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Sir Richard Doll in interview with Max Blythe
Interview I - Oxford, May 1985

MB Sir Richard, you've spent a career in epidemiology. When you started your career in medicine, in 1930, which is some time ago and before epidemiology had really got started, how did you come to be involved in a branch of medicine that was so new?

RD Well, I think it was incidental, really. The fact that I did get involved with it, in practical terms was just because I got an association with Bradford Hill and it all developed from there, but the background as to why I was interested in it really dates back to my days at school before I even started medicine. You see I didn't plan to be a doctor from the very first. In fact, whilst I was at school I always intended to be a mathematician. I remember I was taken to see the professor of mathematics in Cambridge by my father and he said well really the only thing I could do if I did mathematics was astronomy or teach, and as I didn't particularly want to do either I finally gave up the idea of doing maths and accepted my father's suggestion, he was a general practitioner, that I do medicine instead. I was interested in anything that was scientific so it wasn't a difficult break and so in 1931 I went to St Thomas's and lived at home and started on a medical career and never regretted it for a moment. But I've always looked for ways in which one could apply numerical techniques to medical research, so I had that background. And I suppose the other main reason was because when I was a young man, particularly as a medical student, I got very interested in social factors in disease. It struck me at the time as a medical student that our teachers were interested in diagnosis and would prescribe some treatment, but they were not particularly interested in whether the patient could afford the treatment, for example, or when he left hospital, whether he was going back to conditions which would cause a relapse of the disease. Of course in those days there was no national health service and social factors of poverty were extremely important in determining a person's reaction to his illness. The sort of thing one used to see in those days was children being brought into hospital in late stages of diphtheria, just because, the parents couldn't afford to have a doctor to come and see their child. Doctor's fees in those days were half a crown [£0.125], they couldn't afford it, and the result was when the child came into hospital, he was too late in the disease and died of diphtheria. This sort of experience had always interested me in social factors in disease. So I had these two formative interests: mathematics and social medicine.

MB I know something of how strongly these social factors moved you and later on you were to have some influence in pressing for a national health service. I think you represented a committee at the Royal College of Physicians that was pressing for a national health service.

RD Well indeed, I was very interested in the idea of a national health service and before the war I was a member of a small and little known society known as the Inter Hospitals Socialist Society and in fact that is where I met my wife.

MB That was confined to London?

RD That was confined to London. Yes, it was at the London Medical Schools. I'm sure there were similar things in the other schools, but this was a London University one.

MB And you were saying that you met your wife there.

RD I met my wife there. She was a member of it too. We were a small and dedicated group, in fact I was an officer of the St Thomas's Hospital Socialist Society and was had up by the Dean on one occasion. He said, 'You cannot have a hospital socialist society. There's no such thing.' I said, 'Well, I'm sorry but we've got one.' He said, 'Well, you mustn't, in any circumstances, use that name or put up any notices in that name, it would so discourage our benefactors. We should never get any it would discourage them from giving any money to the Hospital if they thought we were such people.'

MB But you still went ahead...

RD We still went ahead, and in the years immediately following the war I took quite an active part in the 1945 election, speaking on platforms in favour of a national health service.

MB Can I just take you back to before the war again, and then into the war? Before the war I believe you published a first paper giving probably some sighting of where you might go in medical research involving the Chi ^{2}.

RD Yes, indeed, I can't remember where I found any reference to the Chi^2 test, but I did see it somewhere and wrote an article about it for the St Thomas's Hospital Medical School Gazette while I was a student. Looking back it was rather interesting because I applied it to some results which had been published on the value of pituitary hormone treatment for undescended testicle. I forget the actual numbers, but a surgeon reported that previously, out of 20 children that he'd treated the testicle descended in 10, and he then treated another 20 children with the hormone and the testicle descended in 14, and clearly this was a very big improvement. So I applied the Chi^2 test to the results and showed that there was a probability of about 50% that he'd get the sort of results that he got and I took it to the surgeon who was using this treatment, but he wasn't impressed by the analysis.

MB This is a bit early, but a prophetic paper. That was 1937?

RD That was 1936 or 1937, yes.

MB And you were to go into the war in 1939 when it started, right at the outset. What happened in that period '37-'39?

RD Well, of course, like so many young people at the time who were concerned with the rise of Hitler it seemed to us, particularly after Munich, that there was no possibility of stopping him other than by facing up to him in a war and I joined the Army Reserve in 1938, so that come September 1939 I was called up and went with a battalion to France.

MB Can you tell me a little more about your war? You're not reluctant to tell me about it, I hope, because it was interesting.

RD Well I was very fortunate in many ways. So many people were killed and others had a very boring time. I obviously survived it but I also had an extremely interesting time. I had nine months in France during which time I acted as a general practitioner to the local French population which was very interesting. I then came back from Dunkirk and six months later went out to the Middle East where I was attached to various hospitals before ending up on a hospital ship cruising around the Mediterranean for a year, which was really delightful.

MB Did the war give anything towards the medical career that was to follow?

