

## **Chapter 4. Walter and Eliza Hall Institute, 1946 to 1948; Rockefeller Institute, 1948 to 1949**

### **Research on Ectromelia, February 1946 to August 1948**

When I arrived at the Walter and Eliza Hall Institute on 1 February, 1946, almost all the staff there were working on influenza virus, which, remembering the disastrous outbreak of influenza just after the World War I, Burnet had undertaken as his contribution to the war effort. As he had suggested, I undertook studies of various aspects of the epidemiology of infectious ectromelia virus. As I found when I had access to the library there, Burnet's suggestion that I should work on the experimental epidemiology of this virus stemmed from work carried out with it in England (Greenwood et al., 1936). Selection of this virus was made more attractive because of Burnet's discovery (Burnet, 1945) that it was an Orthopoxvirus, i.e., it belonged to the same group of viruses as smallpox and vaccinia viruses.

I used the same animal room as the other research workers to carry out experiments, but had a separate room to house infected mice—a wise precaution in view of the disastrous outbreaks of this disease that occurred in laboratory mouse colonies in Europe and the United States. Throughout this work, Bobbie acted as my part-time and unpaid technical assistant. We started by using cylindrical cages that could be attached together according to the number of mice in the cages, as developed by the British team. The first experiments looked at the effect of vaccination with vaccinia virus, the next two on the portal of entry and the sites of elimination of the virus in naturally infected mice.

At the end of the first year, I learned that the University of Melbourne had just introduced the PhD degree (previously, scientists went to the United Kingdom for their PhD). Since as an ex-serviceman I would not have to pay any fees, I applied to the University to be admitted as a PhD student, only to receive the reply that as a Senior Haley Research Fellow of the University of Melbourne I held too senior a post to do a PhD.

During these early experiments we handled all the mice in the cages every day, and made the observation, not easy because of the hair all over the mouse's body, that those mice which did not die of acute hepatitis usually developed skin lesions all over their body—a generalized rash. This had never been described before and was of particular interest because it suggested that ectromelia would be a good model for studying the pathogenesis of smallpox and other generalized diseases that produced a rash. We immediately undertook experiments to investigate the pathogenesis of this generalized infection, in

particular to find out what happened during the incubation period. We had to use the crude techniques available in those days, namely infecting mice by inoculation of a small dose, in a small volume, in the footpad, and then titrating virus from the internal organs (blood, lymph nodes, spleen and liver) and, when a rash developed, from the lesions and from seemingly uninfected skin. The titrations were supplemented by histological studies, since most ectromelia-infected cells produced very characteristic inclusion bodies. Most of my papers were published in the 'Adelaide journal', the *Australian Journal of Experimental Biology and Medical Science*, but I published the detailed experimental results of the pathogenesis experiments in the *British Journal of Experimental Pathology* and a paper drawing generalized conclusions in *The Lancet*. Nearly 50 years later, the latter paper was republished in 1996, as a 'Classic paper', in *Reviews in Medical Virology*. Over the next two years I published five more papers dealing with various aspects of the experimental epidemiology of mousepox, as we now called the disease and the virus, concluding with a long and comprehensive review in the *Journal of Immunology* (Fenner, 1949). My baptism in virology, the study of ectromelia virus, led to a lifetime's interest in the poxviruses and ultimately to my involvement in the smallpox eradication campaign of the World Health Organization.

#### **Frank Macfarlane Burnet**

My relations with Burnet, who was the most creative and imaginative scientist that I have known, were very cordial. At the time I arrived there in 1946, he and all other staff were working on influenza virus. Burnet kept tight control over their investigations, for in those days of non-existent overseas travel, he thought that he had to compete with large teams in the United States. In contrast, he allowed me complete freedom to do as I wished within my topic, the experimental epidemiology of ectromelia. At that time he worked at the laboratory bench from 9.30 am until 4 pm each week-day, and although we met at the tearoom, he was a reserved man and talked little. However, when I had completed an investigation and written it up I would give the manuscript to Burnet. He would read it that evening, and at 4 pm next day we would meet in his office to discuss its publication, and he would then ask about my current and ongoing work. In contrast to common practice in many laboratories, then and now, Burnet never put his name on a paper involving experimental work unless he had done some of the bench work, and all 11 of the papers on mousepox were published in my own name, or linked with that of my wife.

## Helping Burnet Write a Review Article and a Book

Unlike most biomedical scientists, Burnet wrote many books as well as scientific papers. Early in 1948, after he had an opportunity to evaluate my writing, Burnet asked me to collaborate with him in an article he had been asked to write for a new international journal, *Heredity* (Burnet and Fenner, 1948). He must have been satisfied with my performance, because he then asked me to collaborate with him in producing a second edition of *The Production of Antibodies*, the first edition of which he had published in 1941 (Burnet et al., 1941). I helped chase up some of the work done since then, notably Medawar's studies of transplantation immunity. Burnet was responsible for all the interpretation and speculation. The second edition is notable because it contains the first mention of the concept of immunological tolerance, the topic cited in the award of the Nobel Prize to Burnet and Medawar in 1960.

