So you want to be a haematologist?

Aditya Tedjaseputra
Fourth Year Medicine (Postgraduate)
University of Melbourne

Aditya is a final year student training at the Austin Health, with an interest in pursuing dual physician/pathology advanced training programs. He graduated with a Bachelor of Biomedicine degree from the University of Melbourne, where he undertook immunology and pathology as majors. He is considering a career in haematology or infectious diseases.

Introduction

Discussion surrounding specialties of preference is commonplace in medical school, across all levels of training. Some are attracted to the breadth of care afforded in general practice, the in-depth expertise of organ systems in physician specialties, or the hands-on experience with human anatomy in surgery. A few of us however, appreciate the opportunity to care for patients by the bedside, followed by investigating their bodily samples under the microscope in search of an answer to their presenting problems.

Belonging to the last group, I present this article which summarises my elective term experiences in haematology at the Olivia Newton-John Cancer & Wellness Centre and the Guy's Hospital. This, I hope, will shed some light on haematology as a potential field of interest for medical students – one that many of us consider 'exotic' and thus, perhaps, less pursued.

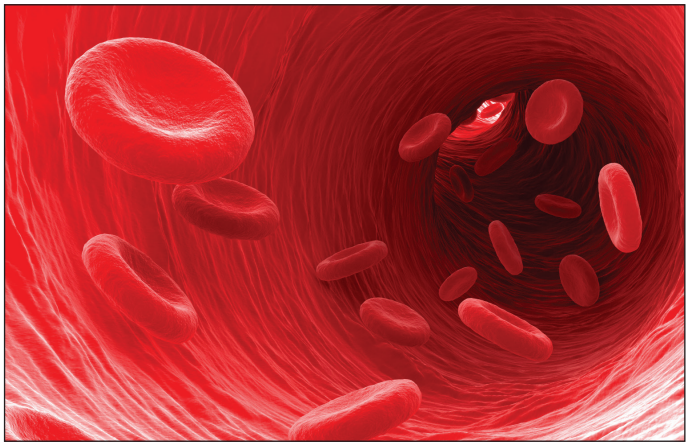
Haematology – what's in a specialty?

Haematology is an integrated discipline that incorporates both clinical and laboratory skills to diagnose and treat diseases of the blood and blood-forming (haematopoietic) organs. [1] The blood's cellular components include the red blood cells, white blood cells and platelets, which are derived from the bone marrow in steady-state conditions. Extra-medullary haemopoiesis in the liver and the spleen occurs in certain disease states, for example in marrow failure syndromes and haemoglobinopathies. In addition, the coagulation factors, which assist clotting, are also an important part of the haematological system. Principally, haematologists treat disorders which arise from derangement of any of these blood components – too high, too low or dysfunctional – as a result of diverse pathological processes, broadly classified as malignant or non-malignant. [2]

Clinical exposure and latest research

To set the scene, my first placement took place at the Olivia Newton-John Cancer & Wellness Centre in Melbourne. A new addition to the Austin Health complex in 2013, it is a comprehensive cancer centre which offers a holistic approach to patient care. On top of routine inpatient and outpatient services, the Olivia Newton-John Cancer & Wellness Centre provides a range of wellness therapies, such as music therapy, art therapy and massage. [3] Following a short vacation, I then set off to London, where I undertook my second placement at the Guy's Hospital, a major teaching hospital affiliated with King's College London. Located in Central London, this is the hospital where Thomas Hodgkin once worked. [4] I would like to share interesting current trends in clinical haematology I came across whilst on this placement.

