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AUDIO INTERVIEW TRANSCRIPT

Elwood, Peter: transcript of an audio interview (14-Apr-2000; 28-Feb-2001)

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Elwood, Peter: transcript of an audio interview (14-Apr-2000; 28-Feb-2001)*

Biography: Professor Peter Elwood FRCP OBE (b. 1930) was a member of the scientific staff of the Epidemiological Research Unit (South Wales) from 1963 and its Director from 1974 until its closure in 1995. He qualified in medicine at Queen's University, Belfast, in 1954 and worked with John Pemberton from 1958 to 1963. He was to retire in 1995 but has ignored the advice and still works almost full time, supported by Janie Hughes and Janet Pickering, a statistician in the unit from 1977 to 1982. He holds Honorary Professorships in the Department of Epidemiology, Statistics and Public Health Medicine in the University of Wales College of Medicine and the Department of Social Medicine in the University of Bristol, and is a Visiting Professor in the Department of Science at the University of Ulster.

AN: Andy Ness

PE: Peter Elwood

AN: Can I start if you like at the beginning and ask a little bit about where you were born and when you were born and a little about your early family life?

PE: I was born in the north of Ireland. I had a very happy childhood, I was one of five brothers all whom did medicine and I think we still hold the record in Queen's University for five brothers doing medicine. I had no idea what I wanted to do when I qualified. I went to Liverpool and did house jobs, I had a brother in Liverpool at that time, and that was the attraction, I did my house jobs, and I enjoyed them immensely. I have always had a great enthusiasm for anything I do and my wife says I am still a boy, I get so much pleasure out of whatever I do and everything is the best yet. I have also, let me get it in now, very little interest in history and I think that is partly because of my enthusiasm for the next study, the next event is going to be the really important one, so I am not terribly interested in what's passed. At the same time I recognize the value of what you are doing. I did house jobs, I did three years of house jobs actually, I enjoyed them so much. Every speciality I went into I thought, oh this might be it, but there was limited intellectual stimulation, and I found myself asking questions, why do we do this? So I went into general practice, and after a few weeks I realized that it was absolutely barren of any intellectual content and no way could I stick it for 30 years.

So I applied to do a Diploma in Public Health (DPH). There was no course running that year. I had to wait and I enjoyed general practice, but it wasn't my scene at all. So I did the DPH and enjoyed it, but again wondered how I would last 30 years in it. John Pemberton was very good to me and he offered me a job as the boy, the junior member of a small team of four people to look at flax byssinosis and I jumped at the chance and just loved it. I have always said that somebody who is into research should be fascinated by the process, not by the answers, and I found the process absolutely exhilarating because we were able to put limits on the degree of confidence. That was the thing that really stimulated me, the statistical estimate of the confidence interval, this kind of thing that clinical medicine was just a fog and you never knew, dealing with single cases, you never knew whether you had any effect or whether any association

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* Interview conducted by Dr Andy Ness, for the History of Twentieth Century Medicine Research Group, UCL, 14 April 2000 and 28 February 2001. Transcribed by Mrs Jaqui Carter, and edited by Professor Tilli Tansey and Dr Hugh Thomas.

was real. Whereas here, dealing with numbers, and with pretty basic statistics in those days, we were able to put levels of confidence on our answers. And I found that, I can remember walking home reading Moroney's *Facts from Figures*, and practically walking into lampposts, I was so fascinated by this, it was such a revelation to me that you could have a degree of confidence within medicine. And this was way back in the late fifties, middle fifties, so statistics wasn't very well developed and epidemiology was rather small print at the end of the book, and not of much importance, but I found it so fascinating that I resolved I would stay in research as long as I could. I didn't think I would be able to stay for long, but I was three years with Pemberton, three wonderful years, he was so encouraging, and I wrote a letter to Archie Cochrane, and Archie invited me over for a few days, and I found that absolutely fascinating. There were so few people wanting to do surveys and randomized control trials were barely mentioned in those days, but I had set up one in Belfast and I had done several surveys. I wanted to – rather than focus on flax workers' byssinosis entirely – I wanted to have a portfolio of research. So I started a few other things. A survey of haemoglobin levels in Belfast, based on a random sample picked from the electoral register, and Archie was absolutely fascinated by this, that I had gone round homes taking blood from people. I also set up a trial of iron-fortified bread within a mental hospital. And just watch how you say that, because that's not acceptable nowadays to use mentally ill patients. But we did then and we randomized a number of the villa accommodation and supplied half the villas with iron-fortified bread. And this all fascinated Archie and he offered me a position within the unit for three years. Those were charmed years and lo and behold at the end of it, I got another two years, and then another two years, and then Archie asked them to make it permanent and I am still here.

AN: Can I go back just a little about your family. You say you are one of five, where were you in the order of these five brothers?

PE: I was number four. And we all did different things. My father was actually a civil servant, but he was in the Ministry of Health, and he rose to be head of the civil service in Northern Ireland, but he never put any pressure on us, but he did betray later in life, he betrayed the fact to me that he had wished that he had done this, so there may have been some subtle influence. But one brother became a pathologist, another an ophthalmologist, another was in public health, and another was in general practice. So we all went different ways.

AN: You say that you were clear that you wanted to do epidemiology. Was there any sense that this was a career path?

PE: No, no. I thought this would look good on my CV and I used to say to Margaret, my wife, that three years with the MRC is worth several MDs. I did get an MD on the basis of the work on flax byssinosis, in fact, if I may slip it in, I got it with honours, but I had no idea that I would stay in research. It was really working with Archie, I just felt that I would prolong it as long as possible, because I felt once I get into something else the opportunity for research will be very, very limited, and so I just tried to prolong it, and I did it very successfully, I say 40 years later.

AN: And do you remember any differences particularly in moving from Northern Ireland to South Wales?

PE: Yes, in that I had far more resources. In Belfast I was doing things on a shoestring, and I really didn't know anything about grant applications. The department applied for money for the flax byssinosis, I paid for everything else I did virtually myself, my own expenses and so on. When I came to join Archie he had a small team, he had just about a year previously separated from the Pneumoconiosis Research Unit, as it was then, and he had brought together a small team, several field workers. Archie was also at that time setting up the Department of Chest Diseases in Sully Hospital. So I really ran the unit and every idea I had was just fed into the home visitors team. Hubert Campbell was a part-time statistician and he spent most of his time actually in the Welsh National School of Medicine and spent very little time in the unit. So I asked for a statistical assistant, because in those days we were using mechanical calculators, I had a Marchant, and I got Janie Hughes, who had a background in punch card operation, believe it or not. I

recognized something exceptional in Janie Hughes and 40 years later all I can say is that there is something very exceptional in her. She has been my right-hand man and absolutely tremendous, dependable, immensely hard-working. And we just got on very well and she quarrelled with me from time to time, because if I let any standard slip, she is meticulous in the standards that she sets, but she's been enormous, and she has been very closely involved in everything I have done. But that was a very significant factor, because I had her to do the statistics, which in those days was very simple, just simple two-way, perhaps three-way, classification. Very simple, covariate analysis, but it was all done on a Marchant.

AN: Could you say a little bit about the work you did with flax workers before you came to the unit?

PE: Yes. The Government had asked the Department of Social Medicine in Queen's University to investigate whether or not byssinosis occurred in the flax industry and if so, what disablement did it cause. Richard Schilling had established that cotton workers' byssinosis was prevalent in the cotton mills, so we did a survey of all the flax mills in Northern Ireland. I think there were about 24 of them. Incidentally, the one mill that would not give us permission to do the survey was owned and run by the then Minister of Health, a man called [Sir John Milne] Barbour, and he refused permission for us to include his mill in the survey. I interviewed all the people, described this study that we were doing, asked the MRC questionnaire on respiratory symptoms, asked them for employment history, and I think I measured height and weight. That was my part in it. Another person did lung function tests and another person made dust measurements in very great detail throughout the mills. Eric Cheeseman, the first professor of medical statistics in the UK, was in the department, and he was an enormous encouragement, a very prickly character, but one who gave me enormous encouragement, and I owe a lot to him as well as to John Pemberton. We saw, my memory says, about 2,500 people in the flax industry, we confirmed that byssinosis occurs in the industry. I was left with some questions, and I very nearly wrote a minority report in the official report of the study, because I felt that there was no doubt disablement from byssinosis, and when the men went in on the Monday and the Tuesday, if they were exposed to high levels of dust, they got quite severe symptoms. In my analysis I found that it was really the smokers who got the severe symptoms. Non-smokers got very mild symptoms. But I was very concerned whether or not there was permanent disability, and so I set up a little study on my own, to follow-up some past workers, and I travelled all over the north of Ireland seeing these past workers, trying to estimate whether or not they had any continuing disability. But that question remained with me, and so about ten years later I went back to the north of Ireland, and I got the survival rates of all the men and women in the study, and I worked out the mortality in the different departments, and I showed that there was no excess mortality even in the men who were exposed to the heaviest dust levels, provided we allowed for smoking and so on. There was no evidence of any mortality and I wrote a paper on that, arguing that byssinosis was an acute condition, and although it led to men having to leave the industry, it did not cause permanent disability. Schilling clashed with me quite severely over that. He remained a friend. I find a lot of these men felt very strongly about their research, but one was able to keep friends with them, and that added to the delight of medical research. There was a lot of controversy, but it was usually with friends. But anyway, I then, about ten years further on, I took the opportunity of looking at people who had worked in the flax industry, and we set up a similar study in the cotton area, and we chose random samples of people in towns in Northern Ireland where flax had been a major employer, and we selected a large sample of people, I think it was about 2,000 people, so that our estimate was that half of them would have worked in flax, and half would not have worked in the flax industry. And we did exactly the same in Bolton and Oldham. We chose I think it was 2,000 people in Bolton and in Oldham and half of them it turned out had worked in cotton and half had not. And we looked at respiratory symptoms and respiratory function in some detail and we published two papers showing, I think, quite conclusively that whether or not there had been byssinosis, whether or not the subjects had worked in flax or in cotton, there was no residual disability. There was a massive effect of smoking on respiratory function, but when we allowed for that there was no evidence of any respiratory disablement from textile dusts. Again, that led to controversy with Schilling and with one or two others, but I think it did establish a very important fact, which sadly was of relatively little importance, because the flax industry died in Northern Ireland, the cotton industry died in Lancashire. So it was a very, very satisfying series of studies over a period of over about 25 years, but of no ultimate consequence in this country. Whether or not other countries take account of it or not, I don't know. But I

was invited to a number of international conferences in New Orleans, in the cotton belt, and oh I can't remember where else, where I presented these results, and it caused quite a stir, but really they were so conclusive when we had finished that series of three studies, the prevalence study, the mortality study, and then the retrospective case control as it were, it really established that byssinosis was still a condition that caused acute disablement, could lead to people having to leave the industry, but was not a cause of permanent disability. And it did lead to very, very great change in the attitude of companies giving compensation, where workers had been claiming disablement, they were able to stand up to them and say no, there is no permanent disablement, and the size of compensation awards and the number of compensation awards fell away to almost nothing.

AN: And you mentioned also in Northern Ireland you did some work on anaemia. I wonder how you became interested in that?

PE: I just wanted to choose some other subject, just to have as I used the rather grandiose term 'a portfolio' of research, and I honestly don't remember what made me think that I would choose anaemia and haemoglobin level, but certainly in those days all the papers and all the reports were that anaemia was highly prevalent and was a very important source of ill health. In fact I remember a statement saying that it was the most important source of ill health in the community and estimates of a third to a half of the women were suffering, that word was always used, suffering from anaemia. Well the first study I did was simply a prevalence survey and I just chose I think it was only about 200 people from the electoral role in Belfast and my wife and I – fiancée as she was then – drove around, wrote to these people, drove around and asked for samples of blood and I did the haemoglobinometry and packed cell volume myself. I published a little paper on this which began a series of challenges, because over the next ten or 15 years, again I did a whole series of studies to evaluate haemoglobin level as an index of health and we looked at symptoms, and that was fascinating. I worked with some psychologists and we devised symptom questionnaires and we applied these to people and looked at the association with haemoglobin level and we found that there was no association until we got down to about 9 grams/100 ml. We then set up randomized control trials, where half the people were treated and we looked at the effect on symptoms and found that until we got down to again about 9 grams there was no effect, no beneficial effect, of treating the haemoglobin level. We then looked at mortality and believe it or not, we had taken blood, an estimated haemoglobin level on 18,000 women in those studies, and I had published a study showing that there was an association with mortality and with cardiovascular disease, but lo and behold the excess mortality was at the upper end and it was particularly with cardiovascular mortality. Now in later re-examinations of those data, when we took smoking into account, where the excess at the high levels was considerably diminished, but it was still there and as I remember it, it was still significant. But that was another series of studies that led to considerable controversy and again a delightful set of friends.

