MSVA 184

Australian Academy of Science - Science education
Interview with Professor Priscilla Kincaid-Smith

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Professor Priscilla Kincaid-Smith, a former President of the Royal Australasian College of Physicians and winner of the Australian Achiever Award in 1997 for a lifetime's work in renal health, was interviewed for the Australian Academy of Science's *Video Histories of Australian Scientists* program in April 1998. The interview was conducted by Dr Max Blythe of the Oxford Brookes University Video Archive in the United Kingdom. Here is an edited transcript.

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List of edited transcripts.

Early influences

Professor Priscilla Kincaid-Smith, you've had a distinguished career in kidney medicine and you have been an ambassador, even a crusader, for many medical interests. Would you like to tell us about some of the early influences on your life?

I was born in South Africa in 1926. We lived in Johannesburg, where my father was a dentist like many of his family. His grandfather was a doctor but his father was a dentist, and so were he and his brothers. My mother was more unusual: she was a graduate in botany, one of the first women graduates of Cape Town University.

She was a great and very enthusiastic botanist. I think she, more than anyone else, fired your early interest in biology.

Yes, certainly in giving me a love of gardens and flowers – not that I've ever spent a lot of time with those.

Was yours a very close-knit family, or did you all go your own ways?

Fairly close-knit. I had two sisters and a brother, and we got on very well.

Was your family prosperous, enabling you go on through education?

Not very prosperous. When my father came back from the war, the money that his father had left for him to go university had gone, so he had to work his way through dental school. But he said to the four of us, 'It doesn't matter whether I leave you money or not; if I leave you with an education I will have left you with something.' He was determined that we should go to university, which we all did. When I was at school, though, I had no particular academic interest or interest in going to university. I was just interested in playing sport, and swimming and so on.

Were there influences on you as a girl in the 1930s because of the sad division in South African society?

It wasn't nearly as sad, I'd say, in the 1930s as it became in the '40s and the '50s. The division was there, and quite unacceptable, but the actual word *apartheid* only came in at the end of the '40s. In the '30s there was a very happy relationship between many black and white people and from the relationships that I perceived, as a child, it was a much happier country than subsequently.

What about school? You have told me you didn't have private education.

I went to the government school, quite close by, and then on to the local high school. My brother and sisters were all better at school than I was – my sisters always topped the class – but I didn't do a stroke of work at school and I was always bottom. It was only when I went to university that I suddenly discovered that I had some ability and used my brain.

Instead of schoolwork you were keen on outdoor activities – riding, and all kinds of sport. Was that partly because South Africa is such a beautiful country?

I always enjoyed the outdoors and I loved nature. I don't think if you lived in Johannesburg you'd ever want to live anywhere else, because it's a perfect climate, the best in the world. The sun shines every day of the year, the rain comes in half-hour bursts in the evenings in summer, and it's just delightful. It gets crisp and cold in the winter but the sun still shines every day. Moving later to Melbourne was definitely downwards, climate-wise.

At the South African swimming championships in 1946 (on left).

I loved nothing better than going out in the bush and camping. I liked going off completely on my own, climbing the mountains and going up the streams. When we went camping at Rustenburg Kloof, near Johannesburg, I used to disappear all day up the river in a pair of khaki shorts, with a few biscuits in my pocket and a swimming costume. My parents of course didn't altogether approve, but I was always a bit of a loner and would just go.

You must have had great independence, even so early in life. And I think that even though you were a great family person, you have always been intensely private as well.

Yes, and I have always loved the outdoors.

The university opportunity

Having reached the university opportunity that your father had always intended you to have, did you head straight for medical studies?

No. I thought, 'Well, if I have to go to university, I'd better do some sport there.' So I was going to do physical education, but being only 16 I was too young. I drifted into medical science, which was part of the medical course. Initially I was doing it just to mark time but once I started doing it I was committed, and I have been ever since. I suddenly discovered that instead of being bottom of the class as I had been at school, I was top of the class. I could do things – I was interested in things and wanted to study. I suddenly discovered what I wanted to do in life.

In London with touring hockey team in 1950 (on right).

That medical science course at Witwatersrand University, in Johannesburg, included things like histology and physiology but didn't quite get clinical. How did you move to studying medicine itself?

I got my science degree in 1945 and then elected to do an honours year, and I went over to medicine after that. I was desperately keen on medicine; I loved looking down a microscope and I still do. I had decided in second year, without any doubt, that I was going to do a medical degree, but I wanted to do the science course first.

You've spent over 50 years being fascinated by 'down the microscope'. Did that begin with the histology and physiology you studied for your BSc?

Physiology, yes, but more the histology, looking at tissues.

Did you have any influential tutors at university?