RD Fortunately I had got my membership [of the Royal College of Physicians] just before the war in the summer of 1939, so that after having served as a battalion medical officer for the first year, I then was moved to a hospital and did become a medical specialist in the Middle East and had fascinating experiences. We treated, actually, the first case of smallpox and the first case of typhus that occurred in British troops in Cairo and I had charge of the infectious disease ward there. An extremely interesting experience, but it was something one lived for at the time and as I say, I was fortunate to have interesting experiences, but it didn't affect one's subsequent career except afterwards I wanted to stay at home and get on with some work. I didn't want to do any more travelling.

MB Right, but a fantastic digression for one who was to specialise in epidemiology later.

RD A fascinating experience, yes.

MB When you returned from the war, you returned to the research bench, as it were. How did that transition take place?

RD Well, when I came out of the Army, I came out a few months early, just around the beginning of 1945 because I'd had my kidney removed the year before for tuberculosis and I did a year's post at St Thomas's Hospital and then other people started coming out of the Army and of course there was no National Health Service then and there were very few hospital appointments. The struggle to get such appointments was really very acute. I didn't like that struggle. I was always keen to do research if I could and my wife to be, we weren't married at the time, she was working for the Medical Research Council and she knew that [Francis] Avery Jones was looking for an assistant to help him in a study of the aetiology of peptic ulcer, particularly to study possible occupational factors in the causation of peptic ulcer. She suggested to me, or rather she suggested to Avery that I might be a suitable person to help him, and he liked the idea and so I started. Well, Avery Jones got a grant from the Medical Research Council and I worked as an assistant to Avery from 1946 to 1948.

MB Where was this work based?

RD The Central Middlesex Hospital and we did a survey of the incidence of peptic ulcer in different sections of the community, trying to see particularly whether irregular hours of meals and shift work played a part in the causation of peptic ulcer, and in the course of that work, which was being supervised by a committee of the Medical Research Council on which Bradford Hill was a member, we succeeded in interviewing, I think it was 98.4% of everybody we set to interview in the factories, and Bradford Hill I know was very impressed by this because often occupational studies in those days got reponse rates of less than 50%. Anyway this attracted him and he asked me to go and work with him on the study of lung cancer.

MB That was the big moment in 1948 the transition from the peptic ulcer field. Just looking at the peptic ulcer research, were the results of that survey good? Did you come out with strong findings?

RD No. I think the main things that the survey did was to establish the incidence of duodenal ulcer and gastric ulcer, show that they had different causes; their social class distributions were quite different, but essentially it was clear that occupational factors were not important in causing them. But I did carry on working with Avery Jones really for the next 20 years and I got an interest in peptic ulcer. If we weren't able to prevent it, then perhaps we could treat it better and after I went to work with Bradford Hill at the beginning of 1948 I continued to work two days a week with Avery Jones.

MB Sir Richard, you must on thousands of occasions have been asked about that classical work that started in 1948, the study of smoking. Can I take you through some of that again please, because it is so fascinating and so important a development?

RD Yes, of course. Well the study in which I was involved arose out of a paper to the Medical Research Council that was written by Percy Stocks who was the chief medical statistician at the Registrar General's Office and he of course was particularly concerned with the increasing mortality rate attributed to lung cancer. It had been an extremely rare disease at the beginning of the century. Indeed when I was a student in the middle 1930s we were taken to see a case if a patient was admitted and this diagnosis was made, because it was considered such a rare disease. In fact, it wasn't all that rare in the middle 30s and clinicians and teachers used to comment on it and say, 'It's an extraordinary thing, that's the second case of lung cancer we've had this month. It's most surprising.' They never really considered that it was increasing in incidence and thought it was just one of those things; 'Cases always run in threes' was the saying that was common in those days. But of course the death rate was increasing inexorably. It had been doing ever since the First World War and this had been noticed by a lot of people and people had written papers on it, but they had mostly come to the conclusion that it was because of the greatly improved diagnosis. One has to remember, you see, that until the First World War you had no x-rays, there was a great deal of tuberculosis, and so there was the possibility that lung cancer and tuberculosis were confused. In the absence of good x-rays, the diagnosis was not easy to make. There was another factor, bronchoscopy was primitive...and there were no sulphur drugs for the treatment of pneumonia. The mortality rate from pneumonia was 20% in the middle 1930s, and this meant that if you got an obstruction to the bronchus, developed pneumonia behind it, the man died of pneumonia without ever having the lung cancer diagnosed. So all these considerations made a lot of people think that the increased mortality attributable to lung cancer was an artefact due to better diagnosis and when the sulphur drugs came in, in the middle 1930s, that it was due to better treatment. But the increase was really getting so great that Stocks felt it unwise to just assume it was a spurious increase and he was rather keen on it being due to atmospheric pollution; coal smoke. He thought that was a major factor, and the Medical Research Council had a committee meeting about it which Kennaway and Bradford Hill were members of, Sir Ernest Kennaway, whose group discovered the first chemical carcinogen and isolated 3,4-benzpyrene. Kennaway was not at all impressed with it being coal smoke. He said that here had been much more smoke in the atmosphere in the 1890s than there was in the 1930s. He thought it must be something else and cigarettes were one of the things which were mentioned at the meeting.