## Overseas Study at the Rockefeller Institute for Medical Research, August 1948 to July 1949

During the last few months of the war, Bill Keogh had travelled overseas and made arrangements with several funding bodies, notably the Nuffield Foundation, the Carnegie Foundation and the Rockefeller Foundation, to enable men who had been in the Directorate of Hygiene and Pathology during the War to gain overseas experience. He had visited and been impressed by René Dubos at the Rockefeller Institute, and after discussion with Burnet they had agreed that I should go to work with him, in what was then the leading medical research institute in the world. I received a Rockefeller Foundation Fellowship of £3,000 and a grant of £300 from Burnet to help cover travel costs. Before I left, Burnet told me that, when I had spent a year at the Rockefeller, he would provide me with a job at the Hall Institute, perhaps as Deputy Director, or, he said, there may be a job in 'Florey's new institute in Canberra'.

Before we left, I wrote to the senior virologist at the Rockefeller Institute, Frank Horsfall, suggesting that I would like to bring some ectromelia virus with me, so that I could make use of some of the more sophisticated equipment there. This was greeted with horror, because of the bad reputation that virus had of decimating colonies of laboratory mice, a matter on which I spoke at a conference in New York as late as 1980 (Fenner, 1981). Instead, knowing that Dubos was working on mycobacteria, I took some strains of the newly-discovered 'Bairnsdale bacillus' with me.

After shipping our heavy goods to New York, Bobbie and I went by the *Aorangi* to Vancouver. Travel was arranged so that the ship would stop for at least one day at several islands: Auckland in New Zealand, Suva in Fiji and Honolulu in Hawai'i. At each of these places we spent an interesting day travelling around the city and the country near it, all quite different from Australia or the countries

of the Middle East, where Bobbie and I had been during the War. Burnet had written to Dr C. E. Dolman, Professor of Bacteriology in Vancouver, and he met us and took us all around Vancouver and its environs before we boarded the Canadian Pacific Railway to cross the continent. We had hand luggage only, and stopped off at Lake Louise for a day to see the mountain scenery, which was breathtaking. Then through the Rockies to the prairies of Saskatchewan, Manitoba and Winnipeg to the Great Lakes. We got off in Toronto, where we met up with van Rooyen and Rhodes, authors of the book on medical virology that I have mentioned earlier (see Chapter 3). After an interesting day there we went south, spending a day at the Niagara Falls, then by train to New York.

### **Accommodation in New York**

Arriving at New York Central Station at 9 am on 20 September, we booked in at a hotel near the Rockefeller Institute, which was located on East River between 39th to 42nd Street. After meeting with Dubos and his team, one of them drove us around looking for a suitable apartment. In 1948–49, New York was an exciting city, clean and still reasonably safe, if one didn't wander into some parts of Harlem (as both Bobbie and I were warned by bus drivers, on different occasions). We eventually finished up sharing a flat with a 70-year-old Georgian Jew, Mr de Kika, who had a large apartment at 141 West Street, on the opposite side of town from the Institute, which we arranged to share at a cost of \$80 monthly. That evening we met up with my old friend Noel Bonnin, who was in New York for a few days on his way back to Australia from England. After getting our heavy baggage out of Customs we set up at the flat. Early in our stay in New York, we visited scientists who had been working with Burnet when we were there, Fred Nagler in New Brunswick and Bernard Briody at Yale University. We also visited some of the marvellous museums in New York, the Guggenheim, the Metropolitan Museum, the Museum of Modern Art and the American Museum of Natural History. I enjoyed the bus trip across the city, which with delays and walking took about an hour each way, because it was a great chance to see something of this great city and its varied inhabitants. We also went to the Metropolitan Opera several times; I remember particularly Wagner's *Tristan and Isolde* and *Siegfried*.

It would have been difficult to live and travel as we did on the £3,000 of the Fellowship if Bobbie had not got employment to look after the young child of a local doctor, Dr Grogan O'Connell. On 19 December, we both moved into his large apartment at 438 East 88 Street, rent-free and within easy walking distance of the Rockefeller Institute.

### **My Research at the Rockefeller Institute**

Dubos had laboratories on the third floor of New North Wing, just below the laboratories of the Rockefeller Foundation, where Nobel Prize winner Max

Theiler worked, with a number of other distinguished arbovirologists. Just along the passage were three other distinguished scientists: Peyton Rous, who was to receive the Nobel prize in 1966, 50 years after his demonstration that Rous sarcoma virus was responsible for malignancy; Rollin Hotchkiss, who was patiently demonstrating that pneumococcal ‘transformation’, discovered by Oswald Avery, was indeed due to DNA and not a protein; and Merrill Chase, who had just escaped from the teutonic supervision of Karl Landsteiner to carry out important work on tuberculosis, independently of supervision.