But perhaps the most ambitious study that I have ever conducted was a preventive study. And we set up in the Rhondda valley, we set up a study of the effect of iron in bread on haemoglobin level and we surveyed, as I remember, about 8,000 women in the Rhondda valley. We identified those who had haemoglobin levels below I think it was 11 grams per 100 ml. We gave them a month's treatment to bring their haemoglobin level up and then we put half of them on bread fortified with an iron salt, and half on ordinary bread, and we watched the fall in haemoglobin level over the next two years. We wanted to look at prevention, not treatment, with iron in bread. So we raised their haemoglobin levels, knowing that they would slowly return to what they had been over the next year or so, and we gave half of them bread. We estimated that the absorption of iron from the bread was only about 4 per cent and when I submitted the paper to journals they all refused it, and said this cannot be right, we all know that iron is absorbed from food at the rate of about 30 per cent in women with low haemoglobin levels, this cannot be right. And I had great difficulty publishing the paper. In the end we did publish it and over the next five, ten years, it gradually became apparent that iron absorption from food stuffs is about 4 per cent, so we were shown to be right in the end. But that was another fascinating set of studies and again I just valued the opportunity to follow through an idea and look at the distribution, look at the association with indices of morbidity, to look at mortality, and then to run randomized control trials to look at prevention.

AN: You did some iron studies in Bury I think with South Asian women as well.

PE: That is perhaps the most fascinating story of my life. We had done studies of the absorption of iron from bread. These were radioactive studies. They were done when immediately I came to the unit, I set up these studies, and we used radioactive iron, because we could make such precise measurements of iron retention, and I got friends and colleagues, I think it was about 120 friends and colleagues to come to the medical school on Newport Road [Cardiff] in those days and have a special breakfast, in which we had two forms of iron. One was given as a control, golly I have forgotten the design of the study now, but at any rate we had baked some iron 59, radioactive iron, into bread and we gave people a slice of bread with this, and then a fortnight later, we asked them to go to Harwell and have whole body measurements of the iron that had been absorbed from the bread. And we were able to work out the absorption. The absorption was almost nil actually, and that's another story on the form of the iron that was being added then to bread, which we were also using at that time. But anyway, I got a bit of publicity because of this, both in this country and in the States and I was asked to join the WHO Committee on Iron Deficiency and one of the first things the Committee said to me was that my work on bread was of some interest but really almost totally irrelevant to the countries where anaemia is undoubtedly a real problem, where chapattis or tortillas are eaten and bread is not eaten. They said we do not know what fermentation does to the iron, would you repeat this study using chapattis? So I set up a study to look at radioactive iron absorption from chapattis and we made this, we wanted to mimic the real life situation as closely as possible, so I got an Indian woman to help me make the chapattis. We made about 200 chapattis, we measured the amount of radioactive iron in each chapatti, and we stored them in a deep freeze. I then went up to Coventry where there was a fair-sized Asian population, and with the help of the health authority and one selected GP we selected 20 women, I think it was 20, or 22 women, Asian women. We did rough calculations. In those days we did them on the back of an envelope and we estimated that the method was so precise that we could get very accurate measurements from a quite small number of women. So we selected 20 women. The criteria of selection were that they were all to be over 50 and they were not to be suffering from any important disease and so on, but we didn't want to include any woman who might become pregnant. So I then, with one of the field workers, Tom Benjamin, we took the chapattis up to Coventry and we asked the women to include one chapatti with a meal each day for one week. And each day Tom Benjamin would visit each of these women and deliver a chapatti on dry ice and the women would defrost it and just eat it as part of her meal. We then a fortnight later drove the women to Harwell, and Tom Benjamin really went over the top in making these women feel valued and welcomed. He arranged a visit to see something of interest during their trip to Harwell, which was a day's journey, a day's outing. He visited Oxford, took them round one of the colleges, he took them for tea, he arranged to have tea breaks on the way there and on the way back, and really I think I made 20 friends on that project, they were so friendly to us. We found that iron was no better absorbed or no different from chapattis than from bread, and this study was a seven-day wonder, and everyone forgot about it.

Twenty years later, perhaps more, 25 years later, I had a phone call from a reporter who said they were making a programme for television on the uses of radioactive iron in medical investigations and they wondered had I done anything. And I said 'no, oh yes, I did look at the absorption of iron from bread, and I was also asked to look at it from chapattis'. Well the television programme blew up this story of the radioactive chapattis in an incredible way. I watched the programme with my daughter-in-law, who is a nutritionist, and she was absolutely incredulous at what they did. The general theme of the programme was that medical investigators had broken all the ethical constraints and had looked at the effect of radioactivity in samples of subjects, in order to estimate what would happen if there was a nuclear explosion, and the programme claimed that massive doses of radioactive substances were given, by deceit, were given to people most of whom either didn't know what was going on, or were incapable of giving informed consent. And they showed a number of studies in America. I doubt the truth of this, knowing what they did to my study, but at any rate they showed programmes and interviewed people who had been involved in studies using mentally backward children, using pregnant women, using psychiatric patients, all kinds of odd groups of people, they claimed had been exposed to massive doses of radiation, deceitfully. Oh I must mention that during the programme, there would be intervals, and they showed an atomic bomb explosion with this huge mushroom cloud and so on, and my daughter-in-law would nudge me

each time this came up and said 'that's another of your chapattis has gone up'. So anyway they then at the end of the programme said 'and similar studies have been in the UK' and they interviewed one of the women and a relative of another woman, and these women made extraordinary claims that a research worker from the MRC, they didn't name me, but they said a research worker from the MRC had given them chapattis and I ate a chapatti each day. Some of them claimed that they had eaten two chapattis for weeks on end, all kinds of claims were made, but they said they were then driven in secret to a military establishment where they had a whole lot of measurements made and they then went on and said, the woman who was interviewed, said 'my hair fell out, I began to get pains and cramps, I became arthritic, I am now diabetic, and if only I hadn't touched those chapattis I am sure I would be fit and healthy'. The relative of the person, the subject who had died, said 'my mother's health failed from that day on and she would be alive now were it not for those chapattis'.

Well the health authority, at the request of the Asian community, set up an enquiry and I went up to Coventry and I was met by the Chief Medical Officer who told me, 'look let's go in by the back door, there's a huge crowd of reporters, and Asians, and they are out to get you, they really are very, very difficult'. We went to the meeting and I had prepared over the weekend a very full account of what we had done and I had clipped to it an account of the original study published in *The American Journal of Clinical Nutrition* and I asked the chairman of the meeting if I could give an account of what I had done before there were any questions and I did that. Well the meeting was exceedingly hostile. The health authority were obviously keeping neutral, but one or two of the people there were very, very hostile, in particular a representative of the Asian community who made it perfectly obvious he wasn't going to listen to anything that I said, and at the end he beat the table and he shouted at me that I had been in league with the War Department and the Ministry of Defence, that these poor women had been duped, that I had deceived them, that they were all – he had managed to trace half a dozen of them by then – that they were all in ill health, mind you they were all in their eighties by then and one or two had died, and everything that was wrong with them was put at my door. Over the subsequent weeks, I was accused of all kinds of things. And I mentioned one or two things, that Mrs Butts, an Asian health visitor had been with me on this study and she could testify the fact that I had explained to these women all about the study and so on. Mrs Butts refused, she said she had never met me, she had never had any part in the study of chapattis, and she knew nothing about it. Janie and I returned to the unit and Janie spent a day or two going through the basement, going through all the letters, and she dug out letters, for example a letter from Mrs Butts, saying how much she had enjoyed the study and how well the people had been handled, and how delighted they were to take part and so on, and it just refuted many of the things that had been said. Janie also dug out a letter that I had written to the son of one of the women, who was doing medicine at the time, and this was a complete description of the study. She also dug out letters from the physicist who had prepared the radioactive iron and we submitted that to a number of experts. I should say that was submitted independently to a number of experts, who said that it was an extraordinarily low dose of radioactivity. That by the way was why we had used Harwell, we didn't use the ordinary hospital counters, we wanted to use as small a dose as possible and Harwell had the most sensitive counter in the whole country. So the thing took a long time to die and I had numerous interviews with the Indian press, and they worked at it for a long time, but eventually it died. But just one little codicil to that, I was in India a few years ago and one of my contacts there asked me about this event. He said it had been raised in the Indian Houses of Parliament, and had been in all the Indian papers that this terrible chapatti experiment led to the death and ill health of 20 poor illiterate women. That was another thing they said, these women were illiterate, that I had purposely chosen them so that they wouldn't understand. Well I had letters from about three of them thanking me for the most interesting study, written in perfect English. No I have no doubt somebody could say well they got somebody to write that letter, they didn't write it themselves, but these were, they were very pleasant women to talk to and I have no doubt that many of them, quite a number of them, were well-educated. Anyway that's a long ramble about something.

AN: Going back to when you joined the MRC unit, you brought with you your interests in flax and in anaemia. What did you work on when you first joined the unit?

PE: Mainly anaemia and we set up large studies in the Rhondda valleys to look at this. I was opportunistic, I was looking for everything possible that I could set up and I would have to go through my publications to remember what came next and when it came next, but one thing Archie complained endlessly about was dust from an asbestos works, which was in Aberthaw near his home [in Rhoose]. So we set up a follow-up study to look at mortality in asbestos, it was actually white asbestos, which doesn't really carry any great hazard, and then 20 years later we went back and did another mortality follow-up, so that again is one of the things that I value in an MRC unit – I think it is a shame that MRC units are being run down – the opportunity to go back 10, 20 years later, and reopen a question. Somebody pointed out to me, Sir Peter Froggatt, pointed out to me in my very first job in Belfast, he said 'remember that it is research that you are doing, and you will go back and back and search past figures, past surveys, past populations again and again'. It is research and the researching goes on and on. And I certainly have found that in my career, in many things that I have done I have gone back to.

AN: So in your first ten years you would be doing some studies initiated by Professor Cochrane, some things that you brought yourself, and then gradually you developed other interests.

PE: I should have thought about this and prepared myself, because it's hard to remember how things developed. With haemoglobin levels we looked at this, we tried to investigate this apparent deficiency of cardiovascular disease at low haemoglobin levels and an excess at high haemoglobin levels and we looked at the association between blood pressure and cholesterol level with haemoglobin level and we found that there is a positive association with cholesterol level and this seemed to me to be an explanation of why there was this gradient, but that was perhaps the first study we did on ischemic heart disease. We then had contact with [John] Yudkin [Professor of Nutrition at Queen Elizabeth College, London], who had gone overboard on sucrose and we incorporated a questionnaire on sucrose intake in one of our anaemia studies and looked at sucrose intake and cardiovascular disease. I think we did ECGs on all the women in that study and we published one or two papers showing no association. Well that was trivial, it was a daft hypothesis anyway.