MB Sir Richard, can I just ask what other things people were thinking about at that time, apart from cigarettes?

RD One that was commonly mentioned was the tar from roads. Of course, the motor car was something that had increased enormously in the first 30 or 40 years of this century and roads were being improved and they were being tarred and people were looking for sources of 3,4-benzpyrene which was really the only known chemical carcinogen, something to do with roads, something to do with motor traffic and the exhaust fumes of motor traffic. One of the things that has always slightly amused one is the way in which I've had letters way up into the '70s saying 'Why haven't you thought of diesel fumes as being the cause of lung cancer, they so obviously are.' Well, of course, it was the first thing that was thought of, not diesel fumes actually because they weren't introduced until the middle '30s, but motor exhaust fumes in general. So, those interested in the causes of lung cancer were thinking about motor cars, roads, industry in general, gas works, pollution in general, with smoking a possibility. There were other remote possibilities: some of the new treatments such as the use of arsenic which had greatly increased in the treatment of syphilis, there were a number of minor possibilities like that.

MB But out of that Committee came your chance to work with Bradford Hill?

RD Well the conclusion of the committee was that they couldn't prove that there was a real increase in lung cancer, but it would be unwise to assume that the increase was all an artefact and Bradford Hill was asked to carry out a study, in which Kennaway and Stocks were to be advisors, to try to find what the causes of the disease were. And Bradford Hill asked me to join him to actually do the work and I started on that in January, 1948.

MB A great moment. Can you take us through the stages?

RD Yes, it was a very exciting period. The way we planned it was to get notifications of patients with lung cancer from twenty London hospitals and, in order to try and avoid the interviewers being biased by the knowledge of the disease, we asked the hospitals to notify us of any patients with lung cancer, gastric cancer or colon cancer so the interviewer would not know which disease the patient was suffering from ... and then they were to interview the patient and choose in the same ward, a patient of the same age who was in at the same time with some other disease. It didn't work, of course, because the sister in charge of the ward would say, 'Oh you've come to see the lung cancer patient in bed so and so' or 'the gastric cancer patient.' So we got the interviewer to just make a little note as to whether the diagnosis was known or not known when interviewed. Fortunately, however, we did find another way of eliminating interviewer bias from the results of the study, because by interviewing people on admission to hospital with suspected diagnosis, it meant that when I went through all the notes afterwards, one found, I forget the actual proportions, 10-15% or even more, proved not to be lung cancer and of course the interviewers didn't know that at the time and one was able to compare the patients who were proved not to have the disease with those who had the disease. This was a very important part of the evidence. Well we started collecting cases and interviewing people about their past histories of exposure to all the factors I was mentioning earlier and we noticed quite quickly that very few of them were non-smokers, but what was more impressive was that when I went over the notes subsequently, I found that those few that were non-smokers nearly always turned out not to have lung cancer, they turned out often to be bronchiectasis, or sometimes secondary cancer, or sometimes very unusual types like sarcoma of the chest wall, fibro-sarcoma or something like that. So this was most impressive and actually within a year Bradford Hill and I were reaching the conclusion that really smoking must be the principal factor. We did not formally reach that conclusion until we had seen some six hundred patients, which was early in 1950. We wrote the results up then and took them to Sir Harold Himsworth who was secretary of the Medical Research Council and sought his advice on our interpretation. The one thing, looking back, I have been very pleased with was that we did say that our conclusions, taking all the evidence into account, and of course we looked at all sorts of evidence, not just that obtained in our study, but we looked at the distribution of the disease in different countries in relation to smoking habits, for example, it was very impressive that Iceland where cigarette smoking was not introduced until the 1930s had no lung cancer. So we took all that evidence into account, the difference in the two sexes, the time relationship to the introduction of cigarettes and the increase in lung cancer and we did put in writing in that first paper that we concluded that smoking was a cause, not the cause, was a cause of lung cancer and I have never had any reason to regret our decision about that. But when we showed this to Himsworth he was quite happy with the argument, but he said, 'You know, you've limited your study to London and there is just a possibility, I can't say how it would work, but you really ought to show that these results are typical of the country and not just of London.' That must have been at the end of 1949 because we then extended the study to five centres outside London, Newcastle, Cambridge, Leeds, Bristol, well that's four centres, and by the time we could see that the results from these centres were being identical, and Himsworth said, 'Well, go ahead and publish,' and we published in September 1950, I think, our paper on the London data. The delay had been slightly unfortunate because it resulted in the American paper of Wynder and Graham coming out a few months earlier, but as they had not drawn the conclusion that smoking was a cause of the disease we didn't mind that so much.

MB This was a time when you must have seen tremendous social implications in what you'd found. It must have been quite staggering.

