

AUSTRALIAN BIOGRAPHY

SERIES 11

A SERIES THAT PROFILES SOME OF THE MOST
EXTRAORDINARY AUSTRALIANS OF OUR TIME



DONALD METCALF

MEDICAL
RESEARCHER



DONALD METCALF (1929 - 2014)

INTRODUCTION

This program is an episode of *Australian Biography* (Series 11) produced under the National Interest Program of Film Australia. This well-established series profiles some of the most extraordinary Australians of our time. Many have had a major impact on the nation's cultural, political and social life. All are remarkable and inspiring people who have reached a stage in their lives where they can look back and reflect. Through revealing in-depth interviews, they share their stories—of beginnings and challenges, landmarks and turning points. In so doing, they provide us with an invaluable archival record and a unique perspective on the roads we, as a country, have travelled.

SYNOPSIS

Professor Donald Metcalf is internationally renowned for his pioneering medical research on the control of blood cell formation. This fundamental research has been used in the treatment of millions of cancer patients around the world.

Born in 1929 in Mittagong NSW, Donald and his teams of researchers at the Walter and Eliza Hall Institute in Melbourne made their scientific breakthrough in the 1960s when they began the task of isolating and purifying colony stimulating factors (CSFs).

Donald and his colleagues researched for over 20 years to show that the CSFs, when injected into animals, stimulated the formation and activity of white blood cells.

After successful testing on humans, the treatment was accepted worldwide and has helped millions of cancer patients in accelerating the regrowth of blood cells following treatment and bone marrow transplants and for increasing resistance to infections.

His work on the control of blood cell formation has revolutionised the understanding of many diseases of blood cells and their treatment.

In this interview, he discusses his early life in country schools, his attraction to research, the competitiveness in trying to be the first to make a discovery, the exacting work of spending years at a microscope and writing some 680 scientific papers, why he returned to work the day after officially retiring and the reasons he continues to strive for new discoveries.

CURRICULUM LINKS

This program will have interest and relevance for teachers and students at secondary and tertiary levels. Curriculum links include General Science, Biology, Philosophy of Science, History of Science, Medicine, Biological Sciences, Biochemistry, English, Media Studies, Personal Development and Career Education.

Before watching

For each of these questions, just note what sort of impressions you have gained from the media and other sources. These are not questions for you to research, but just to give you some notes to reflect on once you have viewed the program.

- How do you feel about the role of genetic engineering in modern society?
- What do you think is the role of the drug companies in medical research?

Create a glossary

The following vocabulary will help in watching the program. Write the meaning of each of these terms in your own words.

haematology

leukaemia

lymphoid leukaemia

macrophage

thymus

virology

At the microscope

'My colleagues say I will be found dead working at the microscope...' are Donald Metcalf's opening words in the program.

- How old is he now, and how many years has he been 'at the microscope'?

Metcalf officially retired as Assistant Director of The Walter and Eliza Hall Institute in 1996. As he says in the interview: 'I just turned up the next morning, seven o'clock, started working again...'

- Can you imagine what career you might have which would see you going to work every day until you are well into your seventies with the sort of enthusiasm Donald expresses? Describe what this career might be for you.

Early life

- Donald describes being moved from school to school throughout his childhood. How do you think your class would respond to a student two years younger than the rest of the class suddenly arriving in the school? Do you think that his 'mischievous behaviour' was a response to this situation?
- Donald's parents wanted him to be a doctor; during his studies when the opportunity arose he moved into the related field of medical research. How much influence do you believe parents have on the chosen paths of their children? Quote some examples of famous people you have researched to support your claim.

Overcoming hurdles

Professor Metcalf overcame many hurdles in his career, and persisted for year after year on research that may have led nowhere. Use the specific examples from his life to answer the following questions:

- Donald was keen to work on cancer research, especially on leukaemia. What was it about leukaemia that made him so interested in it?

The Carden Fellowship

The Carden Fellowship is awarded by the Anti-Cancer Council of Victoria (now the Cancer Council Victoria) as a result of a bequest from G F Carden in late 1947. It provides a salary for a researcher into the study of cancer. Donald was able to spend his entire career funded by this Fellowship as long as he kept writing academic papers. Approaching 80 at the time of interview, Donald is the ongoing holder of this Fellowship—53 years later.

