IT'S IN THE BLOOD

A CAREER IN HAEMATOLOGY PROVIDES THE OPPORTUNITY TO BE PART OF THE FULL RANGE OF PATIENT CARE FROM THE CLINIC TO THE LABORATORY AND TO WORK IN A FIELD WHERE MAJOR TREATMENT ADVANCES ARE BEING MADE, WRITES **TONY JAMES**.

Blood, they say, is thicker than water, and if you ask a haematologist you can find out exactly how thick. In literature, blood is a symbol of life and death, of relationships and of sacrifice.

That's all very well, but the pathologists who specialise in haematology can't spend all day sitting around pondering the big picture; they have small matters to be concerned with – blood cells and their precursors in bone marrow, to be precise.

The numbers, types and structures of blood-forming cells contained in a bone marrow biopsy, complemented by information about circulating or peripheral cells, provide haematologists with a finely detailed insight into numerous diseases and the body's response to them.

Red blood cells, the simplest cells in the body, account for just under half of blood volume. While they spend their four-month-long lives ferrying oxygen from the lungs to tissues and returning carbon dioxide in the opposite direction, white cells are helping to defend the body against infection and foreign materials, and platelets are getting on with their coagulation role to stem bleeding. These white cells and platelets make up only about 1 per cent of blood's volume.

Minus the red and white cells and platelets, the remaining half of blood is plasma, a fluid loaded with nutrients, proteins, enzymes, hormones, electrolytes, waste products, and sometimes infecting bacteria and viruses.

Formed in bone marrow, blood cells develop from stem cells that evolve through a series of generational steps into early, intermediate and late precursors of fully differentiated white cells, platelets and red cells.

Joy Ho, a staff specialist in haematology at Sydney's Royal Prince Alfred Hospital, says the discipline provides a unique opportunity for doctors to be part of the full cycle of patient care, combining clinical medicine, laboratory science and close interaction with medical colleagues.

"For example, in a disease like multiple myeloma (a cancer of the plasma cells in bone marrow) we will assess patients when they are first referred for specialist assessment, organise investigations, perform a bone marrow biopsy and make the diagnosis under the microscope," Dr Ho says.

"In most centres, haematologists will be closely involved in administering chemotherapy and in supervising a bone marrow transplant, if that ultimately becomes necessary, and then in long-term follow-up."

The exact roles of haematologists and other specialists such as oncologists vary between hospitals, depending on the expertise, interests and resources of the specialists involved.

One of Dr Ho's special interests is thalassaemia. She directs one of two Sydney clinics that treat adults with this inherited defect of haemoglobin formation. In response to inadequate oxygen transport, the body attempts to boost red cell production, leading to expansion of bone marrow and the creation of blood-forming tissue in other sites such as the spleen and liver.

Regular red cell transfusions become necessary in some patients, but this overloads the body with iron. As a result, patients need treatment virtually every day with a drug called desferrioxamine to enable excess iron to be excreted. Patients administer the compound using a pump to deliver a slow overnight infusion. Alternatives taken orally have been developed but their role is still being confirmed.

"Thalassaemia is a terrible burden for patients, and they need all the support we can provide," Dr Ho says. "The good news is that their long-term outlook is much better than in the past. Once they were considered lucky to survive until their 20s or 30s, but life expectancy has been increased by decades as a result of careful treatment."

Dr Ho is also a research associate at the Centenary Institute of Cancer Medicine and Cell Biology at Royal Prince Alfred Hospital. There she pursues a long-standing interest in the molecular genetics of multiple myeloma. Transfer of DNA during cell reproduction is thought to be a critical step in the onset of myeloma, and understanding the exact genetic characteristics of the abnormal cells provides information about the outlook for

Dr Joy Ho studied medicine at the University of Sydney then trained in haematology at Royal Prince Alfred Hospital and obtained a PhD at Oxford University. Dr Ho is a staff specialist at the Institute of Haematology, Royal Prince Alfred Hospital, Sydney, research associate at the Centenary Institute of Cancer Medicine and Cell Biology, and clinical senior lecturer at the University of Sydney.

Photo: Paul Jones

One of Dr Ho's special interests is Thalassaemia, the inherited defect of haemoglobin formation.

individual patients, guides their treatment and increases understanding of the disease as a whole.

The Australasian Leukaemia and Lymphoma Group provides a network for researchers and clinicians in the area, assisting with co-ordination of clinical trials and the national and international exchange of information and experience.

Like most Australian haematologists, Dr Ho holds fellowships of the Royal College of Pathologists of Australasia and the Royal Australasian College of Physicians. The training starts with three years as a physician registrar and completion of the first stage of the physician examination process. This is followed by four years of advanced training in haematology both in the laboratory and direct patient care.

Dr Ho has seen the advent of major advances in haematological treatments. One is imatinib (Glivec), heralded as the first cancer therapy specifically targeted at a molecular abnormality underpinning the disease. Imatinib inhibits an abnormal enzyme created by the so-called Philadelphia chromosome that occurs in chronic myeloid leukaemia.