RD Oh, it was indeed, but Bradford Hill always taught, and I think he was right on this, that one should try to divorce your thoughts about that from your scientific thoughts as to the extent to which you had proved something was a cause of a particular disease, on the grounds that if you started saying what ought to be done or what the implications were for society, you would get emotionally committed to the findings. He always impressed on me, and I accepted this from very early on, and I try to convince other people that the same still applies now, that if you are investigating a problem, you must remain objective and you must try to disprove the association between smoking and lung cancer for if you get committed to what should be done on the basis of the results then it becomes much more difficult to accept some other evidence indicating that your conclusions are wrong. And for many years after that I always refused to make any comment as to what I thought ought to be done about it. I'm prepared to now, but it is a long time after the initial event.

MB Can I come back to that later? I'd be very interested in your thoughts on what should be done even today about the residual problem, although much change has taken place. Sir Austin Bradford Hill is a remarkable man. You have already said how much he influenced your thinking and perhaps you'd even say more about Bradford Hill's contributions.

RD Oh Bradford Hill was indeed and is indeed a very remarkable man. Those of us who went into epidemiology, people like [Archie] Cochrane, Jerry Morris, Charles Fletcher and myself really all feel that we owe our scientific methodology and enthusiasm for the subject to Bradford Hills's teaching. Bradford Hill was an extremely modest man himself. He was not medically qualified, but he always wanted to do medicine and he had a real feeling for biology and really was the first person to introduce the controlled trial to medicine. Of course, the controlled trial had been introduced into biology by Fisher some time before, but it had never been introduced into medicine and Bradford Hill introduced it for testing streptomycin in the treatment of tuberculosis. Now you might say that a controlled trial really wasn't needed to demonstrate the effectiveness of streptomycin and that it wasn't ethical not to give patients streptomycin, but the position was very different in the late '40s. One thing was that it was extremely expensive and there wasn't enough streptomycin in the country to treat more than a very small fraction of tuberculous patients and by entering patients into a controlled trial you at least gave them a 50% chance of getting streptomycin, which they wouldn't have had otherwise. I was working with Bradford Hill when he introduced the controlled trial and I was immediately impressed by it's value and quickly started applying it in testing treatments of peptic ulcer. I must just tell you a story about the scientific methodology in testing new treatments. Before the war, most people just used to treat series of patients and compare their results with results they'd had before or results that other people got and the consequence was that frequently a lot of their conclusions were erroneous because the patients in the two groups being compared were entirely different in character. And then a few people had begun to realise that this was not the best way to make comparisons and they started allocating treatment to alternate patients and this was a great improvement. I was taken by this in the late '30s, just after I qualified, and in the Army I put up a proposal early in 1940 that when hostilities started, that I should be given enough sulphonamide to give alternate wounded some sulphonamide prophylactically because in those days it wasn't clear whether it would help or not. I was sent for by the ADMS, as he was called, the senior medical person in Division, and told that this was entirely unacceptable, that either sulphonamide was good to give prophylactically, in which case I would give it to all the wounded, or it was no good, in which case I wouldn't waste the Army's money on it. So I said, 'Well which should I do, Sir? And he said, 'Oh that's nothing to do with me, you'll have to decide that.' So I never got my sulphonamide and I wasn't able to do a trial, regrettably. I was interested in the methodology of trials though and was immediately convinced of the value of the random allocation, which avoided this terrible bias that you were liable to have as to whether you should regard the next patient as suitable or not. If you were very keen on a treatment and the patient who was due to have the treatment was extremely ill, then you might say, well he's too ill for treatment and not include him. With random allocation that was avoided and it was very quickly proved that this was much the most powerful way of getting a correct result when you tested a treatment. So Bradford Hill really introduced the controlled trial and he really introduced the precise methodology of epidemiology in its application to chronic disease. Percy Stocks had done case control studies of cancer in the 1930s, but they hadn't been developed and it was really with Bradford Hill's rigour and his very logical mind that we were able to work out what were the appropriate conditions and what conclusions you could draw from them.

MB By the early 1950s your findings from the first smoking study were published and were bringing attention in the literature. Then started an even bigger study, a study with British doctors.

RD Yes, indeed. Well, as I said a moment ago, our responsibility having concluded that smoking was a cause of lung cancer was to see if we could disprove it and the obvious way to try to disprove it was to say, 'Well, does it predict, does knowledge of smoking habits predict whether someone will get lung cancer or not?' So we thought we'll approach the medical profession and ask them for their smoking habits, and then we can follow them up. The idea to approach the medical profession was Bradford Hill's and it had a lot of attractions. They were easy to follow, because once on the Medical Register you're kept in sight of the General Medical Council, so they are easy to follow. We thought also they'd be co-operative and tell us details of their smoking habits. Now, I may say that when we wrote to them in the first place we wrote a very cagey letter and didn't say, 'We're going to keep our eye on you and see what you die of.' We carefully avoided that but I suspect that most of them guessed it. So, with the help of the British Medical Association we wrote to 60,000 doctors on the Register in 1951, got replies from over 40,000, and then followed them up to see what happened. We wrote to them periodically after that to get information about changes in their smoking habits and we've followed them, in fact, for 30 years. I'm still following them as a matter of fact, and, within a couple of years that study confirmed our results. We started that particular study in 1951 and it was 1954 before we had enough data and our 1954 paper also drew attention, I think for the first time, to the relationship between smoking and coronary thrombosis, though we didn't feel on that data that we could conclude that smoking was a cause of coronary thrombosis.

