.

UNMC have a very developed Intestinal Rehabilitation Programme, of which Professor Mercer is the director, and this, combined with their high volume of intestinal transplants (the highest volume worldwide), made this a particularly appealing institute for me to visit.

After a few emails back and forth between Professor Mercer and myself during the latter part of 2015, a letter of approval from my programme director and a letter of support from the director of the transplant unit at UNMC (Professor Alan Langnas), the visit was set up, and we laid provisional dates for me to visit the unit.

I was very grateful to be awarded the ACPGBI/Dukes' Club Travelling Fellowship Award 2016 which allowed me to fulfil this ambition, and without which this visit would not have been able to be seen through to fruition.

My Visit

The dates we set for my visit worked out very timely indeed. After completing the FRCS viva the week before, and handing my final master's project report in on the Monday morning, I made the long-winded journey to Nebraska very early the following morning. As you may imagine, there are no direct flights to Nebraska from Newcastle, so a few changes combined with storms cancelling flights into and out of Chicago, turned my journey into a 27 hour one, but nonetheless, I arrived to a very hot Omaha late the following evening.

Week 1

Having spent my arrival night in a hotel, I made my way to UNMC, and checked into my student housing accommodation, which was ideally located on campus, just a short walk from the main hospital.

I initially met the international fellowship coordinator, who looks after all fellows visiting the department, and we went on a short tour of the hospital and particularly the transplant unit. There was some more paperwork to fill out, and practical things like an ID badge to obtain.

Once these were completed I met with Professor Mercer. After introductions, we had a chat in his office, and went over what I hoped to gain from the experience, and he shared with me some more information about the unit, and the type of work he does. He had not long finished a paediatric intestinal failure case that morning, and his fellow was finishing up a line insertion in theatre, where we headed to. I was introduced to one of his two fellows (one being on kidney/pancreas transplant, and the other on liver/intestine transplant), a Canadian trainee, who would be my main port of call during the next two weeks, especially from a transplant activity point of view.

We then went to do rounds. There are two sets of attending (consultant led) ward rounds per day. The first is a paediatric ward round, which starts at 10am, and then the adult round, which starts at 2pm.

This was the first main difference compared to our system in the UK. The daily ward rounds are a big affair. There were between 15 and 20 members of the team on the round, being led by Prof Mercer. The ward round team would consist of the surgical fellows, any residents (none in the department whilst I was there), any interns (again none present whilst I was there), medical students, physician assistants, hepatologists, nutritionists, transplant pharmacists, microbiologists, ward nurses, intensivists, and social care coordinators.

The fellow, who would have reviewed all of the complex and ICU patients at around 5.30am, would present updates on these patients to Prof Mercer, whilst the physician assistants or medical students, who would have reviewed the rest of the patients in the morning, would present them accordingly.

There are four attendings (consultants) within the liver/intestine directorate at UNMC, and they have what is at first sight a complex way of splitting up the ward care, elective care and transplants, but ultimately means that one of them would be responsible for the paediatric rounds and accepting/rejecting the transplant calls during the week, whilst another would be on for adult rounds.

The second stark difference to our set up in the UK was the fact that every single patient in the hospital has their own en-suite room, there are no bays; and the looks I received from some staff at the fact that we still have six bedded bays in our hospitals was quite amusing.

This first ward round itself was fascinating, and I was really provided with a flavour of what was to come over the next fortnight.

The first patient I met on the ward round from an intestinal failure point of view was a young man who had sustained a self-inflicted gun-shot to the abdomen. This had resulted in multiple enteric injuries, leading to complex entero-cutaneous fistulation, which had led to a short bowel syndrome. He was now two months following an isolated intestinal transplant, however he was struggling with graft rejection. Although being on high doses of immunosuppressant's, he remained dependant on TPN for the time being, whilst his graft was regenerating, which his recent small bowel biopsies had shown evidence of.

I was amazed to hear that 30% of all small bowel transplants performed in the USA are secondary to trauma (both gun-shot wounds and RTA's).

Other intestinal failure patients I met on this initial ward round included a patient who kept suffering with pneumatosis intestinalis, of unknown aetiology. There was no ischaemic element to it, but it was occurring due to presumed recurring bacterial translocation. On this occasion she had suffered with a

small bowel perforation leading to widespread contamination, and had required a substantial small-bowel resection, from which she was recovering.

