The Royal College of Physicians and Oxford Brookes University Medical Sciences Video Archive MSVA 056

## Dr Denis Burkitt CMG FRS in interview with Dr Max Blythe Oxford, 26 February 1991 Interview Three

MB Dr Burkitt, when last we talked together we had got through your career as far as Uganda, some early work in plotting diseases, but we'd arrived at the plotting of the distribution of a cancer that was to become known as Burkitt's lymphoma, right across an equatorial belt of Africa and in a tail somewhere down this eastern side. How did that early mapping all of a sudden lead to concern for considerable journeying down this eastern side of the country?

DB Well, when we had the initial map of tumour distribution across Africa, running approximately 10° North and 10° South of the equator, with this tail down the east coast, the obvious thing was to say if we could find very accurately some part of the edge of this distribution then one would be able to look for some environmental factors which were operating that side of the line but were absent that side. And the question was where we should concentrate our attention to look for the edge of this map. Now, along the top was out, because people disappeared into deserts and you can't have tumours without people. In West Africa the tumour went as far as the palm beaches, the whole way along, and you can't got into the sea looking for tumours. There was a revolution on in this area so we decided to give it a miss and that left us with the south-east portion as the one to investigate. Now, we thought we were going to find an edge of a tumour distribution but it didn't turn out that way at all – it turned out much more exciting actually. But we planned to do a journey, which you see depicted here, from Uganda down through part of what was then Tanganyika, which is now Tanzania, round Northern Rhodesia, which is now Zambia, the whole length of what was then Nyassaland, which is now Malawi, Swaziland, South Africa, Zimbabwe, which was then Rhodesia, and so on back to Uganda. Now, we had to plan this very much in detail and the first thing I had to do was to get permission to go, which my director of medical services allowed me. We assumed that this would take us ten weeks to do 10,000 miles. We visited something over fifty hospitals. I had to choose companions because you can't go alone for a journey like that. If you only choose one companion and he gets flu just before the enterprise starts you're stuck. So I chose two friends both of whom were medical missionaries. They had long experience of Africa. One of them had been brought up in East Africa. One of them was a superb car mechanic and when you're within perhaps 500 or 1,000 miles from the nearest garage you must have someone like that. And you must have people who get on with each other. We were already close friends. So I chose two friends and we wrote letters to all the hospitals along that area, and optimistically – but we pretty well kept up with it – we told them what day to expect us, what day we would leave them, to put some time by to speak to them. We made an album of photographs showing clinical pictures, x-rays, pathology, so that we could sit down like you and I are at the moment now and turn the pages over and say to the doctor, 'Have you see this or have you not?' And he would say, 'I remember a girl or something.' And we'd say, 'Where did she come from?' and we would put a little mark on the map, that's the way we did it. So the man who looked after the car was my very old friend Ted Williams, whom I'm still in close touch with, and he bought – this was at the time of the revolution in the Congo, the Simba revolution and many of the missionaries were being turned out by the revolutionaries - and we bought a second hand Ford station wagon very cheaply – I'll show you the figures later on. We planned all this. We had metal plates welded on to the bottom of the car so that when we went over rocky roads we wouldn't perforate the sump or the tank or so on. We carried all the reasonable things for spares – camp equipment. We planned it in great detail and that is what brought us into starting this long safari to try and find out if we could get an edge to the tumour belt somewhere.

MB Before we get to the starting line, I'd just like to take a detour in two directions. First, I think while this operation was being planned you took a break and had time to come over to England and you made an important meeting with Tony Epstein.<sup>1</sup>

<sup>&</sup>lt;sup>1</sup> Sir Anthony Epstein and Dr Denis Burkitt were recorded in conversion on 20 March 1991 for the Medical Sciences Video Archive of the Royal College of Physicians and Oxford Brookes University (MSVA 091).