We called that an association and said it would have to be looked into to see whether it was causal or not.

MB But the results of that particular study have gone to enormous lengths to confirm the position in regard to lung cancer and heart disease.

RD Oh yes, indeed. I think the fact that the data were being obtained from the observation of doctors went a long way to convince the medical profession that it was a real causal association, and they were impressed by it themselves. Certainly the British medical profession became convinced of the importance of smoking as a cause of disease a long time before other medical professions. America wasn’t so far behind. It was interest at first, I think. If one had made a survey in the early ’50s probably most people would have said, I’m talking about most scientists, most doctors, would have said that it wasn’t proved, that it was an association and that there must be other explanations. In fact a number of people wrote letters to that effect in the medical journals, but [Harold] Himsworth at the Medical Research Council was quite convinced that it was causal, that the relationship was causal, on the basis of our case-control studies and he told the Department of Health that it was so and that there was no need to do any more research, quite early on the ’50s. But it wasn’t until 1957 that, at Government request, the Medical Research Council wrote a formal paper in which they advised the Government that it should be assumed that smoking was actually a cause of lung cancer. So that was 1957 and that was accepted, then nationally.

MB When you were carrying out the survey of doctors there must have been a very curious thing happening, because as it went along you didn’t have a steady process, you got doctors ceasing smoking. That must have had very curious confirmatory effects in another direction?

RD It did, indeed. It provided some of the most important evidence subsequently, because when that survey was started in 1951 doctors were in fact smoking slightly more than the national average. Well, up to the age of about 65, they were smoking the same, and after 65, they were smoking more than the national average. It wasn’t that doctors smoked more it was that older people in the general population smoked less. I’ve always assumed this was because they had so little money as pensioners in those days. They couldn’t afford the number of cigarettes. So on average doctors were smoking more, but by the time we sent our second questionnaire to doctors in 1957 already a high proportion of them had given up and were smoking less than the general public, and of course within ten years they were smoking very much less. So we were then able to make a comparison between the trend in lung cancer in doctors and the trend in lung cancer mortality in the country as a whole. This was quite dramatic. It showed their mortality in relation to that of the general population falling off, and it started falling off from the early ’50s, and within ten years it had fallen very considerably, whilst for all other cancers the doctors rate still bore exactly the same relationship to the national average as it had earlier on. That was an important argument against those who said, ‘Well, it’s not that giving up smoking reduces your risk, it’s merely that people that aren’t going to get lung cancer are people who can give up more easily, so it’s people who are not going to get it who give up.’ By showing that when a proportion of the population gave up, this had an effect on the whole population, that argument was eliminated.

MB That must have been a totally unexpected bonus.

RD Well it was, indeed, yes. We gave up smoking ourselves fairly early on but hadn't expected that there would be such a big response.

MB Sir Richard, while the smoking research forms one of the great elements in your career, which most of us know about and have read about, there were other things going on as well. It wasn't just smoking. In 1954, there was important research on radiation. Can I take you to some of these other areas of research?

RD Yes. Well of course, you can't spend all your time on one study, particularly in epidemiology when it takes a long time for results to come in. I mean a research project may take 5-10 years and so you have to do other things and I started looking around. I was always interested in the social background of disease and I started looking around for other causes of lung cancer, particularly occupations which looked as if there was some suggestion that they might be associated with lung cancer and we showed, based on Kennaways' work, that people that made gas from coal had an increased risk of lung cancer, a small increase, very much associated with the large amounts of benzpyrene in the air to which they were exposed. Also, asbestos, we studied asbestos. Interestingly enough, I had tried to study that at a big asbestos works in London but the industry refused to let us study their workers. And then about a year afterwards I was approached by another asbestos company, Turner and Newall in the North of England, and they quite reasonably thought that the increased mortality from lung cancer that had been recorded amongst their workers might be due to the high proportion of post-mortems that were done trying to see if there was asbestosis, and they thought it was an artifact due to more intense investigation. They asked me to investigate it in order to disprove the assocation, but when we found that the mortality was nearly twelve times as high as the national mortality they were really rather cross. However, we published the results. That was in 1955. I had studied by then: coal gas, the effect of coal gas; asbestos; also nickel refining. So I'd studied quite a number of occupational factors, and all through that time I was doing controlled trials of treatment for gastric and duodenal ulcer.

MB That work was still going on.

RD Yes. We really stopped investigating the aetiology of those diseases quite early as we never got anywhere and even today I don't think people have got very far. It's still a mystery what causes those diseases, but we were doing quite interesting work on the treatment of peptic ulcer. In fact, around about that time we were able to show that what was then the standard way of treating, mainly putting people on 'slops', on milk and fish and not allowing them to eat most of the things they enjoyed...