There was a very interesting and inspirational tutor, Joe Gillman, who went subsequently to Ghana. He was completely unlike most university academics – people regarded his ideas as way-out. He was inspiring because he was so committed to what he did. He was also very left-wing and he probably influenced me in that direction. In my university career I was very much on the left wing of things, which of course wasn't popular at all in South Africa in those days.

What did the war mean to you?

I've always been a great nationalist and a great loyalist, and I was desperate to go to the war. It was all I wanted to do, but not only was I too young, I was also a woman. Although finally I could have got into the army when I was a second-year medical student, because I was old enough, there was no way they'd let me take part in the war – I had to be a secretary or something, and I decided that wasn't for me. I still am a 'King and country' person. It was 'King and country' then, of course; it's now 'Queen and country' and there's a great debate going on. But I belong very clearly on the side of the Queen.

Clinical experience

Your increased motivation and focus obviously switched something on. By the time you went over to medicine, you had already covered the pre-clinical studies, I think.

Yes. My medical science studies had begun with the first and second years of medicine and then I'd gone on to do two years of science. Now I was going back into third year. Having done so much histology in my science, I found it was easy to do things like pathology – which became my main research interest over the years.

Where was your clinical life based?

I was based partly in the Johannesburg General Hospital, which was across the road from medical school, and partly out at Baragwanath Hospital, where I subsequently went to work. That was a very exciting place.

Those clinical years demanded great commitment and indicated the two ways in which your career was going to go. You were going to have a dedication to research; but, also, from very early on you must have felt that you would never be able to leave the clinical arena, working as a physician.

And looking after patients, that's right. I did not enjoy surgery so much, but I thoroughly enjoyed clinical medicine.

I worked very, very hard as a medical student. But also, in those days, I was training very hard in the Olympic swimming squad, three times a day. There was no way I could do both – being in the hospital all night, I couldn't go on training. I've always absolutely loved swimming but I've always loved medicine also. Eventually there wasn't room for both of them and swimming couldn't go on in any way as a real-life interest. I have continued with some sport, though.

Your clinical training time at Baragwanath Hospital, in particular, must have been stimulating for you. Tell us about it.

After the war, a series of very interesting, very good and dedicated physicians went to Baragwanath Hospital, some of them from England and some from other places. These excellent people included some really good clinicians, who were terribly helpful in providing good tuition in medicine to someone who was keen.

The hospital was built as an army hospital during the war and is quite big, with 2,000 beds. It covers a very large area, with single-storey wards that stretch out for miles. On one side of the road there was this great, long Baragwanath

Hospital complex; on the other side of the road was Soweto township. We did a lot of work in Soweto, as well as in the hospital, looking after people from the township.

It was one of the most exciting times of my life. It was real medicine. You felt that you could either cure or come close to curing almost everyone you saw, whether on the medical or the surgical side. It was a very interesting time in medicine. We'd just discovered the cures for a lot of things. For example, streptomycin for tuberculosis was just becoming available and so people didn't have to die any more from tuberculous meningitis. Tuberculous meningitis had been a death sentence – it was called malignant, and it really was. And the experience during the war had made malaria a much easier condition to treat; for typhoid, antibiotics were just becoming available, such as Chloromycetin.

Because this hospital dealt with hundreds of cases of serious infection, you gained great experience with infection.

Absolutely, and at a time, luckily, when suddenly you could treat them all. It was a very exciting time to be there but we worked terribly hard, virtually round the clock. We were on seven days a week, almost 24 hours a day, often up all night. I've never worked nearly as hard and I got terribly tired, but I loved it. I was there for nearly three years altogether.

A change of country, and the riddle of malignant hypertension

The next step took you to London. How did that all materialise?

Well, having such a really great interest in and love of pathology, I thought that was perhaps where my career lay. I went to London to do pathology under Professor Dible, at a very famous school, the Royal Postgraduate Medical School at the Hammersmith Hospital. Even although I had a very great love of clinical medicine, I did think, 'Well, I'll give pathology a serious go,' but I knew almost as soon as I got into pathology that I wasn't going to stay there. It was very useful, because I learned a tremendous lot toward my subsequent research career, but I couldn't have continued to spend my life in the autopsy room looking at sections down the microscope. I had to go back to patients. So I spent three years in pathology and then went back to train in cardiology.

I know that later you studied blood vessels and the circulatory system. Is that where you started when you went into pathology?