Being new to the field, I carried out research suggested by Dubos and some experiments, more or less in parallel, with the ‘Bairnsdale bacillus’. Five papers emerged from my research there, the most important being a method of counting viable tubercle bacilli (Fenner, 1951).

#### **René Jules Dubos**

Dubos was a fascinating character, very different from Burnet. He had five post-doctoral fellows (as I was classified) working with him. He himself did little laboratory work at that time, but planned the experiments and often wrote them up. At the end of each day he would assemble all of us in his office, sit with his feet up on the table, and ask each of us to describe any interesting results. Then he would pick out an ‘interesting result’ and erect what I called an ‘inverted pyramid’ of speculation, which usually fell down but occasionally led to novel experiments. He invited Bobbie and me to his house on the upper Hudson River for weekends on several occasions. I will never forget my first experience of spring in a deciduous forest. He and I developed very close relationships. I always visited him when I went to New York, we maintained an extensive correspondence for many years, and in 1968 I persuaded him and his wife Jean to come out to Canberra, an experience that he greatly enjoyed. He later became an environmental guru who certainly influenced my later life as Director of the ANU’s Centre for Resource and Environmental Studies (see Moberg, 2005).

### **Dubos as a Mentor**

In those days, all the academic staff gathered together for lunch (a substantial meal supplied at a cost of 25 cents) in the Institute dining room. Dubos took special care to see that all of his team met the personalities of the Institute. On different days, he would move with his group from one table to another and initiate discussions with whoever he had chosen to sit with that day—Gasser, Goebels, van Slyke, Stein, Rivers and many others— so I met a wonderful group of medical scientists, which of course was just what Burnet and Keogh had planned. Periodically, Dubos organized dinners at various ‘ethnic’ restaurants

near the Institute, to which all his postdocs would be invited, along with scientists from Cornell University and the Public Health Research Institute, to discuss tuberculosis. I remember particularly Walsh McDermott, Jules Freund and Bernie Davis.

## Other Personal Experiences While at the Rockefeller Institute

A number of other important matters occurred while I was at the Rockefeller Institute. The most important, personally, was that Bobbie was found to be suffering from carcinoma of the uterus and had to have a total hysterectomy. The operation was performed by surgeon H. C. Taylor and our friend, gynaecologist Grogan O'Connell, on 17 June, at the Sloane Hospital for Women, in 168th Street. She was in hospital for four weeks, with daily X-ray treatment, which continued for two weeks after leaving hospital. I commuted each afternoon from the Institute to 168th Street to see her. We remained good friends of Grogan O'Connell and his wife, and over the next 20 years I made a point of visiting him whenever I went to New York.

The other two matters were more pleasant. The first was a letter from Sir Howard Florey, dated 19 December, 1948, stating that he had been authorized by the Interim Council of The Australian National University to offer me the Chair of Microbiology in the John Curtin School of Medical Research. He also mentioned that he had enjoyed reading my paper in *The Lancet* (Fenner, 1948b). He suggested that while in the United States I should look into the equipment and design of microbiological laboratories, with a view to the design of the building in Canberra. I accepted the offer immediately, and said that during the next three months I intended to spend about four days each three weeks visiting microbiological centres in New York, New Haven, Boston, Philadelphia, Baltimore and Washington. He knew that I was leaving America at the end of July, and later wrote to say that the other two men who had been appointed as professors in the John Curtin School, Adrien Albert and Hugh Ennor, would be visiting him in Oxford during the first week in August.

The other very pleasant surprise, in June 1949, was the news that I had been awarded the 1949 David Syme Prize for Scientific Research, given for 'the best original research work in biology, natural philosophy (physics), chemistry or geology during the preceding two years'. It was founded in 1905, was open to all persons resident in Australia for at least five years, and was at the time one of the most prestigious awards in Australia. I was doubly delighted because my father had been awarded the same prize 20 years earlier, in 1929, for his studies in physiography. Since both father and son had had such a close association with Ballarat, in 1978 I presented both medals and accompanying photographs of the recipients to the Ballarat Historical Park Association. Much later, in 2001, when I was assembling my various medals for presentation to the ANU, the

University of Melbourne kindly provided me with a duplicate of my 1949 Syme Prize medal.

## Other Meetings in the United States

As well as the regular seminars at the Institute, many of which I attended, especially those run by virologists Tom Rivers and Frank Horsfall, I went to international and national scientific meetings held in New York, Boston, Denver and Cincinnati. Bobbie and I also travelled extensively, by Greyhound bus, to many places on the East Coast and as far west as Kentucky, with René Dubos' introductions, always being welcomed by the many scientists that I met. Among the most memorable was a drive from Elizabethtown up the Adirondack Mountains to Lake Saranac in mid-May. When we started, the trees were in full leaf. At Saranac Lake there was still snow on the ground and the trees were just coming into leaf. My visa expired at the end of July, so by arrangement with the ANU, Bobbie and I embarked on the *Queen Mary*, to return to Australia via Europe.

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