I then met a Crohn's small bowel transplant patient, whose graft was failing, and who was now also suffering with acute renal failure, but who, due to the chronicity of her disease, had no intravenous access possible. Her IJV's/SCV's, groin and arm veins were un-usable, and amazingly she was currently having haemofiltration via a trans-hepatic vascular access line.

I then met two patients whom I would come to know well over my time in the unit. The first was a 55 year old man, who had complicated Crohn's Disease. He had undergone multiple resections for small bowel involvement, and had exhausted medical therapies. He had most recently undergone a repair of a sigmoid fistula, via a left paramedian incision, in order to avoid his midline, which had been left to granulate, as a roughly 8x12cm defect, following his multiple previous laparotomies and fistulae. Unfortunately he had then started to show signs of midline fistulation, which had been suture repaired 10 days previously. By the time I saw this patient however, he had, separate to that suture repair, developed a very extensive entero-cutaneous fistula, to the extent where this looked like a loop ileostomy had been surgically formed. Whilst addressing his nutritional demands, and sepsis, this was proving very difficult to manage practically, and we discussed our aims and where we hoped to get this patient to. Prof Mercer discussed the options of allowing more of the midline to heal, in order to allow better nursing and practical care to the fistula, which we would treat as an ileostomy, whilst addressing his very high fluid and electrolyte losses, and his nutritional demands. Or alternatively consider surgical intervention, to resect the fistula, and as much involved bowel as necessary in the midline, with the aim of forming an end ostomy of whatever healthy small bowel we could find, and then seeing how his nutritional demands improved with time, with the understanding that he may end up needing a transplant. He was already quite jaundiced, as an effect of his chronic TPN dependence, and so he was counselled that this may well end up being a combined liver and intestinal transplant. We agreed that we would give him and his family the weekend to think about their options.

The next patient that I met was a young woman, 30 years old, who had Gardener's Syndrome and suffered with recurrent desmoids tumours. She had undergone numerous resections of abdominal desmoids, along with small bowel resections and a sub-total colectomy with ileo-rectal anastomosis, but unfortunately now had developed a large recurrent desmoid tumour at the root of her small bowel mesentery, abutting her SMA and SMV. She was suffering with recurrent obstruction, and had multiple entero-cutaneous fistulae, and essentially was awaiting a small bowel and pancreas transplant, should her sepsis be able to be brought under control.

Aswell as these patients, I was introduced to a number of liver and renal transplant patients, along with an array of HPB patients, including a 36 year old patient with Down's Syndrome who had an ASD and VSD. He had presented with a liver abscess, and was found to have a portal vein thrombosis, for which he had undergone a portal vein thrombectomy, but remained on ICU due to respiratory complications, pulmonary hypertension, and on-going sepsis.

Following the ward round we then went to the transplant planning meeting, which takes place every Wednesday afternoon. Here each case is discussed in a great amount of detail, and all of the transplant multi-disciplinary team are present, including transplant co-ordinators, surgeons, hepatologists, nutritionists, psychologists, and sociologists.

The following morning I went on an early ward round with the fellow, before being in theatre for a 7.30am start. I assisted in an HPB list, and in what was to be my only laparoscopic case of the fortnight, which was a laparoscopic liver cyst fenestration, for a symptomatic patient, with a large multi-loculated cyst in segment 7/8.

I found it very interesting that due to the lack of residents and interns in the department, the theatre lists are staffed by attendings and fellows only, and that they only have assistance from medical students when they are on their attachments. During my time there were a large number of medical students around, but it basically means that for the fellows there is always an attending in theatre with them. This contrasts to our system, where a senior registrar would be left to carry on with a theatre list once competent, with the assistance of a SHO/house officer, with the consultant unscrubbed or in their office.

We then went on the paediatric ward round, which, in a similar vein to the adult round the day previously, was with a very large multi-disciplinary team. On this round I met a number of children who had undergone enteroplasty procedures for short bowel syndrome, those who had undergone both isolated small bowel, and multi-visceral transplants, and those suffering with anastomotic strictures, and transplant related complications, including post-transplant lymphoproliferative disorder (PTLD), which is treated very aggressively with chemotherapy, but can be fatal.