No, not initially. I really got interested in kidneys very early on, and became intrigued with the blood vessels in the kidney. Almost as soon as I had expressed an interest in kidneys, Sir John McMichael – the head of medicine at Hammersmith, who was studying the clinical aspects of malignant hypertension – was very keen for someone to study pathology, looking at a big series of kidneys he had from about 200 people who'd died of malignant

hypertension. I was of course delighted to be involved in that. Malignant hypertension being just that – malignant; everybody died in six weeks or so – we had the complete pathology for everybody, a really big series. I started looking at those kidneys and then, because the main lesion in malignant hypertension occurs in blood vessels, I got an intense interest in blood vessels and what happens inside them.

You started to look at glomerular vessels that were deteriorating quite heavily on the inner surface.

Yes. The kidney is a huge mesh of blood vessels leading into tubes that the urine goes down, and so there are the glomeruli and then there are all the vessels as they get bigger. My interest was in all aspects of those, from the glomerulus up to the main renal artery, which still shows the same process. In fact, one of the first papers I ever wrote was about the blood vessels in a particular form of kidney disease, chronic pyelonephritis. That appeared in the *Lancet* in 1955, right across the first two pages.

Was this a pathological commentary on what you were seeing in the kidneys?

Yes. It was on the association between the vessel lesions in the kidneys and hypertension in people with chronic pyelonephritis, many of whom had malignant hypertension. As I say, I remain very interested in what goes on in blood vessels to this day. And that led to all sorts of interests in and understanding of the process of atheroma, which essentially is the main killer of people in the world today.

From what you have said, Sir John McMichael changed the direction of your work and found you a niche that really made all the difference.

That's right. He was certainly the major person influencing what I did and influencing my life at that time at Hammersmith Hospital. He was a great supporter, a wonderful, friendly man. A lot of people found him very stern and so on, but he was the sort of person you could really talk to – a wonderful brain, wonderful intellect, very sharp, always on the ball on any little point, incredible understanding of the pathology, without really having done pathology – a wonderful person to work with at that stage because he had such a great interest in the process. He, I guess, was the first person with whom I discussed the question that in malignant hypertension there must be something other than the blood pressure that does the damage. We got onto that quite early, that you got much worse vessel changes in some people than others and it didn't relate just to the blood pressure. We even talked in those days, the 1950s, about whether the other factor was the newly discovered hypertensin, as it was called then – now called angiotensin II. That was long before hypertensin had been measured in malignant hypertension but it was subsequently found to be extremely high, and it probably is a factor.

You think that angiotensin is the real toxin in this eroding of the endothelium?

It's certainly a very important factor. In a whole lot of situations it's very important. There are many mechanisms now which have been shown to cause endothelial damage through angiotensin, and I've had a very long interest in that area.

The drama of that situation must have involved both pathology and some kind of treatment. The pathology was quite exciting. Were you studying that large range of material from biopsy or from autopsy?

Autopsy. Bob Muercke, who was one of the first people to do real biopsy, came to Hammersmith in about 1956. He taught me how to do it and much of my subsequent interest was in biopsy work, but certainly that first series of kidneys was from people who had all died. Therefore we had the whole kidney to look at, not just a biopsy.

This really was a very rapid and fatal disease.

A really terrible disease. And I was involved with it again, very quickly after that, on the clinical side – in the very early days of its treatment.

From pathology to treatment

What did you actually do? Were you giving people blockers?

Yes. We used a lot of drugs in the early days. I don't think we were ever into the Kempfner rice diet, which was one of the first treatments for malignant hypertension. By the time I joined Sir John McMichael at Hammersmith, he was treating patients with drugs like vegolysin, which was one of the first ganglion-blocking drugs, and subsequently ansolysin and pempidine. There was a great disadvantage in all those drugs, because although they would lower the blood pressure very well when you stood up, they didn't when you lay down. And if they lowered it enough when you were lying down, then you couldn't stand up. We had all sorts of tricks – we always used to have blocks under the head of the bed and so on. But it was absolutely dramatic to see what you could do for people, even with lying blood pressures of 300/150, provided you were controlling the blood pressure some of the day. So it was again a very exciting time, like the time of antibiotics at Baragwanath. It was right at the very beginning of treatment of malignant hypertension. Previously young people had died from it left, right and centre. They just died like flies. It was a death sentence, and a very rapid one.

You were working on that with McMichael in about 1954-56. Were you there when calcium blockers came in? Was that the next step?

No, they were a long time afterwards, coming in right at the end of the '60s.

We were really treating people quite effectively with the older drugs before any of the newer drugs came along. It was the very beginning.

Could you summarise for us what you were seeing when you looked down your microscope at this autopsy material, at these glomerular knots in the kidney?

Essentially what happened was that the endothelium was severely damaged and you saw clotting. You saw great big fibrin thrombi in the vessels, the so-called fibrinoid necrosis, and in the glomeruli. The endothelium was all damaged. And so it went: platelets, fibrin and blocked vessels and death. And it was terribly rapid. Once it started, it just went like wildfire. That disease is gone now, it has virtually disappeared. We never see it anymore, because we're much, much better at treating high blood pressure than we used to be.