DB Yes, when I was planning this trip... and it was actually when I was planning this trip the first paper came out, which really created worldwide interest. I was lecturing at the Middlesex Hospital, largely to medical students and surgeons, because I had lectured there on may of my leaves in Africa describing my surgical experiences, and a young pathologist, Anthony Epstein - Tony Epstein, as we always knew him came into my lecture and sat at the back and as I talked about what we had known to date about the distribution of the tumour, he sort of put two and two together and said this must somehow point to some biological agent like a virus. And that was the first beginning of our close working together. In fact, he asked me after the lecture if I would, or we would send him material from all our tumours and he would look for viruses in them. As you know, they looked for several years and didn't find anything and it wasn't until they cultured the material before they looked at it that they found what became known as the EB [Epstein Barr] virus. But a little interesting thing came out of that; as he left the lecture theatre he pulled off the wall the typewritten notice saying that an unknown guy called Burkitt was going to speak on some tumour in Africa, if it would interest anybody, and he put it away in his drawer, and a long time later he became the senior editor of the first international textbook on the EB virus and the first illustration in the book is the notice about my lecture which he pulled off the wall, because that was his entry into the whole story. So that's really where the EB virus came to birth or to begin with.

MB Denis, how came the link with the Middlesex Hospital, you said you lectured there on many occasions?

DB Well, I had been for years, I had contracts there and knew the professor of surgery, a man call Leslie Le Quesne, and they used to invite me to lecture to students showing them all the bizarre and strange things we saw in Africa over the years previously.

MB Right, the other thing before we get to the starting line, I know you'd like to say something more about Cliff Nelson and Ted Williams, who really were great strengths on this journey.

DB Well, Ted Williams started a little mission hospital in the north west of Uganda; he made his own sun baked bricks, he dammed up the river and made his own water supply, he built his own hospital with his own hands with the help of African labourers, he put in telephone communication, wireless communication and satellites. And he started later a cancer registry in a little hut made of mud dried bricks with a thatched roof – later he was able to put a corrugated iron on it – and what was such a lesson is that when they did a million dollar project years later to try and see the relationship between the EB virus and this tumour, they chose Ted's hospital because of the work he'd done and because of his knowledge of the language and the local people. Now, what was such joy to many of us who worked on this project like Mike Hutt, myself and others, when he came back to England years later he was made a Commander of the British Empire, a CBE, which is something that heads of major research institutes would covet. Now, the lesson that comes out of this is, if you have a good man with poor facilities he can do marvellous work, but if you have a useless chap with all the facilities in the world he can do nothing. So Ted has been a tremendous innovator and we are still in touch. Cliff Nelson...

MB Can I just ask, how did you first make contact with Ted?

DB Well, I'd known Ted a long time because he was brought up in East Africa and his father knew an uncle of mine who was the first surgeon I think in East Africa.

MB The tonsil uncle?<sup>2</sup>

DB That's right, so I had know Ted for a long time and had met him early in my time in Africa. Now, Cliff Nelson had turned down prospects of a good financially rewarding career in Canada, feeling that God was calling him to work amongst the underprivileged people and he came out as a government official, like I was in Uganda. Later he left the government and joined the mission and he is now in Edmonton and I'm expecting to stay with him in June this year. But we both... he knew Ted well, because he ran the government hospital in the area where Ted ran his

 $<sup>^{2}</sup>$  Dr Max Blythe is referring to an uncle, Roland Burkitt, who performed a tonsillectomy on Dr Burkitt when he was a child. This is mentioned in the first interview (MSVA 053).

mission hospital. So that it was so important to have closely-knit people who could work together in harmony over the whole of this trip.

MB Right, I've got you to the starting line, That's fascinating but can we begin the journey?

DB Now, we wrote letters you see to all these hospitals, before we left; we had a plan of action of what we would achieve. Ted's wife stayed with my wife Olive during the time we were away, and we set out with a tremendous sense of adventure and we travelled as I say over these 10,000 miles talking with people all along the line. Now, of course one can't talk a lot about the safari other than to say ... I think we have some pictures coming up now. You see, when people, the ordinary layman thinks of cancer research, he doesn't think of crossing rivers on ferries and all the rest of it; he thinks of albino mice in the laboratory and white coats. But we enjoyed every bit of it, we didn't know we were doing anything of great interest. It never occurred to us that it was going to come out in the *Reader's Digest* later on and so on, in the sort of language of Burkitt and Ted and Cliff turning their back on comfort and everything for the sake of suffering humanity. Actually, we loved it all, it was marvellous fun but we did get a lot out of it, as you know.

MB Can you pinpoint the stages? Would you like to pinpoint the stages of the journey?