At the Guy's Hospital, I was privileged to work with the Myeloproliferative Neoplasms (MPN) Unit, an internationally renowned centre for the care of patients with MPN spectrum: polycythaemia vera, essential thrombocythemia, and primary myelofibrosis. The MPN are characterized by clonal proliferation of myeloid progenitor cells in the bone marrow and in many cases, liver and spleen. [2] The advent of rapid genome-wide sequencing has identified a number of important mutations responsible for these disorders, including mutations in the Janus kinase 2 (JAK2), the MPL proto-oncogene, thrombopoietin receptor (MPL), and most recently the calreticulin (CAL-R) genes. [5] A particularly important 'newcomer' for MPN treatment I encountered there was ruxolitinib, a JAK1/2 inhibitor, which has been licensed for



primary myelofibrosis since the landmark publication by Prof. Claire Harrison in 2012. [6] This paper demonstrates superior efficacy of ruxolitinib compared to conventional therapy (usually hydroxyurea), in improving splenomegaly and overall quality of life. In addition, there is some evidence that ruxolitinib may also improve survival in patients with primary myelofibrosis, although this needs to be further investigated. [7] Witnessing patients' experiences first hand in her MPN clinics was a fantastic experience; especially given the limited efficacy and increased complications experienced with hydroxyurea. [6] At the moment, the Guy's Hospital and other centres of excellence in the UK and Europe are running further clinical trials assessing the use of ruxolitinib in polycythemia vera, with promising results reported in a recent study. [8] With corroborative studies, it is anticipated that ruxolitinib will be incorporated into the standard of care for patients with polycythemia vera as well.

On the other hand, I spent most of my placement time at the Olivia Newton-John Cancer & Wellness Centre on ward service. An important lesson I took away is the clinical care of serious infections in haematology patients. Febrile neutropenia is the most common and important infective issue suffered by up to 80% of neutropenic patients with haematological malignancies on chemotherapy. [9,10] Primary haematological disease, along with high-dose chemotherapy, results in profound neutropenia, putting patients at risk of invasive bacterial infections. Compounding this risk is chemotherapy-induced gastrointestinal damage, which allows for translocation of enteric bacteria into the blood, causing bloodstream infections. [11] In particular, bloodstream infections with the extended-spectrum beta-lactamase and the carbapenemase-producing Gram-negative bacteria pose significant issues as these pathogens are resistant to empirical therapy for febrile neutropenia (which is commonly a broad-spectrum cephalosporin-based regimen with an anti-pseudomonal cover). [12] Increased mortality risk with these multi-resistant organisms is related to delays in delivering appropriate antibiotic therapy. [13] Indeed, we observed one case of bloodstream infection caused by an extended-spectrum beta-lactamase producing Gram negative bacteria, in which the patient remained febrile after a period of empirical therapy with piperacillin/tazobactam, prompting the switch to a carbapenem-based therapy, allowing an adequate antimicrobial cover (luckily the isolate did not harbor a carbapenemase-producing bacteria as well). Antimicrobial stewardship and adequate infection control measures are required to prevent further problems with multi-resistant

organisms, which has been an initiative worldwide today, including in Australia. [14]

Reflections on the elective placements

An elective placement will not be complete without reflecting on what I have learnt whilst there to make me a better doctor in the future.

First, I have come to truly appreciate the importance of research in clinical medicine. Research, both laboratory-based and clinical, provides the essential foundation of what we know at present of diseases and their appropriate management. As an intern candidate sitting interviews in two months time, the way I view my research involvement has been affirmed – it is no longer merely a 'selling point' in my *curriculum vitae*, rather it is something I am truly proud of – it is a contribution to humanity which I certainly would like to keep up. Haematology, in particular, is a very active field of scientific enquiry. In both centres I attended, there are numerous clinical trials that are still actively recruiting patients at the time this article is written. In recent years, 'targeted therapy' and 'immunotherapy' have taken the centre stage and my experience with ruxolitinib described above is one example.

Secondly, good communication skills are crucial for best patient care, especially in haematology. In such a discipline with high throughput of novel, potentially superior therapy, at times quality of life may be neglected (unintentionally) for 'overall survival', which is often used as a measure of treatment success. A career in haematology hence requires the ability of not only to offer hope via new therapy, but also to limit further suffering by the same token. Taking the time to empathically listen to patients' wishes is very important, along with careful considerations on the potential benefit and side effects of the therapy on offer.