Teaching postgraduate students at Royal Postgraduate Medical School, London 1955.

A recommitment to clinical work

The kidney work spanned pathology and the clinical field, being virtually continuous. But the clinical work really did take over towards the end and you got quite a senior appointment, after moving over as a visiting research fellow.

Yes. I was in the pathology department for three years, and then I moved across to work with McMichael in the clinical field, in cardiology. Essentially I was studying in my first year but in the next year they offered me a registrarship in pathology and so I spent two years as registrar. Then I decided I wanted to go back to clinical work, so of course I had to go to the bottom. I went to the house physician level and worked my way up. Eventually I became a registrar, and senior registrar, and then just before I left I was offered a consultant job at Hammersmith – a great feather in my cap, I thought.

So do I. That was a male world, essentially.

Well, not so much in London, I really would have to say that. There was a stage when 60 people applied for two registrar jobs at Hammersmith on the medical side and two women, Lavinia Loughridge and I, got them. So it wasn't a male world. One really felt that one had a fair go.

And Sheila Sherlock was there as well, founding an entirely new way of

dealing with liver disease.

Sheila was there. She did liver biopsy. She was a superb clinician; we all used to go to Sheila's round. She'd be as rude as anything to you on the round – really pick you out and say, 'That's absolute rubbish,' and walk on to the next patient. But she was tremendous, a really wonderful clinician. She has had a wonderful career and made great contributions, founding the science of hepatology.

People like Chris Booth were also coming on stream there.

Yes. Chris and I were contemporaries, registrars together. I knew them both very well.

The other physician on the McMichael unit was Malcolm Milne, who I guess was England's first nephrologist. He certainly inspired me on the clinical side in the renal field. I learned a lot from him. He used to get a lot of important visitors – people like Belding Scribner, who started the artificial kidney off in America, came to work with him. At Hammersmith, actually, we had the first Kolff rotating-drum kidney. I was the registrar in charge of that and so I used to sit there all night watching this huge drum going round and round, with yards of cellophane wrapped round it. We did all the dialysis for the south of England, so I had a very good training in that part of renal disease. Malcolm Milne later went to Westminster.

As you say, he was one of the pioneering nephrologists. That is why to this point I've been talking about 'kidney medicine', because this was only just beginning to be a discipline.

The name 'nephrology' for this science was first used in about 1960. But he was there before that, of course, and my interest in kidney pathology stood me in good stead in my work with him because of the importance of biopsies.

Marriage, and another change of country

What else was there about those Hammersmith years?

The life in London. Even although I'd always been an outdoors person and loved the sunshine, and hated the climate in London, I adored London because it was such an exciting city. I was terribly poor – we used to get only about £6 a week – but I could still go to the theatre once a week, and go to a concert once a week, and do all those exciting things you do in London. I wouldn't like to bring up a family in London, which is a different sort of place now, but I loved living in London in those days.

And you met Ken there, bringing two essentially medical families together.

Yes, Ken Fairley, who was over there training in cardiology. Ken's father and all his father's four brothers were doctors. His uncle was Sir Neil Hamilton-Fairley, famous in the tropical field of malaria. The family was Australian-based, but Neil became Professor at the Tropical School in London. And then his two sons, also, were doctors. Gordon was tragically killed by an Irish bomb in the 1970s.

Ken and I met in May 1958, got engaged in June, got married in July and came out to Australia at the end of the year. I was 31 – Ken is the same age as me. He had spent four years in London, training with Paul Wood at the National Heart Hospital, and was just about to come back to Australia when I met him.

And your careers were going to converge on the field of kidney medicine.

Yes, they did. We both, interestingly, trained in cardiology – I trained in pathology and cardiology. There was no nephrology as such at the time, but I had been lucky enough to work with Malcolm Milne, as I said.

Ken was coming back to Australia to an appointment, but you had to begin your career over again, essentially, in Australia. You came from being senior registrar. What happened then?

I'd been senior registrar and I'd been offered a consultant position at Hammersmith, but when I came to Melbourne nobody wanted me. Married women were unemployable, virtually. In Australia, when women married they lost their jobs. You couldn't be a married woman and employed in a university or hospital position. So to my absolute amazement and dismay, I was jobless. I did do a bit of research, but I had no status and I had no base or patients or real responsibility for a number of years. I was really frustrated in those first few years, because I had a lot of things I was interested in and wanted to do but I had no way of doing them. It was very, very disappointing.