Treatment reduces the proliferation of abnormal white cells and encourages the normal process of programmed cell death. "Imatinib is a major advance and the results of treatment are extremely encouraging," Dr Ho says. "There are some remaining questions about the durability of remissions, the causes of resistance and how to quantify the response to help determine the longer-term prognosis."

Haematology treatments have benefited from a range of genetically engineered recombinant products. For example, granulocyte colony stimulating factor (G-CSF) developed largely as a result of pioneering research in Melbourne, has had a dramatic impact by helping support patients through chemotherapy that is destructive to blood-forming tissues, and aiding in bone marrow transplants.

Erythropoietin treatment increases red blood cell formation in patients with chronic kidney failure and some types of malignancies. Genetically engineered coagulation factors are now available for patients with haemophilia, removing their dependence on factors extracted from large numbers of donated blood samples. Research is continuing on products to increase platelet numbers.

Bronwyn Williams, a haematologist at the Queensland Health Pathology Service, originally pursued a career in paediatrics. She became intrigued by the process of observing blood cells, making a diagnosis from what she could see under the microscope and applying the results to clinical decisions and patient care.

"I was always interested in cell morphology, the challenge of recognising distinctive patterns of cells and making an informed visual interpretation," she says. "This led me into the formal four-year training for haematology."

Dr Williams is based at the Royal Brisbane and Women's Hospital. About 80 per cent of her time is spent in the laboratory, where she examines cells from peripheral blood and bone marrow, determines additional investigations that might be needed and interprets findings from more routine, and often highly automated, tests such as cell counts.

Dr Bronwyn Williams completed her undergraduate medical degree at the University of Queensland before training in paediatrics and then haematology in Adelaide and Brisbane. She is a specialist haematologist at the Queensland Health Pathology Service, providing laboratory-based services for the Royal Brisbane and Women's Hospital, and also provides laboratory and clinical haematology services to the Royal Children's Hospital.

Automation has not replaced the skills of an experienced pathologist in understanding what can be seen down the microscope. "Very often, it's not a textbook case, and it's an intellectually rigorous process to make sense of a slide, come up with an accurate diagnosis and provide accurate clinical advice," she says.

Dr Williams also provides clinical and laboratory services at the Royal Children's Hospital, where she pursues her special interest in paediatric haematology. "Together, the laboratory and clinical work gives me contact with patients and their families, doctors from other specialties, nursing staff and laboratory scientists," Dr Williams says. "I'm also actively involved in teaching haematology and paediatric registrars, laboratory staff and nurses on the wards."

Although treatment of blood cell malignancies in Brisbane is managed by specialist haematological oncologists, Dr Williams is often involved in their diagnosis. "For example, a blood test might reveal a low white cell count, and further investigation shows immature cells in the circulation that raise a suspicion of leukaemia.

"We would take a bone marrow biopsy, stain and examine the cells, and provide a diagnosis within hours. This would usually prompt some other investigations to confirm the type of leukaemia and identify the cytogenetics of the malignancy, which could influence treatment decisions and help define the prognosis."

Immunology is one area that often interacts with haematology. In children, for example, immunodeficiency disorders frequently result from white cell disorders and may produce abnormal blood counts. These require teamwork between the two disciplines of pathology in diagnosis, treatment and follow-up.

In addition to red cell and white cell disorders, haematologists also manage the diagnosis and treatment of coagulation disorders such as haemophilia and Von Willebrand's disease and platelet disorders that also result in excess bleeding. Then there are the thrombotic disorders that predispose people to obstructed veins.

The entire field of transfusion therapy is under the control of haematologists, from donor collection through to blood banking, production of specific blood products and their administration to patients.

BONE MARROW TRANSPLANTATION

Haematologists are closely involved in bone marrow transplantation, a procedure that is increasingly common and used for an expanding range of diseases. More than 50,000 bone marrow transplants are performed annually around the world. Their success depends on the resilience of blood-forming stem cells in bone marrow, which have the capacity to differentiate into the full range of blood cells. Cells from one person can be injected into another and stimulated by various treatments. It is also possible to remove the patient's own stem cells, preserve them by freezing and then return them later.

Allogeneic bone marrow transplantation involves a donor and recipient who are not immunologically identical. Immune cells that are transplanted can react against the recipient, and the recipient's immune system – although usually failing or suppressed – can react against the graft and reject it. Matching donors and recipients as closely as possible remains a significant challenge for haematologists, and has led to the formation of donor registries and occasional media pleas from patients in search of a compatible donor.

Autologous transplantation involves the removal and storage of a patient's own bone marrow cells, which are returned following radiotherapy and/or chemotherapy. This option avoids problems of incompatibility but poses a risk of returning malignant cells, even though the graft is usually processed in an attempt to remove them.

Bone marrow transplantation is used in nonmalignant diseases including immunodeficiency disorders and haemoglobin disorders, and it is being trialled as a treatment for autoimmune conditions such as rheumatoid arthritis. Patients with malignant diseases including acute and chronic leukaemia, some lymphomas and progressive myelomas can also benefit. And returning patients' own removed bone marrow cells can help restore blood cell levels after high-dose chemotherapy to treat solid tumours.