The natural history of malignant haematological disorders often alternates between periods of remission and relapse – at which a new treatment modality is usually offered. However, it is not uncommon that these 'salvage therapies' are offered on a clinical trial basis, where there is an uncertainty of whether or not we are doing more good than harm. Numerous times I had observed careful, empathetic listening followed by the question 'is this what you really want?' which revealed the true desire of our patients – that they prefer to embrace the time that remains free of side effects (nausea and fatigue are common ones) and are able to treasure their loved ones with minimal medical interventions. In such cases, close liaison with palliative care services is crucial in ensuring that we always act in our patient's best interest. Having learnt this firsthand observing the consultants I had worked with in my electives, I most certainly will remember to put my patients' (true) wishes first in my future practice.

So you want to be a haematologist (in Australia)?

There are three training pathways available in the Australian system (Figure 1). I will briefly discuss the joint RACP/RCPA training pathway here as it is the most commonly chosen pathway, and was the only pathway the registrars I worked with had undertaken. [15]

After completing their Basic Physician Training (BPT) program, candidates are eligible to apply for the joint RACP/RCPA accreditation in haematology. This involves the completion of four years of advanced training in haematology, usually comprised of two years each of clinical and laboratory training (minimum requirements of two years and one year in laboratory and clinical haematology training, respectively). [15]

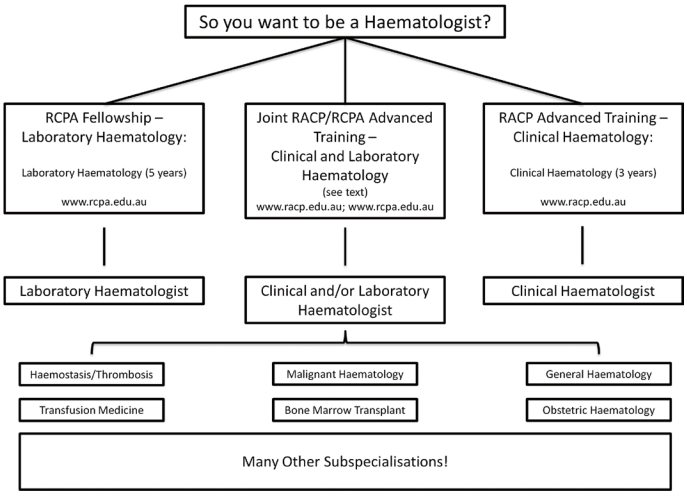


Figure 1. *Haematology Training Pathways in Australia. Haematology affords a wide range of career options and subspecialties depicted here are by no means exhaustive. Please refer to www.racp.edu.au and www.rcpa.edu.au for a comprehensive overview of these training pathways.*

In addition to the RACP written and clinical examinations taken in the final year of BPT, joint accreditation trainees are required to complete the RCPA haematology part I and part II pathology examinations after at least 18 months of accredited laboratory training. [15] The part I examination includes written, morphology, 'wet' and 'dry' practical examinations plus a viva, while the part II examination includes a dissertation and a viva. Hence, those considering haematology as a vocation should take this component of the training into consideration - there will be pathology exams!

Pathways that follow to 'consultanthood' vary, with many fledgling haematologists pursuing further training through fellowship appointments or a Doctor of Philosophy degree (PhD). As a result, haematology affords a wide range of career destinations and many subspecialisations (Figure 1). Those who choose to work as a clinical haematologist provides inpatient and outpatient care, whilst laboratory haematologists hold supervisory role in accredited laboratories. Finally, private practice is also very common in Haematology, allowing for flexibility in matching vocational aspirations with personal pursuits.

For a more comprehensive overview of these training programs, please refer to the RACP (www.racp.edu.au) and RCPA (www.rcpa.edu.au) websites.

In summary, haematology is an attractive specialty as in many cases the haematologist has the satisfaction of seeing a patient clinically, making a diagnosis by looking at his/her patient's blood and finally, offering appropriate treatments. Aligned with a previously published British article by O'Connor and Townsend [16], I think we agree that Haematology is, definitely, a specialty worthy of consideration.

Acknowledgements

None.