MB Yes, milk, fish and chicken.

RD Oh, well chicken was only quite advanced after you were several weeks on milk, and we showed that it didn't make the slightest bit of difference. I put patients on kippers and onions. I can't say steaks because hospital diets didn't run to steaks, but roast beef at any rate, and they did just as well. I have often felt that perhaps it was the greatest benefit I'd achieved for mankind, to prevent people from unnecessarily going on the miserable diet that ulcer patients were treated on. That was with Avery Jones' support. He was terribly keen on investigating all these different treatments, and he and I investigated some fifteen different treatments.

MB You had a long association with him and he must have had an important influence on your work over the years.

RD Oh, he did an enormous amount to help me in my work and I enjoyed working with Avery. Bradford Hill and Avery Jones were marvellous people to work with, both of them, both very supportive, full of ideas and keen to create the conditions for other people to do the work, and always themselves ready to stand back and let the younger person take the credit, not that I was much younger than Avery Jones, a year or two younger.

MB Just a little.

RD He was academically the senior, at any rate, and I loved working with both of them. I went on working with Avery Jones actually for some 22 years after I was formally working with Bradford Hill.

MB By 1955 another problem had raised its head, the problem of test bomb explosions and people asking questions about radiation influences. You became involved with that right away.

RD Yes, I did. Like many people at the time, when the first hydrogen bomb was exploded and there was fall-out throughout the world and questions started being asked as to what the effect of small doses of radiation was likely to be. I was very concerned about this. In fact, I did a course in radiobiology at one of the Polytechnics in London at that time to try to learn a bit about it, so that when the Government asked the Medical Research Council to investigate the relationship between dose of radiation and the hazard to which people were exposed to from it, I had had some background in the subject and was asked to work on it with Court Brown. You see the situation then was very different to what it is now. The idea that cancer was due to a genetic mutation, that this is one of the factors responsible for the development of cancer, was by no means accepted. In fact it was a rather extreme view. Most people thought that you could only produce cancer by doing major damage to tissue, and in fact a few radiation cancers had been described, but of course they were the ones that were recognised following radiotherapy, and you had obvious damage to lets say the skin over a bone and then a bone sarcoma would develop. So many people thought that radiation would only produce cancer if it produced macroscopic pathological damage. The idea that very small doses produced cancer was not accepted. It wasn't the established view by any means. In fact I remember a very distinguished scientist by the name of Austin Bruce, writing a paper in *Science* around about 1944-45 showing how impossible it was that genetic mutations had anything to do with the development of cancer. So, the idea that small doses would do any harm really, I won't say hadn't entered anybody's mind, but it certainly wasn't the accepted view. I don't think that when those test explosions were let off, that the senior military or government had any idea that it might be doing harm.... and then there was a public outcry about fall-out and people said well....they weren't thinking about so much about cancer, they were thinking about genetic damage to following generations and there was this public outcry about it, and the Government asked the Medical Research Council to set up a committee and advise them as to what the actual hazards from ionising radiations were. And when that committee met they realised they had absolutely no data to go on as to the likely risk of cancer and whether there was a threshold phenomenon or whether the effect was likely to be proportional to the dose and they asked Court Brown and myself. Court Brown was a man of about my own age who was Director of a small radiobiological group of the Medical Research Council, and they asked us to see if we could find out the relationship between doses of radiation and the development of leukaemia that had occurred in patients with ankylosing spondylitis who had been treated by radiotherapy. It was thought that this would be a good group to study the effects. Well it was an exciting period then because the committee had to report to the Government, and Himsworth who was the Secretary of the Medical Research Council had Court Brown and myself up and said, 'Well now we want you to try and give us some advice on this and we need the advice by January 1st next year.' So we thought how to do it.

MB When was this?

RD This was 1955, and he wanted the answer by January 1st 1956. So we decided that the only way we could get at all a reasonable answer was by studying all the patients with ankylosing spondylitis that had been treated with radiotherapy in the country, getting an estimate of the dose they had received clearly as possible for close to 15,000 patients. We couldn't get it for all, but we took a stratified random sample of the patients and determined the dose for that. Then we had to work out from the radiotherapy descriptions what the amount of radiation that people had actually received in the bone marrow was likely to be, and then we had to follow up these 15,000 people. It was quite a job to do that in six months. But Himsworth said that money was no object and 'We'll put the whole Medical Research Council staff on assisting you if you need it,' and it really was marvellous. We had three teams of three people going round the country extracting data about patients treated for spondylitis and we had people at the National Institute of Medical Research working out what the dose of radiation that a given radiotherapy treatment was likely to be. Altogether there was some hundred people working on this subject, trying to help get the information and we got death certificates for everybody dying from leukaemia in the country over the previous fifteen years. We could match their names against the names of people treated for spondylitis. That was the way. We weren't able to follow all 15,000 people up individually, but we matched their names against people dying of leukaemia. Incidentally, this turned out to be very effective. We subsequently, in a detailed follow up, found that we'd only missed one case of leukaemia by using this technique, but of course there were no computers in those days. There were some very primitive ones but they weren't being used. You had card sorters, Holorith card sorting machines, and Court Brown and I finally got our answer at 3.00 am on January 1st, as the Holoriths spewed out the last lot of cards. We were sitting there counting and working out the incidence of the different doses of radiation and at that time the results rather suggested a curvilinear relationship and we reported this to the Committee that morning and V Mitchell, Professor Mitchell, subsequently Regius Professor of Physics at Cambridge, I think he'd just been appointed, he was a great radiotherapist, and he didn't like the way we had estimated the dose received and he said, 'It's not good enough' and 'You should do it a different way' and we then took all the data back and spent another six months on re-estimating the dose again, with the assistance of a lot of other people.