The Carden Fellowship was given for the researcher to work at the prestigious Walter and Eliza Hall Institute in Melbourne, whose director at the time was the highly respected Sir Macfarlane Burnet. He insisted that Donald prove himself as a scientist by working for two years as a virologist. Donald said: 'I was thrust on Burnet by the Anti-Cancer Council as a paid Fellow with some research support, but he wasn't particularly enamoured of cancer research, which he saw as a pointless exercise. To him, cancer was an inevitable disease of ageing and therefore neither preventable nor curable.'¹

- Imagine you are Donald and write a letter to a close friend or family member describing the reaction of Sir Macfarlane Burnet to Donald's appointment and how Donald felt about his position.

Donald was only permitted in the main building of the Institute if he was working on virology. Any cancer research had to be done in 'the animal house'.

The animal house was literally that—a place where animals were housed. Institute Board member, Sir Andrew Grimwade recalls:

'...through the jungle of the Royal Melbourne Hospital's grounds. Past the hissing steam and soiled sheets of the Hospital's laundry, I discovered a remote pseudo-zoo with mice, rats, rabbits, guinea pigs, ferrets, sheep and two rhesus monkeys. It was the Institute's Animal House and, above it, was an iconoclastic hermit called Dr Metcalf. Here was one of the World's most brilliant scientific brains. I thought Don Metcalf deserved better and his incredible working conditions haunted me for years.'²

There were 10,000 mice in the animal house!

- Describe what it must have been like for Donald to work in the animal house every day. Make sure you include the way he felt about his research and the fact that he was allergic to animals.
- Write an imaginary version of the first meeting Donald had with the new Director of the Institute, Gustav Nossal. Include an indication of how Donald felt as his fortunes changed.

Growing colonies

- Why was the work of Ray Bradley so exciting for Metcalf and his interest in leukaemia?
- What do you understand by the term 'colony stimulating factor (CSF)'?

A hormone is a chemical substance within the body which controls and regulates the activity of particular cells or organs. All living animals and plants that have more than one cell produce hormones. Each hormone works only on the target cells which are receptive to its action. Colony stimulating factors are a form of hormone which work on white blood cells.

- Why is it so important for Donald to be able to regulate white blood cell production when working with leukaemia?
- Write a script for a short play about the staff meeting when Donald convinced everyone (scientists and ancillary staff alike) in the laboratory that from now on he wanted to collect all their urine in buckets. Create fictional names for the members of the laboratory as you present their hypothetical reactions.
- Purifying the CSF from the urine took a lot longer than expected. How long did it take? Do you believe that most people would have persisted for so long with little to show for their efforts?

Persistence

The CSF made from tissue using Bradley's technique had to be purified. One molecule in a million in the tissue culture would be the right CSF molecule. There were six stages in the purification sequence of one of the four forms of CSF they had discovered, G-CSF. Some of these stages had to be repeated 100 times. They didn't know how pure they needed to make the sample. By the early 1980s, Metcalf had a team of six full-time biochemists working on the purification process, which they calculated would take them 250 years to make enough to test on one patient for two weeks. All that time and effort was needed to learn that what they were doing wouldn't work. The team realised that the only way to make enough CSF to be useful was to use genetic engineering—clone the gene responsible for making the CSF and put it back into bacteria for them then to mass produce CSF.

- Imagine leading a team for years and years and then realising the project goals wouldn't be met. This is quite common with scientific research. Great discoveries come slowly. Using Donald's story as an example, write a description of the

personal characteristics needed to be a good research scientist. Research other great discoveries in science. Is this long hard slog typical of the scientists involved?

When the CSF was finally mass produced, at a further cost of about \$2 million, it could be tested in mice. Donald was finally able to answer his question of whether the CSF did elevate the level of white blood cells. As he says: 'And the answer is, it did. Phew! That was a big relief. Twenty years of work, 15 [years] of purification.'

- Imagine that moment of knowing that the CSF did work. Describe how Donald and his colleagues must have felt. Do you think 'Phew!' fully describes it?

Donald says that much scientific research doesn't lead to positive results. That knowledge was in his head every day as he stared down the microscope.