The unit then began, shortly after I came it began to expand. Archie was brilliant to work under, but Archie had limitations. He had the occasional brilliant idea and will always be remembered for his brilliant ideas, but he didn't do an awful lot himself. Now that's not a criticism, he operated at a very high level and he spent most of his time travelling, meeting people, going to meetings, and he stimulated an enormous amount of work, but he left me to run the unit. There was money available in those days, and so the unit gradually expanded, we took on an assistant epidemiologist and then another statistician, and then another epidemiologist, and so on. Archie, of course, had set up with two ophthalmologists the glaucoma survey and that was a very, very fine piece of work, and it really was a benchmark, set a lot of benchmarks in ophthalmology, but that came to an end and there was very little follow up, and so I inherited one or two people from that team who joined the unit and had no other work to do. Michael Burr joined and he was a real go-getter and set up quite a wide programme on nutritional things and he was great to work with, but he was a bit of a loner. That's not a criticism in any way, but he tended to do his own thing. Then John Yarnell joined the unit and he was very much a loner and wanted to do his own thing, and I let him, I gave him his head. This sounds awfully dictatorial, I don't mean it that way, but he did a survey of HDL (high-density lipoprotein) in women. Now I have got to be careful here, I have a great admiration for John Yarnell, but he has great limitations, he does not work happily in a team, he's very much a loner, and I recognized the potential of what he was doing, and so I encouraged John after his survey of HDL in women, which really didn't go very far, didn't get very far. John had a small team, but he didn't really manage them well, but I recognized John's potential, he's very bright, but has this limitation in working with others. And so I encouraged him to set up the Caerphilly study and I involved most of the unit in that study. And I think it really has been a winner and my style of directing the unit was to try and be a facilitator and an encourager, but I am very much a hands-on person, in that I ran perhaps a third of the clinics myself, and I handled a lot of the data myself, and so on. Archie's style of leadership was a very much higher level than mine, and he travelled a lot, he talked about the unit and the unit's work, and exaggerated scandalously, but he did an awful lot of good for the unit and an enormous amount of good for epidemiology and for health services research. But I was totally different, I was hands-on and although

I went to a lot of meetings, it was to present the results of our studies on anaemia or on whatever, a very different level, but I wanted to make sure that these studies were of a high level and that the data collected were good, that a high response rate was maintained, that follow-up rates were as near 100 per cent as possible. And I did an awful lot of the hoofing around and taking blood and so on, and persuading reluctant subjects and so on, I did an awful lot of that myself. And I think my contribution has been to pass on that of a very high quality. There are uncertainties in it, there are omissions of course, but I think they are of quite a high quality.

AN: Could I come back to just talk a little about working in the Rhondda in general, because my impression is that the early studies were clearly on the miners and then there were a number of other studies, anaemia studies and so on, in the Rhondda. And then there seems to be a point at which the unit almost withdrew from studies in the Rhondda and moved as you say on to the Caerphilly studies.

PE: That was my decision. The Rhondda in those days was about an hour's journey away and it was really very wasteful. The origin, of course, as you say was the studies of pneumoconiosis and Archie actually got money to put up a very nice clinic in Ferndale in the middle of the little Rhondda, which we used as a headquarters. We had about four rooms in it and we could do a certain amount of technical work and do quite ambitious surveys there. But it was an hour's journey away and it was terribly wasteful of time and so on. I also felt that the Rhondda was a selected population and when we began to study conditions other than those of mine workers, it was quite obvious that there was a social class-biased movement out of the valleys. So I made a conscious decision to go somewhere else and we chose Caerphilly, which we felt was a fairly stable population, was relatively close, and the health authority there and GPs and so on seemed to be very cooperative and have proved to be. And I think the first study that we set up was a study of the elderly and Michael Burr really took over that area of research, but I did the study of folate levels and B12 levels as well as haemoglobin in Caerphilly. And we looked at a number of things in relation to that. Then Michael Burr arrived and he set up studies on vitamin C and on the health of the elderly and respiratory symptoms. He then set up studies on asthma and Caerphilly proved to be very, very suitable.

AN: Can we come back and ask you to talk a little bit about the studies of environmental lead, which I know you worked on?

PE: Yes. Can I mention before we leave Caerphilly one of the other studies that we set up? I had had a lot of contact with the Department of Health, or Ministry of Health as it was then, following the work on iron deficiency, iron in bread and so on, and one of the committees that I got onto was on child nutrition and child growth and so in collaboration with the Department of Health, we set up a study of child growth. And we selected 1,000 pregnant women, 500 in Caerphilly and 500 in Barry, which was another typical town, a fairly stable town, not too far from Cardiff, and we followed those pregnant women during their pregnancy and then their infants we followed to the age of five and we made very detailed measurements of growth in the children and we administered questionnaires on nutrition, on health generally, on psychological state, and a whole lot of other things. And again the point that I made earlier, the ability in epidemiology and particularly in an MRC unit to go back to a study or a cohort, is unrivalled, the ability to do that is unrivalled in a long-term unit with secure funding. But we went back to those children and looked at their school records and their accidents, when the children were aged about seven and looked at their school record and administered a few questionnaires to them to see if their early growth and so on affected their situation later. We also went back at 11 and looked at accidents in children, in relation to a number of things, we had a baseline, but the real value of that cohort is now being shown by the Bristol group (ALSPAC) who have conducted a study on diabetes and early markers of heart disease and I imagine that that cohort of 1,000 adults now is going to be of incredible value over the next 20 years looking at the development of heart disease and diabetes and other conditions. Now you can ask me about lead.

AN: Well maybe we should talk about, because that was linked to other studies in milk, if we talk about that and then we will come back to lead.

PE: Yes the other study that again we set up at the request of the Department of Health was to look at school milk. School milk and welfare milk had been withdrawn and in actual fact I should have made it clear that our study of child growth was set up to investigate welfare milk. Up to that point when we set that up, pregnant mothers and children up to the age of five, had been entitled to milk tokens, which they could exchange for milk. So we set up a trial and half the 1,000 mothers were given tokens for themselves, while pregnant, and then for the child and any other child under five, and we monitored that very carefully, we got the milk delivery men to give us in confidence the records of the purchasers of milk and we showed that two-thirds of the tokens, I think it was, were exchanged for milk. We then administered questionnaires to see how much the child was actually drinking and there was an excess of milk being drunk by the children in that half of the trial. That was the validation of it. But then we also set up a study in seven-year-old children to look at the effect of school milk and we selected schools in a deprived area, and we did this by standard criteria, I can't remember what they were, but they were indices of deprivation and we went to areas in South Wales with high indices of deprivation. We selected from all the schools in the defined areas, we selected children from families of four or more children, and social class three manual or lower, so that we were getting a deprived group of children. We supplied half of them with school milk for two years and we monitored that and paid surprise visits to the school to check who was actually getting the milk and the teachers were all intrigued by this study and collaboration was really very high indeed. And then we analysed growth over that two-year period and we showed a very nice gradient that the children in social class three showed virtually no change in growth. They grew, but there was no difference between the ones given the milk and those not given the milk and when we went down the social class to the unemployed, the non-classifiable, then we found quite a sizeable, still just a few millimetres, but a sizeable difference in growth, and if we multiplied that up by the number of years that the children might have received school milk, it was a worthwhile increment. Now the bottom line of all those various studies that I have talked about – iron in bread, iron added to bread, and milk given to children and pregnant mums, and so on – we showed that the iron that was being added to bread by law in this country had virtually no effect, but it is still added, the Ministry of Health having collaborated with us in setting up the studies on the absorption of iron from bread, took no notice of the answer and it was far easier just to leave the law as it was, and so millers still add a small amount of unabsorbable iron to all white flour in this country. The other study where we showed that school milk did have an appreciable and we felt worthwhile effect on the growth of the most vulnerable children, the Department of Health paid no attention to it and school milk was not reinstated.

AN: You talk there about how the results informed policy or failed to inform policy. How much do you think your research directions were shaped by policy concerns, by outside interests, how much were they just something that you had read about. I am just trying to get a feel for where your ideas came from.

PE: I think very little. I became very friendly with the Chief Medical Officer in the Department of Health, William Berry, Bill Berry, and he became a good friend. He was 10, 15, 20 years older than me, but a very, very good friend, and a great encourager. And he put ideas my way, but I am not a political animal at all, and I have always felt, I have two little dictums, one is that one must be interested in the research, and the other is that the process must be enjoyable. If you don't enjoy fieldwork or whatever it is, then it will be a bad study. And the team must enjoy it, and so I made every effort to keep my team informed. We had regular meetings to discuss projects and I made it as enjoyable and as entertaining as I could. Otherwise I felt that the quality of the data will fall off. But political effusion and so on, I feel that the Government and civil servants are very, very bad taskmasters. They either ask a question which cannot be answered, or they ask a ridiculous question, and really ideas have to arise, I think, have to arise spontaneously out of the interest of the person who is setting up the study and I think he has got to pass on some of his interests, some of his enthusiasm to the team, or if the work becomes dull routine, then the quality will immediately begin to fail. I have often wondered how do you stimulate good ideas and I have tried to remember where I was, what I was doing when my good ideas occurred. I have only had two or three good ideas, one arose during chatting in the car to somebody, an idea occurred, and the other was in the bath, so I don't think it is very helpful. But I think it has got to arise out of wide discussions, chatting about studies, 'flying kites', a

good background of reading, to know where uncertainties lie, but I think it is impossible to know what are the conditions, what are the situations, in which good ideas arise.

AN: Which good idea did you think of in the car and which one in the bath?

PE: The idea in the car was the randomized control trial of iron in bread and I was chatting to somebody about the problem of anaemia, as I thought it was at that time, and how could we do something that was relevant to it. Giving tablets through GPs was obviously achieving very little, what could we do? And so the whole field, which lasted about ten years and ended with the radioactive chapattis, all started with an idea in the car as I was chatting to somebody about the work on anaemia, which at that time had only extended to symptoms and the effect on the cholesterol level and blood pressure. Now the other one, I can't remember, it's so long since I thought about this, but I can't remember, no.

AN: Next time you are in the bath, it will come back to you. So can we talk just a little about environmental lead now?

PE: Yes. Lead was a very, very hot issue and it really all focused on lead in petrol and the group was set up led by a politician and by a doctor from Wales, Robin [Russell-Jones], who was an extraordinary character, exceedingly forceful character, who really dedicated himself, and set up CLEAR (Campaign for Lead-free Air) that doesn't spell CLEAR, but the campaign was called CLEAR at any rate. Well I took a somewhat passing interest in the letters to the journals and the occasional article and I found that I became more and more angry at the bad epidemiological methods that were being used and I wrote one or two letters to this character Robin Russell-Jones, pointing out that the data that he was quoting and the comparisons that he was making and so on, were totally invalid. For instance, oh I won't remember the details now, but he was comparing populations and talking about lead levels and I pointed out a total, total inconsistency in this, which I can't remember, and lo and behold he continued to write letters and at a meeting I attended he quoted these data to establish his point. Well I was so incensed by this, I wrote to him and pointed it out a number of times, but I felt really somebody has to do some good surveys. Now that sounds very arrogant, there were one or two people doing good surveys, but I felt this is an area in which we should make a contribution, so I set up one or two studies to look at lead, and we made blood lead our starting point, and we tried to estimate the contributors to blood lead and we looked in particular at air lead and we measured air lead over many, many areas and related air lead levels to blood lead levels.

We also looked at water lead. The Welsh office was interested in that, they had also played a part in the early days, by asking us to look at water lead, because some of the areas in Wales have a very acid surface water and old lead pipes and one or two little studies had shown that the lead levels in the water were really quite high, higher than the WHO recommendation and so on. So we went to North Wales and did a number of surveys of water lead and blood lead and estimated the contribution that water was making to blood and that was quite substantial. Off-hand I find it hard to remember, but in the high lead areas it was making a very substantial contribution, whereas air lead, no matter where we went, we couldn't get estimates higher than about 10 per cent. Now there were uncertainties in this. Food lead was obviously a very important source and in the old days food handling wasn't nearly as careful as it is now and I suspect that on a conveyer belt if there was damage to one of the conveyor belts they would quite happily use lead solder, whereas now they wouldn't dare have lead solder anywhere near food handling. And I suspect that the fall in lead levels, which has been shown quite conclusively in many studies, the fall in lead levels over the years has I think, and I think there is scrappy evidence to support this, been largely due to a reduction in water lead and in food lead. We certainly showed that the lowering of water lead was important, was effective. On two occasions we were alerted to the fact that the Welsh water authority was going to change the pipes to an estate or to a village, and so we went and got blood lead levels and then we followed the blood lead levels following the change, the removal of the lead pipes and the putting in of copper pipes, and we showed very nicely the fall in blood levels and we showed the sort of half life of blood lead from those studies, which led to some quite nice publications. We also went to East Anglia and we selected a town there that had a lot of lead pipes, but had hard water, and we showed that there was a very substantial difference in both water lead levels in the hard water area and the soft water area and very

substantial difference in blood lead levels and the relationship between lead in the water and blood was the same, but one was higher up the curve than the other in soft water. And we published a number of papers on that. We then went to an area in West Wales, where they weren't removing the lead pipes, but they were putting in a hardening plant. They were as I remember it, they were importing a calcium rock from Italy for some reason, it was more soluble, and they were putting this into a huge filter and the water was being sent through this, and we tried to monitor the fall in blood lead levels once this calcium filter was put into the distribution system. That sadly got into difficulties and we didn't really show anything conclusive in it, but certainly water lead levels fell and I am sure blood lead levels would have fallen, but I can't remember what difficulty we got into.