DB Well, roughly what we did, you see, we went down the east side of Uganda and really along Lake Victoria, then we went down the whole length of Western Tanzania, which is enormously isolated, almost uninhabited country. We went round Northern Rhodesia, as it was then, but is Zambia now. Then we went into Southern Tanzania and down the whole length of Malawi. I might say that going round Northern Rhodesia, we crossed over the path of David Livingstone and his history was of interest because Ted had gone out as a medical missionary largely through the impetus of learning about David Livingstone.

MB That was a great memorable occasion crossing the tracks.

DB Then we went right down the lake – Malawi. We went into Swaziland, South Africa, Zimbabwe as it now is, but was then Rhodesia, and then through Tanzania again. Now, we were going to go through Rwanda Burundi but there was such terribly bad weather, the bridges were all washed away, we had to get our car on to the back of a goods train and then on to a ship to get through, but later on – we shall come... I don't know later in this interview – we managed to go by air into these countries Rwanda and Burundi, but we found the same message.

MB Denis, you started in October, on October 7th 1961, and it did take about the ten weeks that you envisaged. It was a pretty accurate trip around and as you said you got to most places within a day or so of having promised to be there.

DB That's right.

MB What were the main recollections of that – close co-operation with people in the hospitals?

DB Well, I think the message was – and I didn't realise then that it was going to be so important, because we carried on the same sort of study all over East Africa later on – is that if you... two things: first of all, it's the man in the mission hospital who tends to be able to provide the most information because he might spend twenty or thirrty years in his job, whereas in district government hospitals, every six months or so the doctor is changing. Moreover, the man in the mission hospital, he wouldn't be there unless he was a dedicated chap. So we found that if we met people, got to know them, talked to them, then we could run an ongoing project and they would support you with all kinds of other information. And when we got on later to the story of Western diseases, when we get beyond the lymphoma, this was built on personal contacts over a wide area with people who were prepared regularly to give information. So really we collected an enormous amount of data, not what we expected, work which we had to reinterpret – let me know when you want the interpretation of it.

MB Right. What I was going to ask was: while you were *en route* did you begin to feel patterns forming or did that happen when you came back?

DB No, the important thing was we did the whole thing on the ground together. If we had been given the opportunity to zoom from station to station with an aeroplane, it would have been quicker but we wouldn't have had the time to all the time throw back and forwards our thoughts. And I mean it wasn't Denis Burkitt's thoughts, I mean Ted or Cliff probably did just as much as I did, but we were able to throw it back and forwards as we went along...

MB Just spending a lot of time together.

DB ... you see, which we would have lost by going zooming around by air.

MB And did you have long evenings to talk in camp, in camps that you struck?

DB Yes we did, in guest houses and mission stations. Of course, we got to know each other better, but I think it was this criss-crossing of information with people that became so invaluable because there were then, and there may even be now, people who will call all this kind of evidence anecdotal and they will brush it off, but if you have a hundred or five hundred, whatever it, hospitals all telling the same story, it is or it isn't there, then we found that people begin to listen. If you can put a lot of consistent anecdotal evidence, it is anecdotal, and there was no chance of getting detailed age... incidence rates but we got a lot of very consistent, reliable anecdotal evidence.

MB When you got back you started to really put this together – to pin out your map.

DB Well, when we got back... you see, as we went along we found out that at the equator the tumour stopped at about 5,000 feet. When we got a 1,000 miles south of the equator it stopped at about 3,000 feet, it was only at the sea coast and around the valleys and the rivers and so on. When we got 2,000 miles south of the equator it

stopped almost immediately we left the coast. So we had a tumour which was dependent on altitude, but the altitude varied progressively in distance from the equator. Now, this was interpreted, I think, probably by a senior entomologist Professor Alexander Haddow as being actually a temperature barrier although it was reflected in an altitude barrier, because what we found... that we never found the tumour to be common anywhere where the mean temperature anytime of the year fell below 60° Fahrenheit. So the finding of this safari was a form of cancer which is related to temperature, which had never been even suggested before – that was in a nutshell the finding.

MB You say that when you got back Alexander Haddow looking over the maps that you were constructing started to think in terms of a temperature limitation. He was an entomologist.

DB And a virologist.

MB Right. Did he start to think in terms of insect distribution?

DB Yes, he did and he, as I'll show you... because when we finished with West Africa, it was he really who showed that the map we drew of tumour distribution related to both temperature and, we'll see later, rainfall, which brought everything into the idea of having a biological agent because it can't be due to minerals or anything like that if it's related to climate.