The following day after early rounds I assisted in a theatre list with Prof Mercer. The case was a 23 year old lady who suffered with bullaemia. Due to her chronic binge eating she had presented to a different hospital in September 2015 with gross gastric dilatation (with a gastric body distended down into her pelvis). She had undergone an emergency sub-total gastrectomy and roux-en-Y reconstruction, however unfortunately had leaked from the gastric anastomosis. She then developed a number of entero-cutaneous fistulae and was referred on to UNMC. Prof Mercer did a laparotomy on her in December 2015, resecting the residual stomach and creating an oesophago-jejunostomy, with the roux-en-Y, and repairing/resecting fistulating points, however again unfortunately she developed further midline entero-cutaneous fistulation.

As we explored her wound it was evident there was a small pinhole in the lower midline into a loop of small bowel. We performed a contrast test through the pinhole using gastrograffin and fluoroscopy, and there were no obvious other fistulae. We closed the pinhole defect directly and left a penrose drain. As she began to wake up there was a further large volume of enteric content that discharged from the wound, so we immediately re-explored. On further exploration there was a large laterally located entero-cutaneous fistula, which after a lot of difficulty in identifying the borders of, it was clear there was very little possibility to mobilise this loop safely, so we closed it primarily over a mallecot catheter which was purse-stringed in situ.

I took the opportunity after afternoon rounds to find out some more information about the IF practice here. At any one point in time, the department are managing up to 50 children and up to 100 adults on home parenteral nutrition. These patients could be located anywhere in the country, as many patients travel a large distance to attend the clinic at UNMC. The healthcare industry in the states is set up well for this, and there are large homecare companies and dietician/nutrition services that are able to provide for these patients on a day-to-day basis.

In terms of intestinal failure itself, the main causes that are seen in the paediatric population arise due to either gastroschisis, NEC, intestinal atresia or volvulus (leading to anatomical short bowel syndrome), or due to aganglionosis, pseudo-obstruction or MVID (leading to a functional short bowel syndrome).

In adults, the anatomical causes can be due to catastrophic causes (mesenteric vascular events, volvulae, internal herniae, surgical injuries, trauma), and non-catastrophic causes (desmoid tumours, multiple resections, Crohn's, fistulae), whilst the functional causes tend to be due to dysmotility syndromes, recurrent obstructions/adhesions, and radiation enteritis.

Week 2

The second week started with a very long but very fulfilling 48 hours.

We began by taking the lady with the recurrent desmoid tumour at the root of her SM vessels to theatre, as she had a small bowel perforation, diagnosed on CT overnight, and was grossly septic. This was an ischaemic perforation, and we ended up being forced to perform a complete enterectomy on her, with en-bloc resection of the desmoid tumour, so she was left with an oversewn rectal stump (from her previous sub-total colectomy) and a stapled off D4 with a foley catheter drain to her duodenal stump, and a further duodenostomy from an enterotomy in D2/D3.

The plan for this lady should she survive this event, was for her to be established on full parenteral feeds, and eventually hopefully be a candidate for a small bowel transplant.

We then revised an abdominal wound in a patient who had suffered multiple entero-cutaneous fistulae due to abdominal gun-shot wounds and the massive blast effect that had arisen from this injury. This patient had duodenal, enteric and colonic fistulation, and was dependant on parenteral nutrition.

Following this theatre list we headed to the HPB MDT, which was relatively similar in its format to our MDT's in the UK, however there was guaranteed food!

From the MDT Prof Mercer and I went to the Intestinal Rehabilitation Program (IRP) clinic, this had been something I was looking forward to from the start, as they have developed a very well structured and organised intestinal rehabilitation set-up that other centres are now following.

The key messages that resonated from this clinic were the importance of a multi-modal and multi-disciplinary approach to these patients, addressing the effects of their TPN requirements, monitoring metabolic and nutritional demands, and planning definitive surgical procedures in a timely fashion.

I would like to refer to three patients whom I met during this IRP clinic.