The other study which got the headlines for a short period of time was we went to traffic-less islands and we decided to go to areas with heavy traffic and areas with very little traffic and estimate water lead, blood lead, lead in the dust, we also did children in those days and dust lead was a very important source, we used to swab the children's hands and measure the amount of lead on their hands and relate that to blood lead. But the most delightful studies were in traffic-less islands. We chose three areas in Wales with different levels of traffic, from a rural area, to a very heavily polluted area. The heavily polluted area was Port Talbot, where there's a motorway which is elevated above houses and we chose houses along this motorway which were on main roads and the motorway over above and we did lead sampling – lead air sampling – and confirmed that the lead levels were very, very high, air lead levels were very high. So we took blood from those women, from Beaufort at the top of one of the valleys, where there's quite high traffic, from Porth where there's a one-way system and very heavy traffic, and, oh dear where else. But then we went to three islands. Now unfortunately I didn't go myself, I got a colleague in Ireland and another colleague to do the surveys and I regretted not going myself. But my colleague went to Tory Island off the north coast of Ireland, a rather isolated community, and this we were told had no petrol traffic at all, never had and there was never likely to be any petrol traffic. And my colleague went out and was appalled to see a petrol-driven van sitting on the harbour, or some little distance from the harbour. So he made inquiries about it, and he found – now remember it was an Irish island, an Irish community – he found that about two years previously the local authority had given a petrol-driven van to the islanders because there were two communities on the island and the school was at one end of the island and the plan was that on wet days, the van would collect the children from the other community. Well they had explained to the islanders, this is true, they had explained to the islanders that you put petrol in at the back of the vehicle, and that you put water in at the front. And the islanders had very faithfully done that, but they had forgotten to tell them that you also put in oil from time to time to lubricate the engine. So the van ran very happily for I don't know, three, four, five, six months, and then it seized up and they just left it where it had seized and never bothered with it again. So we felt that with that background we could call it a traffic-less island. The other island, by the way we took blood from every adult, we swept every house to get lead in dust, and we measured air lead, we had air samplers, one or two air samplers on the island. We then went to Aran Island off the west coast of Ireland, and again my colleague was appalled to see a petrol-driven Hillman car on the island and he made inquiries. And he found that the district nurse on the island had brought a car over, I don't know 10 years previously or whatever, and every time she went to the mainland, which was only at most once a month, but probably not even that often, she took her petrol can and collected two gallons of petrol, put it into the car, drove the car until the petrol ran out, and then just left it wherever it was, until she next went to the mainland. So again we felt that we could call it a traffic-less island.

The other island was truly traffic-less, and that was Sark in the Channel Islands and we asked the doctor there, a doctor Robb living on the island, would he take blood for us and he agreed. He got permission from the Monsignor, there used to be a Dame of Sark, and one of the laws of the island of Sark is that only the Dame or the Monsignor is allowed to have a bitch, others can have dogs, but no bitch, and no-one is allowed any mechanically driven vehicle of any kind, lawnmower included. So we truly did have a traffic-less, vehicle-less, island, and we got blood from them. Well it was delightful that study and a lot of funny stories about the various visits, but we found that the lead levels were almost identical to the areas in Wales, there was very little difference between them. Tory Island was a sad venture because we found that there was a terrible problem of alcoholism there and it may be that alcoholics do raise their blood lead

for that reason, wine does contain lead, used to contain, because they used to seal it with lead in some way, but really there was very little difference. We wrote that up and got a little bit of publicity for it, and it was a delightful study. But I reckon that all the work that we did on lead was I think good epidemiology. I think that instead of doing all those studies, we should have done one really big study. Oh there was one much bigger study. There was a survey of Wales, health in Wales, in connection with health promotion in Wales, and the Welsh Office had funded a group to do a study right across Wales, about 2,000 people were examined across Wales in relation to heart disease, one of the heart prevention projects. Well we asked the team for a sample of blood from every person, so I got I remember two or three thousand samples of blood and we looked at that and the one paper that we published was on blood lead and blood pressure. That was quite an issue and we entered into that debate as to whether or not lead is related to blood pressure. The most curious publication of all that we got out of that was blood lead and platelet function. Blood lead is negatively related to platelet function, so we published a paper somewhat tongue in cheek, and I think it actually asks the question at the end 'Does this mean that people exposed to lead have a lower risk of ischemic heart disease?' but it was rather tongue in cheek.

AN: So I guess this leads us quite nicely onto the studies of aspirin that were done.

PE: Yes. Well just to finish the remark I think I started was the studies on lead I think were good epidemiology, they weren't very big, I think we lost out in that way, but they achieved virtually nothing and CLEAR was so I think it was scientifically scandalous, the way they distorted data, the way they did their best to make out that I was paid by the lead manufacturers, and they couldn't pin anything on me. I got involved actually in the international debate and I was at several conferences in America and I can admit to you now that the international lead and zinc organization paid my fare, but they did nothing else. I did a lot of criticising of papers for them, but I never received a penny from them, but they did actually pay my fare, but we did it in a roundabout way so that CLEAR wouldn't get to know even that, but they did all they could to character assassinate people, and I couldn't care less whether there's lead in petrol, I have no axe to grind, but I felt it was scandalous the way that scientific data were being misused and misinterpreted by them for their own purposes.

AN: What's the big study you would have done?

PE: Oh I think by measuring air lead and blood lead, water lead, dust lead, and trying to look at the contributors to blood lead. We did that in several small studies, each one got slightly better than the one before, but we never involved more than I think probably a 100 or 200 people in it. I think if we had that done in several thousand people, it would have hit the headlines, because it was a good model. The one thing we couldn't do was food lead, that was just too difficult and estimates of lead in food from food tables and so on were pretty useless, probably misleading. Yes, aspirin is another totally, that is how I got into heart disease, that's right. I got into heart disease through aspirin. I suppose that just from reading the literature and I remember one meeting in America that I went to where I spoke on iron deficiency, but I went to some of the other meetings, and I heard somebody talking about heart disease, talking about platelets, the role of platelets in heart disease, which was not well established in the middle sixties, that's when my interest in aspirin started, late 1960s perhaps.

There was talk about platelets possibly being a key role in myocardial infarction and I talked to the platelet experts at that meeting and I remember the guy who had given one of the main papers told me that one of the best measures of platelet activity was to take a slide, scratch it with emery paper, put a sample of blood on it, leave it for two minutes, wash the blood off, stain the film, and then look at it, and if the platelets remain circular, then there was no platelet activity. If the platelet had pseudopodia along the scratches, then that was an active platelet. And I thought well how can I do that in an epidemiological study, this is just amateurish technology, there's no way. But I talked to a lot of people about platelets. I came back to this country, I visited [Gustav] Born and others and I talked to them about methods of estimating platelets and really there was no way. So by default the literature had an occasional, and this was going over a number of years, the literature had an occasional letter from John O'Brien, a haematologist in Portsmouth, and Harvey Vice, a haematologist in the States, and there was an occasional letter that I came

on, saying that aspirin had a very marked effect on platelets and platelets were much more active when the patient had taken aspirin. And John O'Brien showed that aspirin was so active that one tablet a day was enough to reduce platelet activity. So I felt, well, here is a way of testing the role of platelets. One would like to do it in a conventional epidemiological model, measuring platelets and then following up the cohort and see how it relates to vascular disease. But I felt well here's another approach. We can clobber the platelets of a group of men and see what their experience is. So I started discussions with a number of people in pharmacology here in Cardiff, and in, oh I don't remember, but I got in touch with one of the drug firms, Astra Nicolas, long since absorbed by another firm, and they were very encouraging and said yes this looks good. So we set up a study and in order to make it efficient, we took patients who had had an MI [myocardial infarction] and we thought we would give half of them one aspirin a day and we will see what the mortality is. And we decided we would use mortality, we decided that the identification of a second event was too uncertain and there could be bias in it, because aspirin might even at one tablet a day, might reduce their pain, and we might not ascertain as many infarcts in the group on aspirin as in the placebo and we made this decision, we will use an index of death or survival. So we set up the trial and we started admitting patients and with great difficulty, because the consultants were very, very reluctant and they thought this is a madcap scheme, this is absolutely daft, aspirin, you are not serious, but I showed data on aspirin and platelet function and there wasn't a general acceptance that platelets played a key role, so I wasn't on a very easy wicket talking to them. When I went to patients I well remember some of the patients saying to me after I had explained it all, they would say to me 'oh of course doctor I am all for research, I will help you, but tell me what's really in these tablets, you are not serious that it's aspirin, tell me what's in it?' And I had great difficulty in setting up the trial. Well we stumbled on and kept the trial going and it was very, very carefully done, totally blind, and so on. Incidentally, the aspirin was in capsules, so there would be no difference in taste, we concealed it that way.

After the trial had been running about six months, nine months, it doesn't matter, a year, I had a phone call. Now Archie's account of this, it was so exciting that Archie went over the top and he tells it in a much more dramatic way than I do and he is the focus of everything, whereas it was actually me who took the phone call. I was in the unit on a Saturday morning, in those days we used to go into the unit on Saturday mornings, rather casually, but I got a phone call and it was from America and it was, oh what's his name, he's Professor of Epidemiology there, not [Hershel] Jick. No Jick comes into the story, but a younger chap, between us, it will come to me, because he really deserves a lot of credit. But anyway this guy was on a sabbatical or a visit from Oxford to Jick's unit in America. Jick set up a fishing expedition, where he asked every patient coming into a number of hospitals, and eventually it was about six hospitals in six countries, and on the third or fourth day after admission somebody would ask the person 'what drugs were you taking in the week before you came in?' and then he linked these 40 or 50 drugs with diagnoses and he was looking for interactions, harmful side effects, that people taking a rhubarb tablet came in with liver disease, where this had never been expected, this kind of thing. And he produced a whole battery of tables with sort of 10 or 20 diagnoses, and 30 or 40 drugs, and just risk ratios or some index like that across for admission with that drug compared to all the other patients with that diagnosis. And the one thing that stood out like a sore thumb on this, was a risk ratio of about 0.3 as I remember it for aspirin and myocardial infarction, and extraordinary deficiency far greater than almost any other. I mean there were things that you expect, and people taking certain drugs had certain side effects, which were known about, but he was looking for the unexpected, and this was certainly unexpected. Now there were two explanations of that. One was that if a patient had taken aspirin and got an MI he would die suddenly, it was harmful and he would die quickly, and wouldn't survive to be questioned. So you would get a deficiency of aspirin taken in the week before admission. The other was that if somebody had taken aspirin they wouldn't get an MI and wouldn't come into hospital.