MB Denis, you've just mentioned West Africa, you felt you had to go to West Africa to check on edges?

DB Well, you see we had to got to West Africa because it was beginning to emerge, and we were able to confirm it, that not only is this the commonest tumour of children in West African countries but it is commoner than all other children's tumours added together. Now, this was an unpopular statement to make because if you describe something new it's meant to be rare. If you describe something new and you say it's the commonest, as you can understand, it's not a very popular approach to

take. Now, I didn't have funds to think of bringing anybody else to West Africa with me. I was, you see, by this time getting a hundred dollars from this institution and a hundred and fifty from another, we didn't have masses of funds. And, as I think we'll be showing on the slide in a minute, the whole of this 10,000 mile safari for ten weeks for three people, including the money lost in buying the car and selling it again, the total cost came to something a little over six hundred pounds. So it was totally cost effective.

## MB Research on a shoestring.

DB And the lesson that comes out of this - which I still try and proclaim in America - there is a concept that research is like a sausage machine and the more dollars you put in one end, the more ideas come streaming out the other. Now, I think you can put in ideas and get out dollars but you can't turn dollars into ideas. I think the idea in America that we solve cancer by the enormous amount of money that Nixon put into it, that has proved a failure. But to go back, I wanted to do West Africa, I did the western part of the Congo at the same time. Now, I flew by myself over there and then I travelled by myself a good deal of the journey by train and by car because then you can see the lie of the land and the climate and get at the idea, but if you go by air you miss all that. But travelling around West Africa on those occasions, I only did Nigeria and Ghana; subsequently I've been to the Ivory Coast and Liberia and so on -it's all the same. And what we found there was that in the southern part of West Africa, which is tropical rain forest, this tumour was exceedingly common but when we got into the north, Kaduna(?) three million people within thirty miles no evidence of tumour at all. So getting the maps out for the various school departments and things, one discovered that the tumour only occurred when the rainfall was over twenty inches a year, so that we came back then to our base in East Africa with that added dimension that not only was the tumour dependent on temperature but it was also dependent on rainfall, and that made a biological agent, presumably an insect vector, almost inevitable. Now, with Alex Haddow's help and others we looked at then distribution of trypanaosomiasis and yellow fever, yang yang(?) fever, diseases which we knew to be due to insect carried viruses, to see whether they fitted in, and they more or less fitted in. Now, all this evidence of relationship to some insect, we

were like a magnet we drew in people from all over the world who were interested in trying to be the first person to show that a human tumour could be due to a virus, and of course Tony Epstein was one of them but there were lots of others; there was Bob Harris from the Imperial Cancer Research Fund, and there was [Neville] Stanley from Australia and the Japanese and the Americans, but the search was on as it were then to see whether...

MB Denis, can I must ask about that search because you facilitated it by sending tissue on a regular basis from sufferers of this disease to Tony Epstein?

DB Yes we did, we sent it to several people. We sent it to Tony Epstein. He would have it met... actually, Dennis Wright did most of the giving, but we'd give it to the crew of the British Airways at Entebbe and then Tony would meet it at London Airport, Heathrow.

MB This was ice-packed and sent off in special containers.

DB That's right, that's right. And as I said, he looked at the tumour for years and it wasn't until he cultured it first of all that he found a specimen full of viruses. He was so excited he tells me that he turned off the electron microscope because he was afraid the light might burn out the viruses, and he walked round the block to clear his mind a bit and he turned it on again and it was still full of viruses, and he got all his friends to have a look. And within forty eight hours it was on the aeroplane, on the way to the Henles [Werner and Gertrude Henle] in Philadelphia and they said it was a new type of herpes virus which hadn't been described before and that was the beginning. Now, I would like to say this, there were other people looking for viruses and they looked for reoviruses and so on. And I think research is a little bit like going out of a maze. You see if you've got a team of people in the middle of a maze and they've got to find the way out, some people go down a track and it's a blind alley so you can close it off; another fellow goes down a blind alley and you can close it off, and as all the blind alleys are closed off it's easier for the rest of the team to get out. So that it isn't a failure closing off a blind alley, it's got to be done.

MB Right and the nice news is that Sir Tony Epstein is going to come into the studio at the time of our next meeting to talk with you over this exciting period.