The first was a 25 year old man, who had suffered with bloating and erratic bowel function from his mid-teens onwards. Once he hit his 20's he suffered with gross abdominal distension and then profuse diarrhoea on an alternating basis every few days. He simultaneously was losing muscle mass and having less and less oral intake to try to avoid these episodes. This got to the stage where he was TPN dependant due to his poor nutritional status. All the investigations he had undergone revealed a pseudo-obstruction picture only, with marked small bowel dilatation. Prof Mercer therefore decided to intervene three months ago, and performed a tapering enteroplasty procedure, covering the entire length of his small bowel from DJ flexure to TI. At the time of the laparotomy his small bowel calibre was 10cm in diameter. The aim of the enteroplasty procedure is to restore a more normal volume to surface area ratio of the small bowel villi to the enteric contents, and he did this down to a diameter of 4cm. The small bowel histopathology report was very interesting and revealed a Cajalopathy (an absence of the interstitial pacemaker cells of Cajal). There are only three reported cases of this in the worldwide literature.

He was doing well following this procedure, tolerating some oral intake, with supplemental nightly TPN. His bowel habit had been increasingly loose recently, and therefore the decision was made to commence him on Creon (although his pancreatic exocrine function is undisturbed, the increased gut transit time limits the capacity for absorption), and cholestyramine.

The second patient to mention was a 40-year-old lady with Peutz-Jaghers Disease. She was diagnosed aged 15 years, and underwent her first small bowel resection due to an intussusception at this time. Since then she suffered multiple further intussusceptions requiring further resections, and subsequently suffered with recurring bouts of adhesional related complications, also demanding further laparotomies. She had undergone a TAH which had required a further small bowel resection due to dense adhesions, and she was now in a position where she was taking very little oral intake due to chronic abdominal pain exacerbated by oral intake. She had been losing weight for some time,

had already had a trial of a feeding jejunostomy which had the same effect, and now she was TPN dependant with short bowel secondary to all of her interventions. She was in a very desperate position, willing to try anything to overcome her debilitating pain. It was difficult to discern whether her pain is primarily due to adhesions, or hamartomas intussuscepting, a test capsule endoscopy was unsuccessful, and an MRE was unable to differentiate multiple small filling defects. So after a length consultation, it was agreed to offer this lady a laparotomy with on-table double balloon enteroscopy, try to identify any further hamartomas and resect as necessary (endoscopically ideally), perform an adhesiolysis, and take it from there. The aim was to wean her from her TPN, and to fit a feeding gastro-jejunostomy at the time of surgery also.

The final patient to mention was a 52-year-old lady who had flown up from Texas for the clinic. She was diagnosed aged 40 with a rectal cancer and had undergone long-course neoadjuvant chemoradiotherapy followed by an APER. For the following 10 years she suffered with daily vomiting and a picture of sub-acute obstruction that was put down to radiation enteritis. She had undergone 2 laparotomies that had yielded no improvement in her symptoms before being sent to the UNMC clinic. Due to her inability to eat secondary to her abdominal pain and vomiting she was now TPN dependant.

Prof Mercer had performed an extensive adhesiolysis on her initially and resected a significant volume of small bowel involved and stuck in her pelvis with an entero-colic anastomosis. Unfortunately she had leaked following this and had developed an entero-cutaneous fistula. She then underwent a further laparotomy mandating further resection of very damaged and friable small bowel, and now had only 50cm of small bowel remaining. She had been losing a lot of weight recently, and it was decided to re-start her on TPN, as in order to rehabilitate someone's short bowel their malnutrition must first be addressed. The medium-term plan was to build her up so that in four to five months time she would be able to commence a trial of Gattex (Teduglutide) a GLP2 analogue that can increase villous length, however with potential significant side effects, and at great expense (\$300,000 per patient per year). This drug can lead to a 20% decrease in TPN requirements at six months, so if you can save money in the long term with reduced TPN, then the cost of the drug can be recovered many times over.

Following this very interesting IRP clinic there was a liver transplant to do, which I assisted with. The recipient was a 40 year old lady with autoimmune hepatitis and a MELD score of 36.

The liver transplant went very well, and following this we had received an isolated small bowel retrieval call. This was from an 11 month old little boy in Atlanta, and was a brain stem death donation. There was already a cardiac team flying over from Illinois, and a liver team from Chicago, and we were offered the bowel, and after accepting were asked to retrieve the kidneys also. So, two hours later we took off from Omaha airport in a private jet for Atlanta.

