

ELECTIVE (SSC5b) REPORT (1200 words)

A report that addresses the above four objectives should be written below. Your Elective supervisor will assess this.

I have been fortunate to spend my elective at the Oxford University Clinical Research Unit based in Ho Chi Minh City, Vietnam. The unit's research programs focus on infectious diseases relevant to the population of Vietnam and work alongside The Hospital for Tropical Diseases, on whose grounds it is based. It has been a hugely stimulating and enjoyable placement, one that I would recommend to anyone with an interest in infectious diseases, intensive care medicine, or clinical research.

My time has been split between morning ward rounds, tutorials with teaching faculty, lab work, academic meetings, and ward work. I met with members of the CNS infections, TB, Dengue, Malaria, Mathematical modelling, bioinformatics and Medical Economics groups to discuss their work and areas of interest in their fields. This gave me an understanding of how a research unit operates and the interaction within and between groups. I was introduced to some new fields in biomedical science including bioinformatics and mathematical modelling.

The experience has given me some insight into life as an academic clinician. I witnessed some of the challenges, including balancing a demanding working schedule, the need for a broad skillset and flexible approach. But also saw what a stimulating life it can offer, allowing for travel whilst working in a dynamic, diverse and intellectually stimulating environment.

I was fortunate to be introduced to spend some time in the lab, initially given a tutorial by a hugely experienced Microbiologist who talked me through some techniques used in microbiology. I was then able to assist with a few simple experiments involving culture and PCR of samples taken from patients with *Cryptococcus meningitis* as part of the Tamoxifen study. I valued this opportunity as I had no previous laboratory experience and so served to demystify the work that takes place there and broaden my understanding.

I was delighted to give something back by teaching English to one of the ITU doctors preparing to study in the UK.

Learning Objectives and Responses

Better understand the presentations and management of some of the diseases commonly managed at the HTD.

Spending time on CNS infections ward I was able to learn about a number of rare diseases and place my reading into context.

I learnt about two large clinical trials assessing the use of corticosteroids in patients with TB meningitis. The 26TB trial is comparing steroid use against placebo in HIV positive TB meningitis patients. In the 27TB trial for HIV negative patients, patients are grouped according to their LTA4H genotype and then for CC and CT genotypes are randomised to receive either steroids or placebo. Discussing these big trials with the doctors involved and watching its progress over my time at the unit was a great learning

opportunity. Watching difficult decisions be made about adverse and serious adverse events and the withdrawal and inclusion of patients. I also gained context to my understanding of tuberculosis as a disease particularly TB meningitis.

I encountered patients with anti-NMDA receptor encephalitis, a very rare auto-immune encephalitis that typically affects young adults, more commonly females and is associated with teratomas. This is a disease with a long recovery phase and avoiding complications is a significant aspect in the management of these patients. Despite severe clinical features some patients are able to make a complete recovery. I also met patients with cryptococcal meningitis, both of HIV+ve and -ve status, reflecting the increased prevalence of the *Cryptococcus Gattii*. The time I spent with the lab team involved culturing CSF samples from these patients and then performing PCR for speciation. Seeing the study from bedside to bench was a valuable experience. I learnt of the typical temporal lesions in Herpes encephalitis and was reminded of the importance of a good history and of CSF analysis in the diagnosis of patients presenting with symptoms of meningitis.

I was able to better understand the basis of evidence based medicine and the evolving nature of our understanding of disease. How best practice in disease management is subject to constant update. I discussed with some of the doctors the importance of critical appraisal skills in enabling the clinician to make intelligent and informed clinical decisions.

The intensive care unit had a number of tetanus patients at various stages of recovery throughout my stay and so I learnt a great deal about the prolonged recovery phase of this condition and managing autonomic dysfunction and pneumonia secondary to prolonged intubation. I also learnt about the presentation and management of Dengue and Japanese Encephalitis whilst on the PICU.

Describe the pattern of health provision in Vietnam and compare this with my experiences in Northern India during my SSC and the NHS in England.

I have found gaining an understanding of the Vietnamese healthcare system difficult during my time here. The care for patients enrolled in a study is paid for by the study as required by the Vietnamese government. However more generally the public are required to pay into a national healthcare insurance scheme on a means tested basis. The coverage for this scheme was 71.4% at the end of 2014 (1). There are a number of public hospitals based in the large cities throughout Vietnam that are covered in this scheme and also a number of private hospitals that require health insurance or paying an upfront fee. Vietnam spends only 0.9% of its GDP on healthcare and as such there are issues with staffing levels and overcrowding in its public hospitals.

I was interested that patients in trials not only had their costs covered and were also likely to receive a higher standard of care due to better staffing on the wards where study patients were placed.

Deepen my understanding of the interplay between HIV and Tuberculosis as a cause of disease.

I was interested to learn about the relationship between HIV status and its effect on the course of disease in TB and Cryptococcal meningitis. I learnt how a study performed at OUCRU demonstrated that HIV+ve patients have a paradoxically higher rate of both pro and anti-inflammatory cytokines, but also lower survival rates than HIV-ve patients.

The same study showed that patients with the “TT” LTA4H genotype (a gene that codes for a protein important in leukotriene synthesis) in HIV-ve patients had higher rates of both pro and anti inflammatory cytokines than CT and CC genotypes. These patients conversely had an improved survival.

These findings suggest that the HIV status is causing specifically a dysregulated hyperinflammatory response to the TBM and this is contributing to worsened outcomes in the cohort.

The questions raised by this previous trial, whether or not giving steroids to HIV+ve patients and CC and CT genotypes is appropriate given their inflammatory responses, are what the 26 and 27TB trials aim to answer.

I found understanding these trials, their aims and methods, improved my appreciation of the research process, something I will take with me into my medical career. I also gained a better understanding of TB meningitis as a disease process.

Spend time in the intensive care unit, familiarising myself with the clinical environment and techniques applied there.

I was fortunate my visit to the unit coincided with an ITU consultant from the UK, who came to teach ultrasound techniques to the Vietnamese ITU doctors. From this I learnt about the use of ultrasound for central venous catheter insertion at the internal jugular, subclavian and femoral veins. I also learnt some theory and practice of the four main views applied in Echocardiography and its use in scanning the thorax to diagnose effusion or pneumothorax, and in the legs to diagnose deep vein thrombosis.

I also witnessed a number of tracheostomy procedures and central line insertions and had the opportunity to practice arterial blood gas sampling and lumbar puncture. This experience will be valuable when I begin working on my ITU placement in August.

In summary my time at OUCRU has been hugely rewarding and I have learnt so much that I will take into my career. I am enormously grateful to all of the staff at the unit who have made me feel welcome and helped me to get involved.