- Describe the alternative scenario—that the CSF didn't work. What do you think the reaction of all those working in the lab would have been like? How do you think Donald would have reacted?
- At many stages of Donald's life, he persisted for very long times at various projects. Quoting examples from the program, explain what factors in Donald's personality and situation may have enabled him to show such extraordinary persistence with no promise of a positive outcome.
- From what you have seen and heard of Donald in this program, what do you think are the motivating factor or factors which have kept him working so hard for so long?

Genetic engineering and drug companies

Donald Metcalf's work has gone well beyond just leukaemia. Many cancer patients would die if it were not for chemotherapy which kills off the cancer cells. But it also kills off the 'good' white blood cells, which protect the patient against infection. By being injected with CSFs their white blood cells are stimulated to reproduce more quickly, thus increasing the chance of protecting the cancer patient in that vulnerable stage. This treatment has also allowed patients to be given more intensive chemotherapy, thus improving their chance of survival. As mentioned in the program, this treatment has already been given to millions of people with cancer.

The mass production of the CSF hormones was done using genetic engineering by Swiss, American and Japanese biotech companies.

- Has the understanding of the role of genetic engineering in this situation affected the way you felt about genetic engineering before you watched the program?

In the interview, Donald talks about the need for funding for research. Although his own salary was covered by the Carden Fellowship, money is needed for the salaries of assistants and ancillary staff as well as for equipment and materials. Producing the small vial of CSF for testing cost a biotech company many millions of dollars. To bring a drug from the lab to the bedside costs a thousand million dollars and this may not ever give a return on the investment.

Topic: that funding bodies have too much control on what research can be done by scientists.

- Prepare an argument either agreeing or opposing the topic. Use the Donald Metcalf case as the basis for the argument.
- If possible, form debating teams and debate the topic formally.
- Did the understanding of the need for huge financial resources impact on your opinion of the 'drug companies'? If so, in what way?
- What does Donald mean when he says 'It's a real gambler's life you lead'?
- Explain in your own words why Donald believes it is so important to get a patent.

The role of celebrities

The renowned tenor José Carreras was one of the first patients in the world to receive CSF treatment. This one case among the millions who have been treated with CSF is widely quoted.

More recently, Kylie Minogue was diagnosed with breast cancer. Her public battle with the disease is claimed to have been responsible for a much greater awareness of the disease and more donations to research.

- Have you learnt about any disease due to a celebrity who was willing to talk about their condition publicly? If so, who? What did you learn?
- Have you learnt about a disease because someone you know has been diagnosed as a sufferer? What did you learn?

Honours and the team

It is possible to get the impression that honours and awards are easy to win when someone like Donald Metcalf has so many, however most scientists will never receive much public recognition.

- How does Donald respond when asked what all the honours have meant to him?
- How do you feel about his response?
- How important do you believe that communication—through conversation and scientific papers—has been in the career of Donald Metcalf? Use specific examples to illustrate your ideas.

A typical day

- Write a diary entry for a typical day as described by Donald Metcalf. Make it a normal day, but include some fictional and real characters—the people he would interact with over the course of an entire day. Include how he feels about what he is doing, and about his backache! Make sure you include his home and interaction with his family.

- Ask an adult in the later stages of their career to describe a typical day. How do they feel about going to work? Do they enjoy what they are doing? How does their response to the typical day compare to the one that you have created from the biography of Donald Metcalf?
- Donald's work seems to be very repetitive. He has worked at the same sort of task in the same place for most of his life. Compare this to the careers of a number of older people you know. Have most changed jobs and employers? From your small sample, do you think Metcalf is typical?

At the end of the program Donald says: 'You stay a little young person staring out of your eyes and you haven't changed since you were 15. And it's very hard to realise that outside you are getting old and tired and slow looking...'

- Read this quote to three or four 'old people' (as old as you can easily find!) and ask them if that is true for them also. Is Donald talking about only himself, or is what he says true of the other older people you have talked to?
- Imagine yourself as an old person who still thinks like you do today—but everyone around you sees you as old. Write a paragraph describing how you feel. Does this change the way you see old people?

Endnotes

1 <http://www.science.org.au/scientists/dm.htm>

2 http://www.mup.unimelb.edu.au/speech/sir_andrew_wehi_speech.html

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The Walter and Eliza Hall Institute www.wehi.edu.au

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