DB We meet each other all round the world. We pop up on platforms one behind the other you see on several occasions.

MB When was the virus formally recognised – end of the sixties?

DB Oh no, the first paper I think describing the virus was in '64, I think, if I remember rightly.

MB So this was a very quick result.

DB Yes, within a few years.

MB Denis, what does the story lead to next? You've got a pattern, you've got a link with insect distribution?

DB When we had compared the distribution with various insects, it looked as if maybe there be an insect vector involved. Well, now by that time then the EB virus had turned up and so we had to make hypotheses, and you have to make hypotheses and when they're wrong you throw them out. And we said to ourselves, well now, perhaps we have drawn the distribution in Africa of EB virus, but we found the EB virus was just as common here or here where there is no tumour, so we had to get up and say 'I'm sorry, I was wrong.' 'Well,' we said, 'it might be that in Africa the EB virus is carried by an insect and put straight into the bloodstream, or concentrated in the insect or something, and perhaps if it's insect vector it can cause tumours but if it's not it can't. But we found it's never insect vector so, again we said we are wrong. And then we turned again...following a suggestion made years before by a wellknown American virologist, Gilbert Dalldorf, who wondered whether malaria might be involved. And we looked at the map of malaria – which will be coming up, I gather, in a moment - and we found that the tumour distribution both in Africa and elsewhere in the world – and the only othe place in the world that it was known to be

common at that time was in New Guinea, due to the work of Tim Seldon, and subsequently we found that it was common in Malaysia. It is only common where malaria is what you call hyper- or holoendemic, which is intense infestation with malaria all the year round. So then we looked at out own country of Uganda where there had been a survey of the intensity of malaria in different parts and wherever the tumour was common there was hyper- or holoendemic malaria, and in the parts of our country where the tumour didn't occur there was no intensive malaria. And we found that the only part of Africa, tropical Africa, where the tumour didn't occur, were the islands of Pemba and Zanzibar off the coast of Tanzania, and the area around Kinshasa in the Congo. Now, these were the only two places where successful malaria eradication had been achieved and so everything seemed to fit in with the malaria playing a role. And we began to realise then that when we drew this map of tumour, we were actually drawing the map of holo- or hyperendemic malaria; we didn't know it at the time but what we were drawing was the malaria map. So we again, we had to make hypotheses and we said, 'Now, how can malaria play a role in the causation of this tumour?' And we knew that intense malaria caused an enormous proliferation and change in the reticular endothelial system and we thought perhaps in that kind of endothelial system the EB virus can cause tumours, it can't if... but there was no evidence to support it. And then we recognised -I say we because many people were doing this - that hyperendemic malaria causes profound depression of the immune system, and it had been recognised in England that if people had transplant surgery – kidneys or livers put in – they are immunosuppressed by the doctor and they have something like thirty times the risk of getting lymphomas as the normal public, and these are EB virus tumours. So that the concept then came up that the intense EB virus infection together with immune suppression maybe sufficient to cause the tumour and subsequently, of course, years later it became evident that patients with AIDS get this tumour, and they too are profoundly immunodepressed. And about the same time, I might say, as we were doing this, of course, it became evident that this is the most rapidly growing tumour known in man and it is the most sensitive to chemotherapy.

MB Yes, you told me the story of how that success of chemotherapy came about, Denis.

DB Well, you see, the reason chemotherapy is so successful... for two reasons: every cell in this tumour divides pretty well every day and so giving chemotherapy you knock every cell in mitosis, when it is most sensitive; the second thing is the enormous immune response on behalf of the body, because this is a virus induced tumour, there are foreign proteins – I speak from an ignorant point of view and you can correct me if I'm wrong here. But for those two reasons this tumour appeared to be enormously successful to treatment. Now, we didn't have any money for chemotherapy and there was no radiotherapy in tropical Africa in those days so we had to hit on a plan how we could get chemotherapy provided for nothing. Well, my colleagues tell me I did most of my research by what you call blarney and blarney is something like this. We wrote to the big drugs firms in America and we said: 'Dear Sir, we are very enthused with your work and so on but we appreciate that you have a major problem, and the major problem is that all patients you treat with cancer in America have already had radiotherapy, so ever if you appear to get good results, you can't really be certain whether it's due to your drug or whether it's due to the previous radiotherapy. Now, perhaps... we feel we could perhaps help you out of the problem.' And we said, 'We have no radiotherapy so all we would ask for you is to give us free drugs and we'll tell you whether they are effective in the absence of radiotherapy.' And they wrote back and they thanked me for my kind compassionate consideration and told me I could have all the drugs I wanted.