The question of analgesic nephropathy

Ken got a position at the Royal Melbourne at that time. It took a long time, until 1965, before I got into the Royal Melbourne Hospital. McMichael teed up a position for me at the Baker Institute with Tom Lowe, who was the then director of the Institute, and I worked there for a couple of years. The position was very ill-defined. I was a part-time research assistant – I was having children all this time, so I wasn't full-time – and I had no status. But I was able to do research, and the most interesting thing I got into, almost immediately, was the question of analgesic nephropathy.

You were to make yourself quite well known in Australia, although not always popular, by highlighting an enormous misuse of analgesics that you hadn't seen occurring anywhere else. Tell us about that.

The beginning of the story for me was going to the autopsy room at the Alfred Hospital. My practice had been to go every day to the autopsy room to see what the pathology was. On my very first day going in there, I went to have a look at the kidneys, which of course interested me particularly. There on the table were three sets of kidneys with a condition that I'd never seen in six years in London, even although I'd gone to the autopsy room every day. When I asked the pathologist about it, he said, 'Oh, it's terribly common. It's a papillary necrosis. You get it with infections.' I said, 'Well, it's funny, you don't get it with infection in London.' And that was really the beginning of it. I was convinced this was a completely different condition, one that I had never seen in London.

Ken was the first person to recognise the association with analgesics. He, as a very careful historian, had found on questioning some of his patients who were developing kidney failure, particularly after operations – the same group of people had tended to have gastric ulcers – that they were taking vast quantities of analgesics, of Bex and Vincents powders, essentially aspirin-phenacetin-caffeine. Then, because some of these patients passed little bits of black material in the urine, I sectioned those and found they were papillae. I realised these were the same things I'd seen on the autopsy table. So that was how the connection first came up, and it followed on from there.

These patients were taking incredible amounts of analgesics. For example, we had a doctor patient who was taking 100 doses a day. That would kill a person who suddenly took it, but if people get used to it gradually they can get up to that sort of amount. Many people took 30 or 40 doses. What they described was that as soon as they woke up in the morning, with their Bex powders by the bedside, they'd feel they had to have one to 'start the day'. So they'd slug back a couple of Bex powders…

They'd have a dependence on it.

Yes. They had powders, largely, believing they were much more effective than the tablets. They'd toss a couple back and swallow that down with some water, and then they'd feel they could start. It was like people who are addicted to cigarettes and can't start the day without one. Then they would just go on – every couple of hours they would feel that they had to have some more. Often they got a headache, probably a caffeine withdrawal headache, and so they'd reach for the powders again. And so it went on. Many of them took very, very large quantities. In all the factories the powders were provided free of charge.

Was this a peculiarly Australian thing?

At first it seemed to be, but it was similar to the addiction pattern in Sweden at that time and it probably still exists to a certain extent in countries like Switzerland and Belgium, where there hasn't been much control. It was very much a community habit. If you went into the supermarket, every second

trolley that you saw people wheeling out would have two great big gross-boxes of Bex or Vincents on top as their week's supply. I couldn't believe it.

Your deep involvement with that massive social problem went beyond clinical medicine. How did you approach it?

I talked about it a lot at lectures and so on, and the medical community were quickly informed about it. We got together as groups of nephrologists and by the mid-1960s the Nephrology Society was founded. We started going to government then and saying, 'Look, you've got to control this.' Then the Kidney Foundation was formed and managed to persuade the NH&MRC, who eventually – in about 1970 – were able to persuade government to put on some controls. And the disease has disappeared. You never see a case anymore.

The effects of activism

You worked for about 10 years to get that moving, even before you were fully accepted clinically in Australia. You became deeply involved in the voluntary movement for preventive medicine. You talked much earlier about being political – now you felt you had to get into the political arena again?

Yes, but at that particular time and over that particular problem. Obviously, one just couldn't accept that people could take this poison and there would be no restrictions.

Were the companies pleased about this?

Ohh! the companies just hated me. Years later, when finally the restrictions had been introduced, on one of my very rare first-class plane trips I was sitting across the aisle from some people from one of the big companies. I recognised them but they didn't recognise me. They spent the long trip to Singapore talking about me and what they were going to do about it, but then they turned around and said, 'Oh well, Australia's finished now. We'll never be able to sell anything there on a big scale again'. They were deliberately going to Malaysia and that part of the world to introduce the analgesics there. And not long after that the problem started to appear there. It's like the tobacco companies, who know they can't get very far in Australia so they're off to China to sell their wares. I was very, very unpopular. They were very powerful and had a lot of influence in a lot of areas. I know that there were occasions on which I suffered from influence by the analgesic companies.

How was the high profile that you generated in those early years, before you were acceptable in major clinical situations, regarded by the professional community you were joining?