So the phone call on that Saturday morning was to ask me had I any evidence on aspirin and myocardial infarction. Was it killing people, or was it saving lives? Well Archie, of course, was thrown into it, we were all thrown into a dilemma by this. The trial that we were running, and we had – I don't remember at the time – 200 or 300 people in the trial, were we killing them or were we helping them, and we couldn't live with that. And so we broke the code. And as I remember it there were 8 deaths on aspirin and 11 deaths on the placebo and we felt well that doesn't prove anything, but it is most unlikely that we are killing

people. So we decided to continue the trial. I was flown over to NIH [National Institutes of Health] within a few days of the. Jick asked NIH to arrange a top-level meeting and I met some of the great men in cardiology and so on at this meeting at NIH and I was very young in the field. It was a wonderful experience and when we came back here there was another meeting. Jick came over here and MRC arranged a very high-level meeting with a few people to decide what to do about this. And [Richard] Doll was one of them. And Doll was very, very worried about one tablet a day. He said that's homeopathy. He said why don't you start giving a big dose. But I stuck to my guns and I said 'no one tablet is enough'. I gave in on the next trial. We set up a second trial, and I gave in and we gave three tablets a day, but I certainly wasn't willing to change the protocol for the first trial, despite a lot of pressure. And the MRC just said 'look ask for whatever resources you want and we will give you them, expand the trial as much as you can'. So looking back I should have been much more ambitious, but I asked for three nurses, and I got a nurse in Swansea and we started admitting patients and so on. We got one in Manchester and one in Oxford and we boosted the number of patients in the trial. Well we stopped the trial. I don't know quite why we stopped it, we probably should have set up a monitoring committee and asked them for advice, but we decided that 1,400 for two years, I think it was, would give us enough power and we stopped the trial, analysed the results, and we got a reduction of 24 per cent by aspirin, non-significant. Now this was deaths. We had always said that we would analyse deaths, although we did a back-of-envelope calculation with non-fatal MI and it was significant and it went the same way, but we held our guns, we were foolish I think in those days, why not publish this with all the 'ifs and buts', but we were so pure in those days, that I held that information, never even mentioned it at meetings, until a long time later I began to just drop in that well had we put in the non-fatal MIs that actually would have been significant. But we published it, we submitted it to the *BMJ* [*British Medical Journal*] and the *BMJ* dragged their feet for a very long time and it was one of the longest incubation periods that I have ever known. I think they didn't believe it. And they published it eventually under the heading 'For Debate' and looking back I think that was admirable, because you don't want clinical practice to be biased by one trial, particularly when it is not significant, but at the time we were disappointed, because they were obviously dragging their feet, and very, very reluctant to publish it and in fact when I rang up on one occasion to ask what was happening, I got a rather sharp reply from the editor and he said 'look just you remember who you are and just keep quiet and don't bother us'. But anyway it excited a bit of interest, not an awful lot of interest, and we started to monitor aspirin use and over the next 15 years we did four studies of aspirin use by doctors and we wrote to' I think it was 600 doctors or something, just asking them what measures do you use to reduce the risk of heart disease and they listed them and then we analysed these and showed that there was very low use of aspirin, but it did increase slightly over the period, but it was really the big ISIS trial that persuaded people to use aspirin. Anyway that's all by the way. There was very little, I was asked to go to hospitals, meetings and so on, and talk about aspirin and so on, but it was a bit of a joke, it wasn't taken very seriously. But a number of research units obviously took it very seriously indeed and over the next few years six trials were set up, in Germany, in the States, we set up a second trial, and when those trials were published, Richard Peto took an interest in the subject, and he presented an overview of those six trials, and the controversy that had gone on, because I used to go, I did the back-of-envelope adding up of the deaths and placebo of aspirin, and I did an overview and showed there was highly significant if you added them together, but that was rejected at almost every meeting I went to, and they said that's apples and oranges, that was one phrase that came up, you can't do that, they are different trials, and different communities, you can't just add trials like that, and I argued yes, if the stuff works, it should work in America, in Germany, and in this country, it should work with men and women, and old and young. No, no, it's apples and oranges. Richard Peto presented an overview of those six trials and it was subsequently published in *The Lancet* and it was the first meeting of the Clinical Trials Society. I'm fumbling a bit, but it was the inaugural meeting of the Society of Clinical Trials and that was his contribution to that. And, of course, it went on to, I like to think that it played a part in the setting up of the Cochrane collaboration, the putting together of all the evidence, because certainly Richard Peto was involved and has really taken that on at a rate of knots and that was his very first overview published in *The Lancet* and presented at the founding meeting of that Society.

So we set up a second trial. Now again I am coming back to my theme that being in an MRC unit gives opportunity for one to continue and to pick up things and continue them on. I have had enormous

pleasure and satisfaction from aspirin and in the last five or six years I have travelled extensively in the Far East on lecture tours, tremendous interest in aspirin there and there are also new uses of aspirin. I am doing a trial now on cognitive decline because multi-infarct dementia is probably a substantial cause of cognitive decline. There is growing evidence that 22 studies in the literature that suggest that it may be of value in colon cancer, rectal cancer, possibly gastric cancer, and possibly oesophageal cancer. There are six trials that have been set up on those. There's evidence suggesting it may reduce the risk of cataract and there's one study even suggesting it may reduce hearing loss. So it has been enormously exciting. But if I can take you back, my starting point was platelets, and I never lost the interest in platelets and I felt this has become an end in itself, aspirin, very exciting, but what about platelets? And also in relation to aspirin, aspirin is remarkable, because we give aspirin to everybody judged to be at risk, and it reduces by about 30 per cent. We give anticholesterol drugs to those with high cholesterols, we give antihypertensives to those who have high blood pressures, and they reduce the incidence by 20 per cent, 25 per cent, but here's aspirin that we give to everybody, with no selection in terms of the mechanism platelet aggregation or whatever and yet it has this massive effect. Now if there was a screening test, that we could do a test on men and say well your platelets are pretty inactive, you don't need aspirin, but your platelets are very active, you will benefit from aspirins, we might reduce the risk in those men by 60 or 70 per cent, we might. So I think a test of platelets, which is predictive of IHD (ischemic heart disease) would be enormously interesting from an aetiological point of view, but also it might be used in prophylaxis. I have to admit that aspirin is so inexpensive, and being effective at low dosages, probably a man with inactive platelets, you would say 'oh I would take it anyway', so probably it wouldn't have much effect, but it's a nice model to think of.

Well we had contact with, O'Brien was our main haematological contact, and he has been an absolutely marvellous friend and encourager, stimulator, right through the Caerphilly study, from the earliest days of aspirin, right through and still I am in contact with him, even though he is in his mid-eighties, still contributing to my thinking, and my papers and so on. So we talked to him about platelets and there was the aggregation test that he had brought out and Born had also brought out in the same year, but it was complicated, it was difficult, and we really felt that we couldn't cope with it. But then we had contact with Serge Renaud, and it was actually John Yarnell who made the first contact with this Frenchman Serge Renaud. Serge Renaud had gone along a similar path to me, had an interest in platelets, an interest in aspirin and so on, but he had determined to do platelet aggregation studies and so he had persuaded INSERM, the counterpart of the MRC in France, he had persuaded them to give him money to equip a caravan with platelet equipment and he had a delightful caravan which he towed around France and he towed around the south of England, doing platelet tests. He had two plate aggregometers, which were the O'Brien model, but slightly modified, he had two centrifuges, two platelet counters, two of everything, including two coffee-making machines, in this caravan and it was delightful the way it was laid out, extremely efficient in that the subject came into a caravan, then a bed was lowered across the door, it was the only way he could do it, the man lay on the bench, gave his blood, was then thanked and let go, and immediately the platelet work started, so it was done while the blood was absolutely fresh. So Renaud, bless him, agreed to lend us his caravan for however long it took to do all the men in Caerphilly. Well I was terribly apprehensive, I thought that if we parked this outside men's houses, it would be vandalized in no time, but we compromised, we set it up in Caerphilly [District] Miners' Hospital, and Caerphilly [District] Miners' Hospital was marvellous, they put hard-standing and steps for us, they put a cable into it for current, and Andrew Beswick, who has been an absolute brick in the unit, he spent four years of his life doing nothing but platelet aggregation. We asked the men to come early in the morning and give a sample of fasting blood, and Andrew found that he could only do six in a morning, it's quite a complicated test, we did aggregation of three agonists. Well we did these tests and this brings me to another rambling diversion.

I have had fascinating contacts with a number of high-powered technical people, and I find them very interesting. Let me talk about a man called Flower, Rod Flower, who's a very, very elegant worker. He did a method of platelet measurements which I am going to come back to shortly, and he developed this instrument, did a little bit of work on it, including some electron microscopy [EM], which immediately makes people think 'oh this is good science', he has actually had an EM working on this, and he showed

that his method was measuring something in platelets. So hundreds of these machines were sold and he then drops it and goes off on something else and designs some other equipment or gets involved in something else. The evaluation of a test of platelet aggregation in relation to vascular disease takes year and years and years. We did it on 2,000-plus men, these tests of aggregation. Renaud lent us this beautifully equipped caravan, which we parked in Caerphilly Miners' Hospital and the hospital made hard-standing and steps for us, the men came in and gave a sample of blood and Andrew did the aggregation, got pen recordings of aggregation on 2,000-plus men. We had to wait then for cases to occur, and we waited I think five years and then worked on an analysis, and we found no evidence of prediction at all. Now we really went to town on this, because we felt that the standard measures of aggregation, these pen records, rather like an ECG, you know you can make certain measurements and certain measurements had become established as measuring the degree of aggregation. We felt well there may be more to it than that, there may be some other aspect that's being affected, that's related to ischemic heart disease, so we made I think it was about 12 measurements on these traces and then as a final attempt, I gave them to one of the girls, and I said look treat these as wallpaper, just sort them into different patterns, and you don't have to tell me, I mean tell me at the end, how you describe these patterns. So the girl did this and I think she had about ten patterns from no affect at all, to a crazy curve. And we played around with this and got some way of describing these patterns, but still there was absolutely no prediction. So we published a paper in *Heart*, and I can tell you with amusement that in recent days, in the last week, two people have quoted that paper as showing that platelets are predictive, platelet function is predictive of ischemic heart disease. There was one very, very scrappy prediction which I was uneasy about, but if we took the very early heart attacks, there was a vague suggestion that one of the tests might, but after having made 20 comparisons, we felt should we even publish this and probably wrongly we put it into paper, but the very early cases might have been predicted by this one measure. So anyway that was phase one.

Now we then heard about two new tests of platelet function and so in the next phase, five years later, we put in those two tests. They were rather different. One was a method of looking at aggregation in whole blood. See the original test requires platelet-rich plasma, and you have got to spin the blood, remove the red cells and the white cells, and then you count the platelets and if it's not a quarter of a million or something, then you top it up with other platelets or you dilute it, give it a further spin and so on. So there's quite a lot of manipulation of the sample and its plasma and we felt well that's not very realistic. So when this test devised by Rod Flower came along to do it on whole blood, we thought this will be it. So we did that test on every man and that again took Andrew Beswick another four years of his life and John O'Brien meanwhile had devised a very, very simple test, which I thought was particularly interesting, because the background physiology of platelets is that if platelets are damaged or exposed to ADP then they are activated, but if you block that response with aspirin, you can still get them to aggregate if you expose them to high shear and, of course, in atheroma some of the platelets are exposed to high shear forces in the blood vessels and so that might be a separate method of activation. Well John O'Brien simply took a whole blood sample, just the residue in this syringe, stuck it in a little filter holder, sucked the blood through at a pressure which meant that they were going through the filter at high shear and then he did a platelet count on the whole blood and on the blood that came through. He actually had a second measure, which made the test very, very attractive, you simply put the thing on, sucked the blood through and counted the number of drops, and it's anything from, I don't remember, 5 drops to 30 drops, and that the number of drops gives an indication of platelet activity. And he had done EM measures of platelets on the filter and so on and he had managed to get a filter paper from a firm which guaranteed the same mesh and so on, constant. So we did these two tests, and we had to wait, of course, and again it took I think it's ten years ago, and just within the last few weeks, I have analysed the data and they are absolutely intriguing. Remember that the original test on PRP [platelet rich plasma] showed no prediction whatever, so we thought well this whole blood test is so much better, maybe it will show. Let me mention first that the filter test shows no prediction at all. Absolutely nothing, flat as a pancake. The whole blood test we had predicted that if it shows anything, it will show myocardial infarction, but not with stroke just as a sort of vague hunch. We also, with all confidence, said well it will be the most active platelets that will have the highest risk of MI. Well the results that we have have intrigued everybody, including Rod Flower himself and this is really hot this one, it's within the last few weeks. We found that the whole blood test shows no trend when we divided the men into fifths by their whole blood platelet test, there is no trend, there is a

suggestive trend with stroke, but it's not significant. But the men with the most active platelets, the fifth of men with the most active platelets on the whole blood test have a significantly reduced risk of stroke, and it really is quite impressive. It's only one sub-group in the whole table, but the risk we showed is about 0.5 and it is statistically significant. So that has thrown us, it's with stroke, and it's the wrong way round, and I am just writing it up at the moment for publication but I am sending a copy of the paper to, I have sent it already, to about six experts and they have all contacted me and said well have you mislabelled the test, is it the wrong way round? They cannot explain it. So I think that probably is a good point to break.

AN: Thank you very much Peter.

[SECOND PART OF THE INTERVIEW]

AN: I have just gone through the first interview we had and in that we covered your series on flax, anaemia, milk, bread, the work on aspirin, and then on platelets, and what I was hoping to talk about today, was Caerphilly and some of the others, and then reflect back on this period of time. Is there anything else that you think we should talk about, that you think is important, that we have missed out, before we move to Caerphilly.

PE: No I don't think so, I think for the last 10 or 15 years of my life in the unit, Caerphilly became the dominant issue. I kept on a few other things, but I think that's the only other main omission.

AN: Could you tell me a bit about how Caerphilly became to be set up and talk me through the study itself.