MB An offer they couldn't refuse.

DB So we got vincristine, we got Andoxin and we got advice from the world experts, people like Joe Burchenal and Herbert (?) and we said what do we do, because I didn't know. Well, they more or less said you give all the drugs you can without quite killing the patient and then one or two of them might survive. You wait till they have bleeding from the gums and their hair falls out and what have you – about three white cells left. Now, I was running a whole surgical unit as well as doing this research work as a hobby. My patients used to be taken out of the hospital by their mothers in the middle of the night sometimes after they had their first injection; we had to wait about four days to get blood counts back, so I was doing the worst,

most inefficient chemotherapy that has ever been done. But I soon found that we were getting the best results in the world. Peter Clifford in Nairobi was discovering the same thing and we just happened to have a marvellous tumour because although I in my ignorance was probably seeing 40 per cent of jaw tumours or something cured with two injections of chemotherapy, when I was followed by an expert, John Ziegler, he put it way up to 60 per cent or more of all tumours were cured. So the chemotherapy was absolutely marvellous; it cost very little, it could be given in any mission hospital anywhere – you didn't need to have elaborate facilities – because it's no good having marvellous treatment in Africa and it can only be given in some prestigious establishment. So that the results of the chemotherapy again were magical, but I didn't deserve any credit for it, I was just fortunate I had a good tumour.

MB As the chemotherapy took hold and became the right way to go, obviously this disease began to decline widely across Africa.

DB Well, no it didn't decline because you never reduce any form of cancer by improving the treatment. The treatment became very successful, but it's a total fallacy that early diagnosis or treatment ever reduces the evidence of cancer, it never does. Now, cancer in Africa is not an important subject compared to other things. The importance of this tumour was the lessons that were learnt in North America and Western Europe. It didn't really have any impact on health in Africa because although this was the commonest cancer of children, children's cancers are not very common in any case and cancer is immaterial compared to things like malnutrition and all the other things we have in Africa.

MB But I was thinking of the grotesque cases that emerged in that they were treatable.

DB They were treatable but not preventable.

MB Right, but the amount of suffering that there had been before.

DB Yes, we had saved lives.

MB So you must have been enormously satisfied by the whole enterprise.

DB Not only that, but I mean we didn't know that we were doing anything of any value at all. I mean to begin we didn't know that this tumour was going to be the first human tumour shown to be related to viruses, the first human tumour which could be treated successfully with non-toxic doses of chemotherapy, the first human tumour shown to have specific chromosomal changes and so on. So that it became what Sir Harold Himsworth, the Director of the Medical Research Council, called the sort of the 'Rosetta stone', but we didn't know it was going to be that, one doesn't claim any credit for it, but it was fun when it happened that way.

MB Looking back it was a very remarkable story.

DB Great fun.

MB And it took you into the middle sixties.

DB Yes, I suppose I was working on this tumour between about '57 and '67 and I then got on to a much more important field, which really I gather we'll be discussing later.

MB Yes, I was going to ask first about changes in Uganda, because Uganda had been your home.

DB Well, you could never do this type of work now, you see I happened to be just in the place in the time. It would have been difficult to do it earlier, you wouldn't get the co-operation now, you wouldn't have the freedom of movement, you wouldn't get the amount of information. It was something that had to be done I think at a certain time in history and I was fortunate to be there at that time.

MD Yes, but just as that story came to an end life in Uganda promised to come to an end.

DB It did. You see, we left Uganda in '66 and it ticked over fairly well under an African government. I worked for two years after the African government came in but then when Idi Amin came in the whole infrastructure of the country collapsed and of course people were killed by the hundred thousand. It was terribly disappointing. I mean the medical services all collapsed because you can't have medical services when you have complete anarchy. They are only finding their way back gently now, but it was a very sad story.

MB That must have been very depressing, and where did you decide to move to, Denis, at that time?