Conflict of interest

None declared.

Correspondence

A Tedjaseputra: adityat@student.unimelb.edu.au

References

[1] Haematology - Advanced Training Curriculum - Adult Medicine Division/Paediatrics & Child Health Division. Sydney, New South Wales: The Royal Australasian College of Physicians; 2013.
[2] Hoffbrand AV, Moss PAH. Essential Haematology. 6 ed. Hoffbrand AV, Moss PAH, editors. West Sussex, UK: Wiley-Blackwell; 2011.
[3] Olivia Newton-John Cancer & Wellness Centre: About Us Melbourne, Australia: Austin Health; 2015 [cited 2015 19 March]. Available from: http://www.oliviaappeal.com/About-Us.aspx.
[4] Stone MJ. Thomas Hodgkin: medical immortal and uncompromising idealist. BUMC Proceedings. 2005;18:368-75.
[5] Klampfl T, Gisslinger H, Harutyunyan AS, Nivarthi H, Rumi E, Milosevic JD, et al. Somatic mutations of calreticulin in myeloproliferative neoplasms. N Engl J Med. 2013;369(25):2379-90.
[6] Harrison C, Kiladjian J-J, Al-Ali HK, Gisslinger H, Waltzman R, Stalbovskaya V, et al. JAK Inhibition with ruxolitinib versus best available therapy for myelofibrosis. N Engl J Med. 2012;366(9):787-98.

[7] Verstovsek S, Mesa RA, Gotlib J, Levy RS, Gupta V, DiPersio JF, et al. Efficacy, safety, and survival with ruxolitinib in patients with myelofibrosis: results of a median 3-year follow-up of COMFORT-I. Haematologica. 2015;100(4):479-88.
[8] Vannucchi AM, Kiladjian JJ, Griesshammer M, Masszi T, Durrant S, Passamonti F, et al. Ruxolitinib versus standard therapy for the treatment of polycythemia vera. N Engl J Med. 2015;372(5):426-35.
[9] Lingaratnam S, Slavin MA, Koczwara B, Seymour JF, Szer J, Underhill C, et al. Introduction to the Australian consensus guidelines for the management of neutropenic fever in adult cancer patients, 2010/2011. Australian Consensus Guidelines 2011 Steering Committee. Intern Med J. 2011;41(1b):75-81.
[10] Freifeld AG, Bow EJ, Sepkowitz KA, Boeckh MJ, Ito JI, Mullen CA, et al. Clinical practice guideline for the use of antimicrobial agents in neutropenic patients with cancer: 2010 update by the infectious diseases society of america. Clin Infect Dis. 2011;52(4):e56-93.
[11] Blijlevens NM, Donnelly JP, De Pauw BE. Mucosal barrier injury: biology, pathology, clinical counterparts and consequences of intensive treatment for haematological malignancy: an overview. Bone Marrow Transplant. 2000;25(12):1269-78.
[12] Tam CS, O'Reilly M, Andresen D, Lingaratnam S, Kelly A, Burbury K, et al. Use of empiric antimicrobial therapy in neutropenic fever. Australian Consensus Guidelines 2011 Steering Committee. Intern Med J. 2011;41(1b):90-101.
[13] Mikulska M, Viscoli C, Orasch C, Livermore DM, Averbuch D, Cordonnier C, et al. Aetiology and resistance in bacteraemias among adult and paediatric haematology and cancer patients. J Infect. 2014;68(4):321-31.
[14] Gottlieb T, Nimmo GR. Antibiotic resistance is an emerging threat to public health: an urgent call to action at the Antimicrobial Resistance Summit 2011. Medical Journal of Australia. 2011;194(6):281-3.
[15] Advanced Training in Haematology Sydney, New South Wales, Australia: The Royal Australasian College of Physicians; 2015 [cited 2015 April 25].
[16] O'Connor D, Townsend W. A career in haematology. [Internet]. London: British Medical Journal; 30 Dec 2009. [cited 2015 31 May]. Available from: http://careers.bmj.com/careers/advice/view-article.html?id=20000625#