PE: Well we had a post for a junior epidemiologist and it was largely looked on as a training post by MRC, and they had a series of people, I think the immediate previous people were David Bainton, Ian Baker, and then I advertised and we got John Yarnell. And John Yarnell is a very bright person, but a bit of a loner, [he] wanted to work on his own and he set up several studies. He did a bit of work on urinary incontinence, something else passed through my mind, but I have forgotten it, and he put forward a proposal to look at HDL (high-density lipoprotein) in women, HDL. Cholesterol was a big item in the literature at that time, but almost entirely in men, and I thought yes this is worth doing. So he got a bit of money to employ a few people, four women, and he set up a study in 800 women in Caerphilly. So that quite honestly limped along, it was not a very successful study, and I am not sure if anything was published from that, I may be wrong, but I don't think so, but I saw the potential in that study, and I urged John to set up a study in men, a major heart disease study in men, testing a range of hypotheses and taking additional samples of blood and asking additional questions to give a basis for testing new hypothesis which would come up in the future. And that was always in my mind, that any major study like that should always have the potential for testing new hypotheses. If I can extrapolate just a little, it always seemed to me that epidemiology studies are so large and so unwieldy that they pick up a question like the relevance of HDL and it's 10 years, 15 years before any answers emerge. The answers are incredibly valuable, but by then the medical thinking has moved on and other questions have arisen, so any big epidemiological study has to be hung on one or two hypotheses in order to get funding. But really I have felt for a very long time that those questions that it has hung on are of very little value in the end because the answers take so long, and to take extra blood samples, so that retrospectively new hypotheses which arise in the future can be tested, is a very, very necessary aspect of epidemiological studies. And that was in my thinking with Caerphilly. Anyway John did a lot of thinking and put forward a proposal to look at about two and a half thousand men in Caerphilly. I insisted that this was a unit project. I have always given credit to John Yarnell that he set it up, that he did a lot of the basic thinking and organization and drawing of the sample and this kind of thing, but I always insisted that it was a unit project and that we all had a part to play in it, and that's certainly how it turned out. Also with regard to collaboration. We all saw tremendous value in collaboration and so we drew in a number of people on lipids, on haemostasis. John O'Brien was one of the people I collaborated with on the work on aspirin and cardiovascular disease and

he's very much a lateral thinker and so he was involved from the very beginning and suggested a small package of haematological tests and then in the later examinations for men that was expanded and other people were drawn in, like Gordon Lowe. But we set that up and we called it, I insisted that it be called the Caerphilly Collaborative Study, because I felt the real value would come from collaboration with men like Renaud, on platelets, John O'Brien on haemostasis, Barry Lewis on lipids, and so on, and I think that's been the success of it.

Now I don't want to be critical here, but John Yarnell tended to be a loner, wanted to do his own thing, so there was always a bit of tension between John and myself. I was much more keen on collaboration than I think he was, and certainly I forced the issue on many occasions. The involvement of other people in the unit was, of course, absolutely essential. Janie [Hughes] and Marion [Jones] looked after the records, the response rate. Marion was just wonderful in following up men who refused to come to the clinic, she followed them up and offered to do the investigations in their home, and then she would ask me to go and take blood from the men, so we got the whole range of data from them. And without Marion and Janie, the study would have been a relatively average, or below average study, but they put in such a consistent effort, and they didn't have to be asked, they just did this, which was a product of their training over the years, in working with Archie and others, and that really turned it into a very fine study, with a very high response rate, and a very careful documentation and so on.

AN: If you could just talk me through the chronology of when the study was set up, the sort of numbers, what you did.

PE: Well it was launched in 1979, and the first case took until 1983, it took four years to see the men. John Yarnell chose the sample, using the electoral register, and some of the doctors' lists, but we wanted to get a complete sample of men within a certain age range, 45 to 59 years of age, so a questionnaire was sent out, asking a few general medical questions, and asking the age of the respondent, and that was a key factor in identifying this particular age group within the community, and letters were sent out to virtually every male on the electoral role, in order to pick the sample, and get a complete sample between those age groups. We set up the study in church halls, the YMCA, and in doctors' surgeries, moving around the town, and seeing people in the different areas. We had one dedicated person who visited the men and tried to persuade them to come to the clinic, and then in the clinic we had about six 'stations' we called them, where different tests were done. We piloted all this with my friends and contacts and some of my friends from church and from the neighbourhood would ask me at intervals 'well what's happening up in Caerphilly? You haven't had us up for a long time'. But we timed everything and tried to envisage delays in the procedure so that men went through as smoothly as possible. The record keeping and so on really developed ad hoc as we went along, it developed, and one of the very, very big mistakes we made, and I bitterly regretted it, was we just used numbers going up from 1001 upwards and then we discovered later that Speedwell, the study in Speedwell in Bristol, had done the same, and so there was an overlap in the numbers, and that was bitterly disappointing. I had always suggested within the unit that each research topic had a unique number, and for instance our study on school children was if I remember rightly 32s, 33s, and 34s, and those numbers came first and then 01, 02, 03, for the different subjects, and Janie and I developed this system and we were able if we picked up a questionnaire we were able immediately to say which study it came from. But nobody thought much of that when Caerphilly was being set up, and we just used straight numbers, and then we got into a terrible situation over stored samples where Caerphilly and Speedwell had been stored together and it has been very, very difficult to unscramble the two sets of stored samples.

AN: Two things that strike one in retrospect about Caerphilly are one its relatively small size, and the second would be that it's a study of just men, particularly as it arose almost from the study of women in the first place. Were you conscious of deciding to restrict the size or to confine it to men? What was your thinking at the time?

PE: In those days 2,500 wasn't particularly small. We would have liked it to be bigger, but I was certainly so insistent that it should be intensive, and that we should collaborate with as large a number of collaborators

as possible and add in as many things as possible. For instance we added in, at a later stage, we added in lead, we added in arthritis with [Professor Alan] Silman, and we added in I can't remember now, but other things, and it was a very intensive study, so rather than large numbers, we were prepared to go on for a long time. You see it was a very stable area. Some of the cohort studies in London and places like that got into trouble in trying to follow up people. We knew that this was a very stable area, Caerphilly, and we expected it to be a very long-term study. Initially we had certainly thought of ten years, but I don't think we had thought of that as an absolute end to the study. Now with regard to women, we were aware of the opportunity that we were missing at not looking at men and women, and so towards the end of the study we added in 250 women, and sadly nothing to my knowledge has ever been published about those women. Because when we started to analyse them, and I took a personal interest in those 250 women, and I looked at a number of things in them, but Peter Sweetnam pointed out that the drift by the laboratory estimations, there was always a drift over time and the women came in at the end, so we would either have to compare the women with the last 250 men in Caerphilly or we would have to indulge in some rather dubious standardization process, with the drift and the changes in the laboratories. So sadly we found it so difficult, but it may well be there were one or two questions about diabetes. I remember, we got into correspondence with a group in America, where they had shown certain differences between men and women in diabetes and we were looking at this, but Peter Sweetnam more or less refused to analyse it. So yes it is a small study, but I think we have gained in other ways in that we have contributed to a very large number of hypotheses and to discussions about a large number of things, rather than a more focused study. But you see it would have been, because John Yarnell's main interest was in HDL cholesterol and he teamed up with Barry Lewis in London and with Colin Bolton in Bristol and we had very, very detailed measurements. We also put in the upper lipid proteins, which were very, very new in those days, and we could have made it a lipid study, and 10 years later we had difficulty in publishing the results of these wretched HDL fractions 2 and 3, which had been done for us. They were old hat, people said 'oh no those methods are not appropriate now'. My own interest stemming from the days of aspirin was in haemostasis, and the involvement of John O'Brien and then later Renaud, the French expert, and then Gordon Lowe in Glasgow, and then Flower in Bath, that has I think been the most valuable single area within the whole of the Caerphilly studies, the haemostasis and thrombosis evidence and the platelets.

AN: I wonder whether if it's worth moving across from Caerphilly to ask more about the Unit, and to your time there, and in thinking about the Unit, what would you say were the strengths of a unit, as opposed to a grant-funded university department, because that's the obvious comparison, the MRC has the opportunity to create a unit or to put its money into a university department. What are the advantages that you think [there were] in setting up the Unit?

PE: Well when I was appointed director, I remember somebody said that I had fire in my belly, and that was one of the strands in thinking and allowing me to become director of the unit after Archie Cochrane. Who could follow Archie Cochrane? Certainly the whole style of the unit changed very, very markedly, but I think one of the benefits was the on-going budget, the rolling budget. I mean in the early days money was very free and I was asked did I need any more staff, and could I do with some more money? I think we did things very, very efficiently, because while we were doing the Caerphilly study I was also running studies on lead, we were also doing the final follow-up of subjects in relation to byssinosis and Janie and Marion would work on Caerphilly for three days a week and the other two days would be off to Bolton and Oldham, or would be up in the valleys taking blood for lead studies. And I think the cost of the various studies was very much less than if funding had been for the complete study on its own. We made very efficient use of time and resources. I think also the unit attracted enthusiasts. Field workers are rather a speciality, and to have a love of going out and meeting people and accepting the challenge of getting a high-response rate and so on demands a certain kind of person and we seemed to get those people. We also could give them a career, and a career structure, both the medical and the non-medical people, and the support staff, they all had career structures within the MRC and permanent posts most of them and this was very beneficial to the development of an area of research, rather than just a one-off project. There was continuity, and I knew that when we followed up Caerphilly, we wouldn't have to start recruiting another set of staff for the Phase two and Phase three, we would have the same people going back and they got known in the area and known by the men and that was a tremendous advantage.

AN: If I could just ask you a little bit about the role of the Unit then in training and in its staff. Initially it seems that there was no very clear career structure in epidemiology in the Unit, it attracted a variety of people, but then training became more formalized, there were master's programmes, working projects, and so on and so forth. And one gets the sense that the Unit then played a less active or was less pivotal in that training role.

PE: Well I think that's true and also the Faculty [of Community Medicine, later Faculty of Public Health]. Archie was always very anxious that field epidemiology played a large part in the activities of the faculty, and the original documents setting out the aims or mission statements or whatever it was at the beginning, talked about statistics and field epidemiology being the basis of epidemiology, but only lip service was paid to that later, and all the training that the faculty introduced was towards community medicine, public health medicine, and the unit lost out very badly. In fact that was very noticeable, because a number of splendid people in the unit like David Bainton had great difficulty in getting their theses approved for their Part Two Membership [of the Faculty of Community Medicine, MFCM], and the view was taken that this hasn't a public health aspect. He looked at temperature and cardiovascular disease. He wrote a splendid thesis. There were one or two others who got into the same difficulties.

AN: So did this provide training opportunities very much on the job, but as training became more formalized, it somehow became a step to a career in epidemiology?

PE: I think perhaps it was me [who] didn't make a bid to play a bigger part in this. But we used to get students visiting, and Cambridge used to send down their students, was it two days initially, and they stayed overnight, and we showed them the field studies going on and a view of the studies in progress. Several other groups, London I think, Michael Marmot used to send down people, and locally, of course, we still put a slot in locally, but possibly if Archie had continued as director we would have had a much bigger part to play within the Faculty. Epidemiology would still have been a significant part, but I just enjoyed fieldwork and testing out so much that I wasn't terribly interested in lecturing and training and so on. But let me say that the people who came to us and took up the training post of junior epidemiologist with us, most of those did extremely well, and it was almost a unique training in fieldwork, because we were so heavily involved in that, and practically nothing else.

AN: Going back to the early years, with a lot of people coming and then going on to greater and better things. One can think of Bill Miall, to be seen to progress. Bill Miall had his own unit in Jamaica, Ian [Baker] went onto other things. So people were moving on and Estlin Waters went onto a professorship and then in the later years if you look at people who came more latterly, the people who came and took your junior jobs, they are not the professors that are dotted around the country now, in the way that say Wellcome Fellows in epidemiology are dotted around the country as professors of epidemiology and I just wondered whether you felt that was the case or not.