DB Well, we moved for two reasons. First of all, it was made clear to me that I wouldn't be wanted to stay on in Africa as a consultant surgeon, because we had been working all our lives in Africa to eventually do ourselves out of a job by training local people, and why should they pay the salary of an Englishman or an Irishman like me to come out if they could employ their own people. So I was told that I wouldn't be wanted for long. Now, about the same time as that, through the help of my senior colleague, Sir Ian McAdam, the Medical Research Council said they would take me on; they had shown a lot of interest. So I was able to stay in the same office in the same hospital for the next two years working on this tumour and then, largely for the sake of our three daughters - we felt it so important they should have a home in England – and also as my work was expanding, because then I was – we 'll come on to it later - but we were investigating seven forms of cancer, not only throughout Africa but we were trying to get information from India and the Middle East; I could really do it just as well from London as from Africa. So we were very sorry to leave we had a very happy time there but we did leave in early '66. But I used to for many years go out twice a year and do very... I'm surprised when I look back on them, the enormous safaris I did all over Africa, collecting information.

MB And you still had many friends there.

DB I did, and of course we built up a network of hospitals so that when I came home to England I was getting 150... about 150 mission hospitals were sending me data on their work every month and we eventually expanded that enormously because we got data from I think from 800 third world hospitals, and it was on that I based my next sphere of epidemiology as it was.

MB I'm just going to bring you back to London initially, Denis, because in '66 you come back and you set up office in London.

DB Yes the MRC gave me a unit...and they were... in those days the MRC tended to work on the basis of choosing a fellow they thought they could trust and then letting him get on with his work, never interfering, never asking any questions. They never asked me what I was doing, they never told me what to do and they gave me what I wanted, which wasn't very much, in the way of travel grants, and it worked like a charm because to be just given a free hand. I had a sort of senior secretary or personal assistant; I had a typist then for a time, I had a part-time statistician and geographer, but that's all we were. But it was great fun.

MB But you became a nucleus collecting information from all over the world about seven cancers.

DB Yes, then mostly from East Africa but then from all over the third world about what is now known as western diseases.

MB And that's another big story. Are we able to go into that now? Can we start and go into that story? I'd like to know about the start of that.

DB Well, it started... when I got back to England I had an office in Tottenham Court Road. I had two but I moved after about a year, and I was working then on the seven tumours. We were getting... hospitals from all over East Africa were sending us particulars on these tumours, so that we could work on the basis that we worked with on the lymphoma, with the help of Michael Hutt, who started cancer registries and gave free pathology everywhere. And the important thing was this: previously

geographical pathology was done by comparing country with country – Nigeria, Ghana, Kenya, Uganda. Now, there's something in that but there are also great fallacies, because that assumes that as soon as you go through the customs post your disease pattern changes – which it doesn't – and if you have a particular area of a thing being common or rare straddling a political boundary, part of it goes into one cancer registry part of it goes into another, it's totally lost. So what we did was to get information from every hospital in the country, not only those with histological diagnoses but on clinical grounds as well, because having worked in an up-country hospital I know that if the doctor has a common tumour, he doesn't send it for histology – it takes a long time to get a report back – and he can make a clinical diagnosis and get on with it. If a tumour is rare, he doesn't know what to do with it so he sends it for pathology. So there is a risk of all the rare things going to the pathologist and not the common things, and you can see how that skews the information. Or if something which is accessible like a skin tumour, that will go for histology, but something like an oesophageal cancer, which you can't miss because if a fellow can't swallow he's got oesophageal cancer in Africa, but that doesn't go to histology unless you have to do an oesphagoscopy and so on. So we did two things: we got information from every hospital in the country and plotted the distribution locally within the country, and we accepted good clinical evidence when we couldn't get histological evidence, although we tried to get histological evidence when we could. And we were able to show enormous changes in disease patterns within countries rather than between countries. So that is what I was working on when we got back to Africa on the seven tumours before I got on to the wider project.

MB Denis, there was a meeting with Hugh Trowell I think around this time.