MB This is the dose getting right through to the bone marrow.

RD That's right, yes. This meant special tests, special measurements. Experiments had to be done on a model man for a given radiotherapy dose to show how much actually got to different parts of the bone marrow and that took another six months, in fact the best part of a year, and we then revised our results and at the beginning of 1957, a year later, we concluded that they really showed there was a linear relationship between dose to the marrow and the development of leukaemia. And in our final report to the Medical Research Council, they eventually published their report to the Government on the hazards of nuclear radiation in early 1957, and in the report we produced for the Medical Research Council we concluded that it should be assumed that radiation produced leukaemia in proportion to the dose received in the marrow right down to low doses, with no threshold. I'm sure our data was the first which suggested that you should assume no threshold. It didn't prove it of course, but it suggested that it was unlikely, and of course subsequent developments of molecular biology made everybody willing to accept that cancer was basically caused by a gene mutation, at any rate at one stage in the development of the disease. The whole attitude has changed since then.

MB Subsequently, there was work in this field published from the Japanese end of the story that validated your findings on radiation.

RD Yes, of course, the demonstration that radiation could cause leukaemia came from the experience of the Japanese survivors of the atomic bombs at Hiroshima and Nagasaki. There had been a little suggestion from occupational studies by radiologists before, but very weak, but this came out in the middle '50s, before the final results of the spondylitis studies. So the proof that radiation could cause leukaemia came from the experience of the survivors of those bombs. At that time they hadn't got a dose response relationship. It took quite a long time to work out what the doses had been that were received by the survivors and it wasn't until after our report that estimates of the dose reponse relationship came from the Atomic Bomb Casualty Commission as it was then called and the experience of the survivors of those two bombs actually gave almost identical results of the estimate of the amount of leukaemia that might be produced by radiation per rad.

MB So you turn in a remarkable second survey. How does that radiation research weigh when you look back and consider the various components of research in your life? Is that 1st, 2nd, 3rd? Can you order it in importance?

RD Well I think from the point of the impact on disease the smoking must be more important, but of course the appreciation that radiation could cause cancer and do it down to small doses has also been of considerable social importance, so that comes second.

MB At this stage in your career in the mid ’50s there was beginning to be a feeling in your mind that cancer was multifactoral in its cause and not a one causal factor business.

RD Yes, indeed. I’d always been intrigued, like so many other people had been, by the age distribution of cancer. Why was it essentially a disease of old age? There are types of cancer that occur in youth, but the common cancers are all very rare in youth and then start occurring in the 20s and 30s and then get increasingly common. There were all kinds of hypotheses. It was said to be just degeneration associated with old age in general, but that didn’t mean very much, and I was interested in the mathematical relationship between incidence, one usually had to work with ‘mortality’ statistics in these days, between mortality and age. And Stocks showed that you could account for this increase with age if you postulated six or seven steps of one sort or another in the development of cancer. Armitage and I took that up and tested it on a number of cancers. We didn’t like the idea much that you required six or seven mutations to cause cancer. It didn’t seem biologically reasonable, but it did seem reasonable that there might be several stages. We tried out a number of hypotheses, the most interesting being that there were two stages and the first change resulted in giving a changed cell some advantage over neighbouring cells, so that its progeny increased in comparison with the progeny of normal cells. Then the second stage turned one of those cells into cancer, and we tested that hypothesis against the distribution of disease with age. It looked as if it was going to work at first, but further studies showed that it wasn’t really an adequate explanation. You really have to postulate I think three stages, and I think various differences in the behaviour of the cells in between, but we published several papers testing various hypotheses against the observed incidence with age. And I think the multistage hypotheses for the induction of cancer, which again wasn’t very popular when it was first introduced, has become the standard concept at the moment. And of course when we found that giving up smoking had an effect very quickly, it fitted in very well with the idea that you had multiple stages, which of course, had been shown earlier by Bembrum and Shubrick, and also by Rouse, that you could have one agent that initiated a cancer and another that did something to make the effect of that initiation more evident, the so called promoting stage. I don’t like to use those words now, because I think they have been given meanings which perhaps aren’t justifiable, but the concept that you have at least two, and possibly three stages, and that the development of cancer is a sequential process is a very valuable concept which is being borne out by laboratory discoveries.