I seemed to get on all right with them but I think I was regarded as an outsider, coming from South Africa – a woman who stirred things up. I don't think I was

ever terribly popular. What bothered me more was that even although a lot of very talented women did medicine in Melbourne and topped their classes, all the women gave up medicine when they became married – often to less capable men – and the men continued to practise.

Attending a medical conference in Sydney in 1963.

And if women were in jobs in medicine, they were the lower-echelon jobs.

Yes. To be perfectly frank, very few of the women who'd gone through the Royal Melbourne Hospital in those days continued to practise. Some of them came back to it in a part-time capacity many years later, but most of them gave up.

Renal transplantation

Eventually you did begin to get further, reasonable work in Australian medicine.

In about 1962 I got a Wellcome Fellowship, my first substantial grant, to work as a senior research fellow in the Department of Medicine at the University of Melbourne. After that I got an NH&MRC fellowship for a year, and that led on to the years when, finally, married women could be employed.

You were a catalyst in the development of kidney transplantation, as early as 1964. Was that program the first in Australia?

It was the first in Australia to use cadaver transplantation, although Adelaide had a living-donor program going in the mid-1960s. I was very much involved in the setting up of the renal transplant program at the Royal Melbourne Hospital. I was a research fellow, with no real status, but nonetheless I was a key person in the process and looked after the patients. The operations were done in those days mainly by vascular surgeons, and the Professors of Medicine and Surgery, Lovell and Ewing, were both very supportive of

transplantation.

I was desperately keen to start it. Dialysis was just starting but we had no facilities, we had no machines – at most we'd only have a machine for one person – and so transplantation was always what I thought we should do. We never seriously tried to set up a dialysis program, except to dialyse people for a very short period of time so they'd be fit for transplantation. Then, if you do transplantation successfully, you treat those patients and you've got room for the next ones and so on. Even by 1967 we had only a couple of renal dialysis machines, but we had set up a very successful transplant program.

Up to that time in the early '60s, kidney transplantation was not going well, despite the efforts of people like Roy Calne, in London.

Transplantation had a very bad name round the world. Several units were doing a little of it. At Hammersmith, my old school, results in transplantation were uniformly bad, but some very good work had been done in Boston in a series of twin cases, and David Hume had done some excellent work. Mary's Hospital had a good program just starting, and Tom Starzl was starting in Denver. I went on a trip in 1964 to look at the transplant programs round the world, and when I came back I decided that we could do it, and how we should do it.

Were you sponsored for that decisive trip?

Yes. I didn't have any money. Somebody invited me to speak and I was convinced. Our program got off the ground very well indeed, and in 1967 we published in the *Lancet* that we had had 80 per cent success – after two years. People could hardly believe it, because around the world the possibilities for cadaver transplantation had seemed quite dismal. But it did work, and it still works. The results we got then were almost as good as the results that we're getting now.

A return to blood vessels

You brought a Sheila Sherlock kind of biopsy into this kidney work, but you weren't at all popular for that.

Biopsies had a very bad name in Australia when I came here, because somebody had done a few at the Walter and Eliza Hall with a francine needle – a liver biopsy needle – and had had disastrous bleeds. So nobody wanted to hear a word about kidney biopsy. We had to re-establish that technique and show that it wasn't dangerous. We were the first to do it in transplants, and we then did it regularly.

That got me back to my blood vessels. Under my eyes, in serial biopsies in the transplant, I could see this whole process of endothelial damage, platelet

aggregation, fibrin, atheroma developing in a matter of six to eight weeks. And that is the now very well-recognised accelerated atheroma of transplantation – the major problem in heart transplants, particularly, but one which we described in the kidney in the mid-'60s.

So getting the transplant surgery under way was actually the bridge to further research on what you'd begun doing at the Hammersmith?

Yes, it was back to blood vessels in the kidney. We were the first to document the transplant atheroma story. I still find blood vessels an absolutely fascinating area, because I think if we could solve that problem we really wouldn't have coronary artery disease. We're getting there. We're beginning to antagonise angiotensin II, which is an important thing. We're beginning to understand a bit more about the role that cholesterol plays. Initially a lot of people thought it was just fat deposition in the vessels, but to me it has always been a thrombosis process rather than a fat deposition process – and very complex, with lots of possible approaches including through chemical factors and membrane interaction.

I'm fascinated by the idea that as a research fellow, on a Wellcome Fellowship, you started a major transplant initiative.

I don't think I was the only person, but certainly I was very much involved. The initial renal unit became a nephrology department in 1967, and I was head of that. By then I had a full-time university appointment as a 'first assistant'. I was head of the department in the hospital, but I ran it as a university employee. I was, of course, supposed to do research, teaching and all those other things that you do in a university position. The position of head of a rapidly expanding renal unit was very demanding and it all took a lot of my time and effort.