It was fascinating for me to be involved with a small bowel retrieval, as I have not had this opportunity during my previous transplant rotation, and was a critical part of what I hoped to get out of my experience here (although UNMC carry out roughly 30 bowel transplants per year, the majority of these are multi-visceral, only about five per year are isolated small bowel). Unfortunately the liver team had inadvertently cut the SMA at its origin (ordinarily we would retrieve the small bowel and SMA en bloc with an aortic cuff), so we retrieved various other potential conduits, including both common iliac arteries and bifurcations, the descending aorta, and the right common carotid artery and bifurcation.

We retrieved en bloc with the pancreas, however since this was an isolated small bowel transplant, on the back table once back at UNMC we resected the pancreas and duodenum to the D2/D3 junction, and prepared the SMA and SMV for anastomosis. We had retrieved as much length of colon as possible with the specimen also, but the distal extent of this was non-viable, so we resected that at the level of the ascending colon (and performed an appendicectomy).

The recipient was a three year old boy who had suffered gastroschisis as a newborn, and had short bowel since a massive resection at that time. He had 10cm of jejunum distal to the DJ flexure only, and a closed off rectal stump.

The initial dissection on the recipient was very challenging, due to dense adhesions to the anterior abdominal wall, and general loss of domain, but we were able to resect back to D3. A proximal enterotomy was inadvertently made in D2, which was where we decided to create the proximal donor-recipient anastomosis (hand-sewn, continuous, double-layered). We fashioned an SMA conduit using the donor's carotid artery, and anastomosed that onto the infra-renal aorta, where we then anastomosed the donor SMA onto. The SMV to SMV anastomosis was more straightforward.

The distal anastomosis (again, hand-sewn, continuous, double-layered) was made between the donor ascending colon and the recipient rectum. We then created a loop ileostomy in the RIF (which would be used to carry out endoscopic surveillance of both limb's mucosae over the coming weeks), and replaced his gastrostomy tube.

The procedure, although technically challenging, went very well, and the patient looked good at closure.

The following morning I was very happy to see that he was still doing well, was not on any vasopressors, and his ileostomy looked pink and healthy, and already had enteric content coming out of it. He was on Tacrolimus as a standard protocol following small bowel transplant.

The following day we had an intestinal failure theatre list and after a couple of further long consultations with the in-patient I had met with the Crohn's entero-cutaneous fistula in week one, we proceeded with the laparotomy. As expected, access was extremely difficult on this patient, as there was only a very thin layer of granulation tissue outside of frank fistulation. We mobilised around the most prominent fistula initially, and gradually developed this further. After many hours of painstaking dissection and using gastrograffin and fluoroscopy via a foley catheter to guide us, we got to a position where we were able to resect a large portion of fistulating small bowel, and mobilise laterally to bring out a proximal jejunostomy. We closed the colonic side primarily, and used a Strattice mesh to close the midline, as there was no discernable fascia, it was matted and fused entirely with the small bowel/abdominal wall. This was a good result for this patient, as we would now hope for him to stabilise on his TPN, and then be a candidate for a SB/liver transplant in due course.

Following this we carried out a re-look laparotomy on the desmoid resection patient, as she had enteric content leaking from her drains. The duodenal stump was leaking, which we repaired over a drain.

The following day I met with a colorectal surgeon, a contact of one of my current consultants. I visited his practice, and went to see some of his in-patients (spread across different hospitals in the city), as well as sitting in on a research meeting of his, and a short clinic of his.

This marked the end of my visiting fellowship.

Of all that I have been exposed to during this time, and of all that I have seen, the two main stand out parts for my learning were the IRP clinic, which I found fascinating and very insightful, and the small bowel transplant, which provided me with a very detailed level of insight into the ultimate management for patients with intestinal failure.

Acknowledgments

This period of time has been hugely valuable to my understanding of intestinal failure, its management, and the aims of not only the surgeon and patient, but of the wider multi-disciplinary approach that is mandatory towards caring for these patients, and achieving positive outcomes.

I am hugely indebted to the ACPGBI and Dukes' Club for the award of this fellowship, and I have no doubt that this experience will be of great importance as I take these lessons forward with me into consultant practice.