PE: One has to say this very, very carefully, because we got some very, very good people, for instance Michael Burr, who joined us as a junior epidemiologist, and has a tremendous record in field epidemiology, but we did have difficulties recruiting people. I tried to attract Michael Marmot to come to the unit in the early days, but he wasn't interested in coming, which was quite sad. We had one or two other people, Michael Lichtenstein, a superb American, Dan Sharp, who is now one of the associated heads of NIH (National Institutes of Health) in the States, but we really had very great difficulty in attracting people to come down to Wales. The Wellcome Fellows would come and I would enthuse about the opportunities down here, but they would shake their heads and say who wants to come to Cardiff for a year, when they can stay in London and have a broader exposure to things in London and the nightlife and so on, so it became increasingly difficult to fill that junior epidemiologist post. But I don't want to put too much emphasis on that, because we did get some very good people. You see John Yarnell took it and he stayed with us probably longer than any of the junior epidemiologists, but he was not a high-flyer, very bright, and achieved a lot, and I am sure will continue to achieve, but he's not a high-flyer and wouldn't look for a

senior post. He came from Bristol, you see, just a move across the Channel. It attracted very few people from a distance. David Wood, he came down here, and I think he actually stayed with me, I don't remember the circumstances, but I tried to attract him, but he wasn't interested.

AN: That's interesting to know. The other thing that strikes me is that at the point that the Unit was set up around 1960, having originally been a part of PRU, but a distinct part, that the rules were almost set for the Unit then that the MRC decided on the number of staff, the number of key posts, and then from 1960 onwards, you were almost stuck with that as your unit. Was that really the case, was it set in stone, or could it have expanded or changed or altered?

PE: Well it became increasingly difficult, but I did manage to get a nutritionist, Ann Fehily, who put a superb amount of very high quality work into Caerphilly, and that was a new post. I also got John Gallacher, I got him with very great difficulty. Now he's a very, very bright original thinker and he put a marvellous slot on psychosocial factors into Caerphilly and later on cognitive function. He also set up a study of stress management within patients with angina, then the MRC pulled the plug on that. But it certainly became increasingly difficult to get more staff, but in the early years it was very, very easy, and I was asked whether I would like more staff and in the early days I said 'no I don't think I would want to cope with a bigger team'. But later, I can think of one or two people that I would love to have appointed or to have offered an appointment to. And the MRC were just not willing at all.

AN: One gets the feeling as you talk about the relationship with MRC changing, that in the early years with Professor Cochrane and in your early years as a director, that the relationship was warm, there was very much a 'what do you need, and how can we support you' and then that seems to have withered.

PE: The way I look on it is that in the early days we were at the sharp end and we were the reason for headquarters existing, and somebody has made that very point to me, that the work that we did secured the future of the whole organization, and so the whole focus was on facilitating units, and encouraging units and so on. Then the MRC Board system was set up. I am not a politician, I don't understand a lot, but my thinking is that the university became more and more jealous of MRC units, which had stable funding and secure careers and people in the universities who were in research had to find their own money and had no stability, not the same stability in their careers. And the Board came in and they were very, very aggressive in the early days and the review process was certainly very, very threatening. This was a total change and it led to changes in headquarters, and headquarters changed from being our representatives in negotiations with other bodies and so on, they became the executives of the Boards and they came down to see us and to put into effect decisions that had been taken by the Boards and the whole atmosphere changed over a very short period of time. The review processes also became very, very threatening and initially very hostile. I submitted my first report on our first five years under the Board system, and I was asked to appear before the Board and one man whom I won't name, attacked me most aggressively and hit the table actually, and almost shouted at me, because of one of our studies, where we had used a method that he disapproved of. And I was told afterwards that because of his performance, it was decided that no director would ever be called to give account in front of a Board again. That was judged to be so discourteous and it was certainly so threatening and so hostile. But that was the general atmosphere of the Board and we never felt that we had friends at headquarters after the Board came in.

AN: And when roughly was that?

PE: That was about 1975, I think, you can check up on that, but it was about 1975 that the Boards were set up.

AN: And also to explore a bit more this feeling of not accountability, but this sense of peer review and oversight, that one of the advantages of the Unit clearly is that one can have a relatively free rein, and pursue ideas and go where one wants. But one may not be subjected to the same discipline as peer review and having to get the money and so on and so forth, and I am just interested not

only in how that balanced out, but also how much you felt there was this process of oversight and review and fitting into ideas. The peer review positive side is that people shape your ideas as much as criticize them. It's not about blocking your ideas, it's about putting your ideas out into public domain and coming back, being reframed, and improving.

PE: Well we didn't experience much of that. I thought that we found it a very threatening and hostile procedure and one or two individuals on the Board of representatives that visited us, one or two individuals were helpful afterwards and dropped a few hints and gave a few suggestions, but I think that was off the record. The procedure was, I never found it helpful in any way. At the same time we recognized that society was changing and accountability was coming in and senior lecturers in academic departments were being looked at and were being subjected to more and more close accountability and that certainly has come in now and there isn't the security that there was in those days. So it looks as if we were different from the universities, I think we changed a bit later, MRC, the accountability and so on changed a bit later in the universities, but it was a very sudden process within the MRC, whereas my impression within the universities was that it came in very gradually over a period of time.

AN: That's very helpful. One of the things that came up in some comments about the early studies in the Rhondda, and perhaps it's easy in retrospect, but some said that maybe this was a missed opportunity, that if one had almost defined a study population within the Rhondda at that time, then instead of doing repeated cross-sectional surveys, but to roll them into some on-going, longitudinal study. My sense is that that didn't fit with epidemiological thinking, because it was too new. It wasn't that people didn't consider that idea, but I wondered if there was any debate or discussion about the Rhondda, because I know that we talked about how in a sense Caerphilly was closer.

PE: No, I don't remember any discussion, but certainly epidemiology, the foundation of epidemiology in those early years was the cross-sectional survey and I can remember lectures I received and lectures I gave, focused on case-control study, leading onto cross-sectional surveys. Intervention trials were rarely talked about in epidemiology. Those were drug trials, and prospective studies, I think. Framingham of course stood out as unique and there were other studies, of course, but epidemiologists didn't tend to think in those terms, I think the value of the long-term prospective study was being slowly established and like the mustard seed it grew, but it wasn't the thinking in those days. I remember my parent department, my original department in Belfast, set up one prospective study which was to run for a year and was to follow cholesterol level and blood pressure in, as I remember it, about 500 men over one year, and this was referred to as a rather unusual prospective study, and the men were to be seen several times, rather unusual.

AN: One of the things, and I think we have touched on this before, just to revisit it a little bit, was about the selection of topics, because one thing when you look at the portfolio, that the Unit developed over the years, it's in a sense quite idiosyncratic it's a real mish-mash of things. Not to be critical in any way, it's refreshingly interesting. And some of the studies seem to have arisen from individual reading, perhaps you could shed [light on] that policy, either policy had changed and you tentatively approached or were perhaps formally asked to do that. I wondered if you were conscious in any way of how you set the shape of things. Clearly you made a conscious decision with Caerphilly, but before that.

PE: I think before that it was very, very haphazard, and I certainly looked on epidemiology as having a potential input to every activity in clinical practice, and my work on iron deficiency, I can't honestly remember why I started that, it doesn't really matter, but I looked on that as being of value in trying to influence the thinking of haematologists and nutritionists and I felt that my contribution was at haematological meetings and meetings of nutritionists, not meetings of epidemiologists, and I would go along to these meetings and I would challenge – the thinking at that time was that anaemia was to quote one statement that it was 'the most serious health problem in the community' and I would challenge that and put forward evidence from my studies, and I felt that as the opportunity arose in different fields that

we had a slot to put in, rather than now where I think the epidemiology has come of age, it is highly respected, and makes a very profound and often paradigm shift almost in disease and areas of clinical concern. I think in those days I felt we just were the laboratory workers, the animal workers, and the epidemiologists, and the clinicians, they all had separate slots to make towards the big picture. Now I feel epidemiology draws it all together as it were and draws on the mechanisms and so on, goes out and gets, works towards the final evaluation of a disease or whatever, and it's a much more respected and much more crucial. As I say 'paradigm shift' is perhaps too grandiose a term, but it's more than putting in a little slot on thinking on the importance of iron deficiency anaemia, is it all that important, does it relate to mortality, and no haematologist had ever thought of that before. Now they say the epidemiology is almost the first chapter in the book and then well how do you explain these findings, rather than as somebody put it to me in the early days, they found it at the end of the book.

AN: That's interesting. Looking back over the areas that you worked on and I think maybe you are underplaying the contributions you made, I wonder what if you were to name three or four, or a few more things, in the 40 years that you had contributed, in a sense one might say with iron deficiency and anaemia, that above a haemoglobin of 9 or 10 and mild anaemia is not a medical problem, but are you conscious that maybe with the aspirin work, what would you want to be remembered for?

PE: Well I suppose the aspirin work, because it actually saves lives. I think it played a very substantial part in focusing interest on haematological mechanisms in cardiovascular disease. In the early days it was all atherosclerosis and vessel wall disease and very little attention was given to haematological mechanisms. Now the techniques were not there and the laboratory people hadn't come up with all the factor 7 and 8 and Von Willebrand's disease and so on, and nor were tests available for platelet aggregation on a large scale and so on. Byssinosis I think we made a real contribution there and the flax industry and the cotton industry was heading towards paying exaggerated claims of harm and I think we stemmed that. Now whether that was a good thing or not I don't know, because I notice in the coal industry that there's now a total rejection of all of our ideas, it seems to me, and I only follow these things very superficially, but it seems to me that there's total rejection of Archie's findings on chronic bronchitis in the industry and on early pneumoconiosis not being associated with death, and presumably with any serious hazard to health, but now that's all been overridden and compensation is going to be given to all these people. So one really wonders is the world driven by truth in the end, or is it being driven by attitudes and impressions and so on.

AN: When I was reading through our previous interview, one of the things that struck me was you describe research as about certainty and clinical practice as being very uncertain, whereas if I was going to characterize the two I would almost describe it as the other way round and say that clinical practice is about certainty, one should work in the areas where one is certain, so when one's certain aspirin works one uses it, and actually when one gets to the edge of knowledge one encounters immense uncertainty in trying to quantify, struggling with new techniques, and how do they get to that, and one step or two steps back, and I was just interested that you saw this as a move from uncertainty to certainty. In my mind I see it as entirely the reverse, and I just wondered what you thought about that.

PE: Yes, I suppose I was referring to the single clinician and the single case, where you can never have certainty and in the epidemiologist with two and a half thousand men a 'P' level of such and such. Were you ever in actual clinical practice?

AN: Oh I did about five years.

PE: Well I just found that so dissatisfying, because in no case could I ever put my hand on my heart and say I helped that person.

AN: I see what you are saying now.

PE: And I found this. We took the credit if a person got better and if the person developed a complication, then we were blamed and we had no defence. We tried to defend ourselves, but we never knew, we had no controls, and just moving from that to where you are looking at putting 'p' levels on things and moving logically, seemed to me to be moving from uncertainty to a search for certainty. You never get absolute certainty obviously.

AN: No, I think we agree now, I think I understand what you were saying. You know if one caricatured a clinician, the certainty they had in their minds seemed to me to be inversely related to the amount of evidence on which they had to base that certainty. Reflecting just a little bit more about how your career worked out and the Unit as a whole, what things if you had the opportunity to go back, might you have changed or done differently?

PE: I think I wouldn't have done any of the lead work, the lead work was very, very entertaining and took me to a lot of meetings, all over the world, and a certain amount of prominence, but achieved nothing useful in the end. I think I wouldn't have wasted my time on that. What else? I don't know I have lived a charmed life. It just wasn't in me, I mean I admired Archie in the way he worked at a very high level, and achieved a lot for epidemiology and achieved a lot for the faculty and so on, and he moved in political and quasi-political circles that I shunned at. I wouldn't change that, not because I don't recognize the value of it, but because it just wasn't me. I think I might have made greater efforts to get one or two more epidemiologists into the Unit. I mean I am sure he won't mind me telling you, but when I was due to retire, I recommended to the headquarters that George [Davey Smith] be offered the directorship of the unit, with George's agreement, and the MRC just ignored it completely. I think if George had come to the Unit, it would have been marvellous, perhaps I should have made bigger efforts on that, but at the same time I have got to acknowledge that he's in a very good position.

AN: You could argue that he has inherited the Unit anyway.

PE: That's right, that's right, and the ethos of the Unit, and the support of the Unit was diminishing anyway. The MRC was running down units, and perhaps he is in a better position yes. Now it's difficult to say what I would change. I loved South Wales, but it's certainly not in the best place for the Unit and yet London or some big metropolis would be the worst place as far as getting stable populations, you can't win it both ways.