We finally got the unit into one place in 1976, quite late. It had been difficult for us, working for at least a decade in almost every ward of the hospital, going round to see transplant patients here and there, and dialysis patients here and there. But we saw it as a challenge, and it worked out in the end.

Trying to prevent renal failure

So where had your work got to in the '70s?

We had moved from the desperate situation in the '60s, when we had to do something about renal failure and get transplantation dialysis established. My interest was never in that end of renal disease but always in the beginning, the prevention of renal failure. The analgesic story is an important part of that, but I became much more interested in trying to do something about the process in the glomeruli in the kidney – especially trying to combat the blood clotting in the glomeruli and the damage to the endothelium.

In the 1970s I worked mainly in the area of glomerular nephritis, which was the major cause of renal failure once we'd got rid of analgesic overuse. We did controlled trials with a combination of immunosuppressant drugs, anti-platelet drugs, anticoagulants. One of the drugs that we got very excited about at that stage was heparin. Although it worked very well, it has got so many actions that it was probably working through different mechanisms than the anticoagulants. Now that time has moved on, I'm doing a trial of an oral form of heparin in glomerular disease, which again we think is working by a different mechanism. So I've continued with that interest in treatment and trying to prevent renal failure.

I was never an enthusiast for dialysis. It was a necessary evil, as far as I was concerned. Transplantation is different – it gives people a completely new sort of life, and I was always an enthusiast for transplantation. But I've always worked very much on the side of trying to prevent renal failure.

Growing recognition and a representative role

Let me summarise where you yourself were by the 1970s. You had been established in the Royal Melbourne since 1967. Your three children had been born in the early 1960s, and your husband was in the same field as you but as a supporter, not a competitor.

A supporter, very much so; never a competitor, because he didn't need to compete. He was for a number of years senior physician at the Royal Melbourne Hospital, but having trained in cardiology – probably the best trained cardiologist at the time that he came back to Australia – he'd moved more into the renal hypertension field. It was probably something we did together, and we did very similar work through those years at the Royal Melbourne. A lot of our publications are joint publications.

By now you had quite an international reputation.

Yes. I was President of the International Society of Nephrology fairly early, from 1972 to '75. I probably had more recognition overseas than in Australia at that time, but I think people took me more seriously when I became President of the Society. Then I became involved in the Royal Australasian College of Physicians. I became the first woman Councillor in 1976.

Was that popular? A few years before that, people wouldn't have believed that could happen.

Well, I must have been popular enough to have been elected, but I don't think I was all that popular round the table in the Council room – it took a while to accept me. From memory, I think it took a few years before there were any other women round the Council table. Even when I became President, in the

late 1980s, there were perhaps only two or three. I was very much committed to and involved in the College of Physicians.

You continued your links with nephrology organisations in Australia, as well as internationally.

Yes. I was President of the Australasian Society of Nephrology in the early '70s, more or less at the same time as the international society, and have continued in association with them. I've continued to be involved in the Australian Kidney Foundation, and particularly interested in their role in the analgesic story and other types of prevention. Involvement with the AMA came later, when I finished up with the College of Physicians at the end of the '80s.

You were elected President of the College in 1986. That's a story in itself, isn't it?

Yes. The President is elected by the Council members, and the Presidential election is like a Papal ballot, with round after round of voting. I think it was the longest one they'd ever had. I got in by a very narrow majority – by one, I think, but I made it!

With the then Governor of Victoria, Dr Davis McCaughey, AC, in 1988.

And you are still the only woman to have been President of the Royal Australasian College of Physicians. You gave that senior role in Australian medicine a lot of your time. Was that a satisfying opportunity to change things?

Yes. The College was involved in many issues, so it was a very interesting time. I remember particularly that the surgeons at that time were very much restricting the numbers of people going into training, but our College never really felt that that was a good thing to do. We've always allowed anyone who is capable of completing the training and passing the exam to come in. Although it got us into a little trouble with our surgical colleagues, we have maintained the view that the more physicians the better. We felt that the more people you had who were properly trained, the better medicine would be

practised in Australia, and I think that view has held up. I was very much involved in the political aspects of that at the time.

We also had a feud with the government, who tried to cut off the physicians' fees. The College was not allowed to talk about money but we just set up another organisation, with the same people in it, to talk about money and we defeated the government. They cut our fees in half in July, we refused to charge any less and got our patients all steamed up about it because they were having to pay half, and they persuaded the government to change it all back in December. They were busy, hard days, but important days in Australian medicine.

Reflux nephropathy

In the 1980s you were still looking down a microscope, still looking at kidney pathology, still interested in research into atheroma of the glomerulus. You were also running a major renal unit. What were the advances that were made in the actual clinical procedure?