MB Sir Richard, in all this time you were associated with Bradford Hill, and you were to stay with him until he retired?

RD. Yes indeed. Nothing could have persuaded me to take any other job as long as he was Professor at the School of Hygiene and Director of the Medical Research Council’s Unit there. He was a marvellous man to work under, but when he retired his empire broke up into three parts and I was asked to be director of the Medical Research Council Unit. Donald Reid became the Professor of Epidemiology and the Head of the Department, and Peter Armitage became the Professor of Medical Statistics. At that point I thought there was rather too much epidemiology concentrated in the London School of Hygiene and Tropical Medicine, also that it would be good to have epidemiology more closely linked with clinical medicine and Lord Rosenheim was very welcoming and the Medical Research Council moved the unit to University College Hospital and the unit was established there from 1962 until I retired from that post.

MB Very early in that post you took a strong interest in oral contraception. That became a new research focus for you.

RD Yes. Of course oral contraceptives were introduced around 1960-61. They came to this country very slowly. This was about the time I had taken on the directorship of the unit and frankly I was a little disappointed that epidemiologists hadn't been consulted in relation to the possible hazards of oral contraceptives. The Medical Research Council had a committee which was entirely made up of endocrinologists who prophesied all kinds of things that didn't actually turn out and they didn't suggest that there should be any epidemiological studies designed to see what their effects were. So I got in rather a huff about it, as a matter of fact, and decided not to do anything, but then there was a report that they might produce venous thrombosis – this was just an odd clinical case that was reported, and I thought well this is ridiculous, this is socially an extremely important thing, one must find out whether oral contraceptives, steroid contraceptives, are harmful or not and what they do. The first thing to test obviously was whether they produced venous thrombosis and pulmonary embolism, and I had a look at hospital records at the Central Middlesex where I was still working, to see how many women in that age group were being admitted with that condition, that wasn't obviously due to surgery, accidents or childbirth, which were the main causes of those conditions, and it looked as if there were just enough cases if one did a study over a whole region, over the North West Metropolitan Region as it was called then. And Martin Vessey had just joined the unit and I suggested that he might like to help on that study and we started working on this ... and of course it has given rise to 20 years work ever since. After the first study, which was a case control study and which was done at the same time as a study done by the Royal College of General Practitioners, a case control study that they did on their patients, and a report from the Committee on the Safety of medicines, the three groups all published a paper in 1967 all leading to the same conclusion, we then decided that we should really try to see what the total effects of oral contraceptives were and so we designed a prospective study just like the doctor's one, on this occasion with the help of the Family Planning Association. And Martin Vessey has taken that over and has been following up 17,000 women ever since.

MB A massive enterprise.

RD Well, it has been that, and along with the study of the Royal College of General Practitioners it really has provided us with all the worthwhile data we have on the harmful effects and the benefits of oral contraceptives, because it is not just that they produce hazards, they have medical benefits quite apart from the social benefits of controlling conception. This is often forgotten.

MB Data arising from that study has probably had enormous effects on the production of oral contraceptives. Is that right?

Rd Oh, I think it has.

MB So that the story is nowhere near the same as it was when oral contraceptives were first introduced here.

RD No. The first important thing being that the dose has been reduced because when these various hazards were shown, it was shown that they were commoner with the higher dosage and the dose of oestrogen and progesterone has been progressively reduced. I'm sure they're much less hazardous now than they were initially.

MB What else was happening to you in that period in the 1960s when you were Director? You were an administrator. How did you find being an administrator?

RD Well I didn't particularly enjoy that, but it did mean that one could get involved in more studies because you had people to help and work with you. We carried on working on some theoretical studies on the multi stage hypothesis, the numerical analysis of the relationship of age and cancer, and a number of occupational studies and I was still doing these studies of the treatment of peptic ulcer. So the smoking, the radiation, the occupational studies and the oral contraceptives kept us very busy.

MB That was all going on through the '60s.

RD All being carried on, yes, because we got more precise information with the greater amount of data. As a matter of fact I'm still studying radiation now, because it is important in estimating what the effect is, to know how long the effect lasts, and we are still following up the spondylitis cases that were irradiated. It looks as if the effect is largely eliminated by thirty years.

MB Sir Richard, by 1969 the news was in the air that you were going to make a change, from London to Oxford.

RD Yes, that was a great surprise to me, I can assure you. An old friend of mine came and saw me one day and said would I be interested in a post in Oxford, which I may say I'd never thought of, and it didn't take me long, after consulting with my wife, to say, 'Yes, it would. I would be interested in it.' I had a number of tempting offers before that, which I'm very glad I turned down. One was to take responsibility for the new international agency for research on cancer, which WHO was setting up in Lyon. That was an interesting possibility, but I decided it was nicer to stay in England and work with the Medical Research Council who were marvellous employers.

MB Sir Richard, with the prospect of discussing the Oxford years in a later interview we will bring todays discussion to a close at this point. Thank you.