AN: Yet it almost came out to South Wales and then was stuck here because of its ability to do the studies and it was handicapped by its inability to recruit and expand.

PE: I think the other thing, which I wish we had done was some more really ambitious field studies. We did one study and getting all the nurses in the country to answer questionnaires on diet and follow them up. Doctors were so obviously an easy follow up, good, as Richard Doll showed. I wish we had done more of that.

AN: So we could have had the British nurses study.

PE: Yes. And we had thought of it. We also thought of dieticians, and somebody actually did do a study on dieticians. Michael Burr did something on vegetarians, but I think we went for the Caerphilly kind of study where we had a relatively small number, 2,500, but went into tremendous depth. Now there's a place for that, but there's also a place for the rather superficial nurses study, health workers study.

AN: So somehow your imagination, your strength, was somehow constrained by this heritage of being able to do high response rate surveys in defined populations.

PE: Yes. And collecting detailed information on things and rather accepting questionnaires as second rate, that's very questionable.

AN: It's hard to make that leap and justify to someone why you needed to be in South Wales to do a national survey.

PE: Oh I would not have wanted to have given up the one, I would have wanted to balance it with the other. And it did come up on occasions, the idea. I remember when the aspirin results came out, I put forward a proposal for a nationwide fairly superficial study. Several actually, now that I think of it, and the attitude in the Unit was our reputation. And I remember Peter Sweetnam saying with great sincerity that our reputation is built on very careful studies, careful data collection, and don't get into that, it will do the Unit no good. And I think it's a pity that we didn't. The value of the US nurses study and health workers study and doctors study has been so great, and it must be very efficient money-wise.

AN: Yes, sure. I mean the scale of the undertaking is clearly huge and cyclical in a way. In a sense I feel that you also had a certain number of field staff that you wanted to preserve continuity, so one was always looking for manageable pieces of fieldwork which would slot into blocks of time, whereas in the free market of the universities one brings in research staff, one hires seasonal workers, one fills a huge space each time one has a cycle for your cohort, and again the Unit made it hard to take on those things.

PE: That's right, the Unit was all built up to do these small detailed studies one following after the other. But would it have been possible? And with unskilled labour you can do these huge things. I remember we made arrangements with the local authorities to use their letter stuffing and folding apparatus and banking stuff. We never used it in the end actually but it shows that I had some desire to conduct large studies, but we never actually did.

AN: To go back to the relationship that Professor Cochrane had with the MRC and yourself, and my sense of the MRC at that time which I think is perhaps necessary is very much being a patrician organization and that Professor Cochrane was a man who had gone to Cambridge, who was one of the club, he had been at Cambridge with the person who oversaw the Unit and it was almost that Cambridge news would be exchanged between them. And I get the sense that you came from a different background to that and that that created some tensions. I mean were you aware that somehow you didn't fit into the Cambridge classes of the day?

PE: I think I am going to have to say that I wasn't aware of it and I wouldn't have cared, because it's not quite me. Archie was a social climber, namedropper, I don't think I am. I just loved the work, I just wanted to get on, and I loved nothing more than setting up a clinic and going and doing part of it myself and then handling the records and so on, just being thoroughly involved in the day-to-day work. Archie didn't really do that, and Fred Moore was one of Archie's great critics, that Archie never bothered with the detail, left it all to Fred, and they made a good team, but it was a very, very different emphasis and I would tend to be a bit more of the Fred Moore than the Archie Cochrane.

AN: But I get a sense that going back that the atmosphere was very clubbish, and it seems from what you are describing that there was a club, and it was a club that you didn't care to be in, rather than in a sense that you were made unwelcome or somehow positively excluded.

PE: Yes I think that's perfectly true, I would have been uncomfortable in that club. Also epidemiology was growing very, very rapidly. And in the early days, I mean when I wanted to move from Belfast, where I had done a little occupational epidemiology and field epidemiology, the only person who came up in discussion with my boss was Archie Cochrane and the unit in Cardiff, whereas now I think there are a dozen places that one would want to either advise younger people who ask me, I say well look what's going on in Bristol. Bristol until the last four or five years or whatever it is, Bristol wasn't on the map at all.

AN: The final thing, I will perhaps put something which is quite sensitive, but strikes me that in a sense Professor Cochrane seems to have no stated faith or belief and yet you have quite a strong faith, and I am wondering if you feel that affected you in the topics that you chose or the way you did things, or the way you ran the Unit. Were you conscious at any point, or do you reflect back, oh I shouldn't have done that, because I don't really believe that it fitted in with my faith or my belief.

PE: No I don't think so. Certainly there was never any conflict. I would find it difficult to say that it helped. I think I am who I am, and I have been very active in church things, for the last 15 years I have pastored a church and I often say that the church gives me fulfilment for the part of me that is a clinician, you know dealing with individuals and dealing with problems and so on, and it complements the more ivory tower academic work that I do here, but I think I would be dishonest if I said that I can think of any benefit or any harm, I think they have worked together in a way that has been very, very fulfilling.

AN: But have you always from a young age had a faith or a belief?

PE: Yes I grew up in a convinced Christian home and I have never wandered from that, but I have never found it restricting in any way. No doubt it has played a large part in moulding my character, and so I don't look for the high social involvement and so on, the way Archie would have done. But I am not aware of any way that it has impeded, it has enriched, and in its contacts it has led to, and also led to a number of people in the Unit, I think a proportion of committed Christians in the unit was higher than in science in general. I never did anything actively, I can put my hand on my heart and say I never was biased, I don't think subconsciously, certainly not consciously, in any appointment, paying any attention to the background of the person with regard to faith, religious practice or whatever, and it never upset my relationships with Archie. I remember in my initial interview with Archie he asked me about religious beliefs and so on, and I told him I said I was an active and committed Christian and he said well 10 years ago I would have argued it with you, but now I don't even care enough to argue.

AN: I suppose the final point, some would argue that epidemiology stems from an almost socialist left-wing tradition, and I suppose Professor Cochrane had left-wing beliefs. One looks at the whole social medicine movement in the 1940s, John Pemberton, your original boss, various people, and it seemed to be coupled with Jerry Morris's MRC Social Medicine Unit and I just wondered whether you felt not religion, but politics, but whether you thought that was part of an ingredient in doing epidemiology, because my sense is that when you moved over to work for Professor Cochrane, there wasn't any political agenda, whereas in other units say Jerry Morris's unit, one would say there was some sort of left-wing political agenda, of a sort, or it's shaped by his left-wing beliefs. I wondered what you felt about the politics in the sense of epidemiology. Was it seen in some way linked to politics? Or was it to you just scientific endeavour?

PE: I suppose we can't step aside from these things, we have some views on attitudes and certainly my Christian beliefs would be very close to some of the fundamental tenets in socialist views, but they are not a driving force with me. I would like to think, this sounds so arrogant, I would like to think that the emphasis on truth in Christianity, Christian teaching, helped to motivate me looking for truth in science and medicine, and no I don't think that's very profitable to follow, but I think it may have had a small effect. Yes the feeling that there are absolutes and there is absolute truth, because this is now rather scorned and everything is relative.

AN: I suppose on one level what you are saying is that Christianity has a strong thread of social justice running through it, which sits comfortably within the left-wing socialist belief.

PE: I think that's certainly true. And I mean all the time that I was director I was visiting the prison and holding classes in the local prison, which was just round the corner. I suppose it certainly arises from my Christian background, not my socialist one. I am not aware of any socialist strand in the background. My father was as apolitical as I am.

AN: That's the other thing I wanted to ask you, but is there anything else you wanted to talk about or think that we have omitted?

PE: Well I may have said it before, but I would certainly like it to go on record, that one of the great thrills that I have had is all the data, samples, records, going over to Bristol, and seeing what I would say is the top epidemiology unit in the country taking on the studies, and the privilege, the enormous privilege that I have had in working with Bristol and in being able to continue work here. I have one or two colleagues who feel very bitter that their life's work lies in a drawer somewhere and the Prof who succeeded them just takes no interest in it, and the heartache that they have. I also go to the library and I see all the pneumoconiosis collection of papers there and nobody is interested in it. I just feel so privileged that our work is being carried on, and the tremendous thrill I got from Stephen Frankel the way he carried forward those negotiations. Tremendous. Because on this side I think I was the only one who showed any worry about all this being lost, and I don't think Peter Sweetnam gave it a thought, John Yarnell wasn't interested, Hugh Thomas thought that the Department of General Practice here might take it all over. I thought that's absolutely daft in the extreme, there was no one there competent or interested, I just got such a thrill, anyway I have said that before probably.

AN: Thank you very much Peter.

[END OF TRANSCRIPT]

Further related resources:

1. Ness A R, Reynolds L A, Tansey E M (eds) (2002) *Population-Based Research in South Wales: The MRC Pneumoconiosis Research Unit and the MRC Epidemiology Unit*. Wellcome Witnesses to Twentieth Century Medicine, vol. 13. London: The Wellcome Trust Centre for the History of Medicine at UCL.
2. Jones E M, Tansey E M (eds) (2013) *Clinical Cancer Genetics: Polyposis and Familial Colorectal Cancer c.1975-c.2010*. Wellcome Witnesses to Contemporary Medicine, vol. 46. London: Queen Mary University of London.
3. Ness A R (intvr); Tansey E M, Thomas H (eds) (2017) *Bainton, David: transcript of an audio interview (11-Jul-2000)*. History of Modern Biomedicine Interviews (Digital Collection), item e2017044. London: Queen Mary University of London.
4. Ness A R (intvr); Tansey E M, Thomas H (eds) (2017) *Hugh-Jones, Philip: transcript of an audio interview (05-Jul-2000)*. History of Modern Biomedicine Interviews (Digital Collection), item e2017046. London: Queen Mary University of London.
5. Ness A R (intvr); Tansey E M, Thomas H (eds) (2017) *Hughes, Janie: transcript of an audio interview (28-Mar-2000)*. History of Modern Biomedicine Interviews (Digital Collection), item e2017047. London: Queen Mary University of London.
6. Ness A R (intvr); Tansey E M, Thomas H (eds) (2017) *Jones, Marion: transcript of an audio interview (10-May-2000)*. History of Modern Biomedicine Interviews (Digital Collection), item e2017048. London: Queen Mary University of London.
7. Ness A R (intvr); Tansey E M, Thomas H (eds) (2017) *Kilpatrick, Stewart: transcript of an audio interview (23-May-2000)*. History of Modern Biomedicine Interviews (Digital Collection), item e2017049. London: Queen Mary University of London.
8. Ness A R (intvr); Tansey E M, Thomas H (eds) (2017) *Miall, William: transcript of an audio interview (13-Aug-2001)*. History of Modern Biomedicine Interviews (Digital Collection), item e2017050. London: Queen Mary University of London.
9. Ness A R (intvr); Tansey E M, Thomas H (eds) (2017) *St Leger, Selwyn: transcript of an audio interview (27-Jul-2000)*. History of Modern Biomedicine Interviews (Digital Collection), item e2017051. London: Queen Mary University of London.
10. Ness A R (intvr); Tansey E M, Thomas H (eds) (2017) *Sweetnam, Peter: transcript of an audio interview (31-May-2000)*. History of Modern Biomedicine Interviews (Digital Collection), item e2017052. London: Queen Mary University of London.

11. Ness A R (intvr); Tansey E M, Thomas H (eds) (2017) *Tudor Hart, Julian & Thomas, Mary: transcript of an audio interview (14-Jun-2000)*. History of Modern Biomedicine Interviews (Digital Collection), item e2017053. London: Queen Mary University of London.
12. Ness A R (intvr); Tansey E M, Thomas H (eds) (2017) *Waters, Estlin: transcript of an audio interview (14-Jul-2000)*. History of Modern Biomedicine Interviews (Digital Collection), item e2017054. London: Queen Mary University of London.
13. Ness A R (intvr); Tansey E M, Thomas H (eds) (2017) *Yarnell, John*: *transcript of an audio interview (18-Apr-2000)*. History of Modern Biomedicine Interviews (Digital Collection), item e2017055. London: Queen Mary University of London.
14. Reynolds L A, Tansey E M (eds) (2003) *The Recent History of Platelets in Thrombosis and Other Disorders*. Wellcome Witnesses to Twentieth Century Medicine, vol. 23. London: Wellcome Trust Centre for the History of Medicine at UCL.