We've just gradually got better and better at treating kidney disease. People have always accused me of being unfocused and being involved in too many things, which is perfectly true. One of my other interests was the toxicity of lithium to the kidney, and also I have continued to have a major interest in the condition called reflux nephropathy, which results from reflux in childhood and infection. I was heavily involved in studying reflux with a great friend of mine, John Hodson, who was probably the world's most famous, dedicated and effective worker in that field. He, unfortunately, died a number of years ago, but I'm still working in the area.

Reflux is probably extremely common, occurring in at least two per cent of infants – perhaps far more. Essentially what happens is that when the child goes to empty its bladder, the urine refluxes up the ureters to the kidney because the ureters have an abnormal opening into the bladder. Somewhere between the pressure of that flow up to the kidney and the role of infection, you can get quite serious damage to the kidneys.

This again has fascinated me because it's potentially a preventable condition. If you can diagnose it early, then you can stop the damage. There are various ways of grappling with it. A research project we did a few years ago was looking at babies *in utero*, following those with a dilated renal pelvis through to infancy to see if they refluxed. The main thing is to prevent infection. You can also screen the children of people who reflux, because it's an inherited disorder. We're still trying to find better ways of doing all that.

The main thing I discovered in relation to reflux concerned the progression. Although it's a mechanical thing initially, with the damage from infection it becomes a type of glomerular nephritis and the progression occurs by

glomerular lesions, by this old process of endothelial damage, thrombosis – right back to malignant hypertension in the beginning.

So you're right back to where you started, in a way.

Yes. In fact, it was the subject of that first paper of mine in the *Lancet*, in 1955. Although we called it chronic pyelonephritis in those days, it was essentially what we now call reflux nephropathy. So I've stayed very much in the same area, in many respects.

The lithium story

You mentioned lithium. What was that about?

We became fascinated by the lithium story when a Swedish group published a paper about a series of patients who developed chronic renal failure on lithium. We found it difficult to believe, but we did a big study on patients taking lithium. Using biopsies we managed to pinpoint the essential lesion that they got in the kidney, and I suppose the long and the short of the conclusion of our study was that it really doesn't cause a lot of damage in most people. If people are on lithium, it's better for them to go on taking lithium than to stop it and have all the disasters that they get with manic depressive disease. So we did, to some extent, exonerate lithium. In most people it does not cause significant chronic damage.

Another new stage in life

In 1991, at 65, you were told you had to retire.

That's right. I was just a little bit too early. A few years later the anti-discrimination legislation was brought in, and some of my friends and colleagues who are a year or two younger are still in their university jobs. But I was kicked out. I had to go and find something else to do.

But you still do kidney work.

Yes. I see patients at Epworth Hospital, a private hospital, in the mornings and I work at the university in the afternoons doing a bit of research. And, as we have said, I have been involved with various political activities which have taken quite a lot of my time.

Although you have very few facilities now for research, I believe you're doing a thousand-patient trial study.

I'm reviewing 1,000 biopsies – quite a big series – and documenting cases, to try and work out the factors in biopsies that predict which way people are going to go. It's fairly low-level research but it needs to be done and I can

probably do it as well as most people. It's a slow business, I've found, but it will eventually be published.

I find it hard to think of you as even part-retired, but does your current work allow you more time to be on the farm and to be with the family?

A little bit more time, not much. I actually work a longer day now than I did, finishing at about the same time as before but starting earlier. Perhaps I'm a bit slower. I certainly don't work any less hard from Monday to Thursday, but we do spend Friday to Sunday at the farm now.

On the farm, Apollo Bay, Victoria.

The farm has been a very important part of our lives. When the children were young, in 1965, we bought a block of bushland to have a place to get away to at the weekends, but it runs us now. It is in Victoria, but 100 miles from here. The trip there takes us a couple of hours because we travel late at night – it would take most people a bit longer. We have a large beef herd, with a couple of hundred cows, and I'm very much involved in looking after them. They come and eat out of my hand, and we mark the little calves. It's been a great interest and I don't like selling them. And I still ride the horse. We have bikes, which are much easier to catch than horses, but I love riding.

And what about Ken and the children? Did any of the children become nephrologists?

No nephrologists. Two are physicians – a gastroenterologist and an infectious disease epidemiologist – and our daughter trained as a vet but is now in the pharmaceutical industry as a manager. She's in the United States right now, actually. And we've got six grandchildren. They all love the farm, and we get together as often as possible. Ken is a senior consultant, and we're both working away.

Let me congratulate you on rising to become President of the College after such a hard start in Australia, and thank you very much for participating in

this interview.

Thank you very much.

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