DB Oh no, that was later. What happened at about this time was – actually, I was looking it up in my diary, it was late '67 – Richard Doll who had an office not far from mine – he's Sir Richard Doll now – well, he rang me up one morning and he said, 'Denis, I have a chap in my office who I think would interest you. He's written a couple of books which as a statistician I would have no difficulty tearing to pieces.' But he said with great perception, 'I believe nevertheless that the guy might be right and I think you'd like to see him.' But that got me interested in this man Surgeon-

Captain T L Cleave, who was a retired naval officer. He'd written several books which he'd got published at his own expense because a publisher wouldn't take them. He was rather poo-pooed by the profession, poor chap. But what he was saying was that many of the common diseases in post-industrialised western countries are rare throughout the third world, were rare even in England or New York until about the First World War, are equally common in black and white Americans, and therefore must be due not to our skin colour or our genes, but to the way we live. Now, this made an enormous amount of sense to me because I knew from my experience in Africa that he was perfectly right saying this. But the profession wouldn't listen to him. He had a certain amount of evidence which they would call anecdotal, but I suppose was, thank God, the only person perhaps then in the world who could really test Cleave's hypothesis, because I was getting these reports on cancer from over 150 hospitals every month and I was able to ask them all: 'Do you see gallstones, appendicitis, diverticular disease, coronary heart disease, you know, what have you?' And I was also able, as I mentioned to you earlier this morning, I had a friend in America, Ray Knighton, who had set up one of the biggest giving organisations to third world hospitals in the whole of America. He had hit on the idea that any drug firm or instrument firm is always going to make more of something than they want. They have to have spare stuff and they throw it away, but if they throw it away, it's a dead loss, but if they give it away to a registered charity they claim income tax off it. And so this fellow set up warehouses and he said he would accept gifts from the drug firms; they would have to deliver them and everything but he'd give them a receipt to say they had given them and they could get tax off them, and they gave millions of dollars worth of free drugs to mission hospitals, irrespective of denomination, around the world. And I hit on the idea that if people are getting presents of a thousand dollars worth of free equipment from someone like Ray Knighton and the medical assistance programme, and you enclose a little pro forma and you'd say could you answer these ten, fifteen questions, almost certainly they'd be answered because after all the chap's given them a huge gift, whereas if you just write out of the blue and they've never heard of you, it will go in a wastepaper basket. So through Ray Knighton's help and also through my enormous contact with missionaries and missionary societies round the world, we were able to get replies from something near to a thousand different hospitals. Now, if they all say that in a third world situation

there's no coronary heart disease, there's no gallstones, there's no hiatus hernia, there's no this and that, then although it's anecdotal evidence people will listen. And I can remember well being asked to present my information to a meeting of the Royal Society of Medicine in London, and I was giving cancer figures from different parts of Africa on a ratio basis: here is 2 per cent of all cancer of the oesophagus, here is 50 per cent and so on. And somebody got up in the audience and they said, 'We don't accept you work at all, you're only giving ratio figures, you're not giving rate figures,' which of course I didn't have and you couldn't get them. And I didn't know that Sir Richard was in the audience, but Sir Richard turned to the chap and said, 'Can you give me any instance where somebody has published ratio figures which have been significantly altered when rate figures became available?' And the chap sat down, and I've always been grateful to Richard for that encouragement in those days, you see.

MB Yes. And what patterns began to emerge that really impressed you, because for the rest of your career you have really pursued this field of research more than any other?

DB Now, let me emphasis this. Other people deserve the credit and they had said before me that certain diseases which would fill the hospital beds in this country are rare throughout the third world. Now, Hugh Trowell had said that in a book he published in 1960<sup>3</sup> and it hardly sold a dozen copies. It wasn't referenced in any article of English literature. I think it got destroyed by damp or something, but it was totally unknown. But looking back it was an epoch making book – we'll talk later. I met up with Hugh Trowell again...

MB This was the meeting I got to, too early.

DB We worked together for years and years, we co-edited three books together, many scientific papers, and I think that observation of his, which was also made by T L Cleave. We went back in a... although Cleave only mentioned perhaps 12 or 15 tumours, conditions, Trowell mentioned over thirty, but they both came in unknown to

<sup>&</sup>lt;sup>3</sup> Trowell, H C., 1960. *Non-Infective Disease in Africa*. London: Edward Arnold.

each other towards the same thing. Looking back on this story, many workers have had a vision of this, independent of each other and they were all like little streams running together to make a huge river, which is the whole concept of western diseases now, which according to Thomas McKeown, the former professor of epidemiology and vice-chancellor of Birmingham University, a very highly respected man, he says that the biggest advance in medicine in the last century was the observation that infectious disease, then the major cause of death and disability, was due to environmental factors which could be controlled, and so they were. The conquest of infectious diseases had nothing to do with therapy, it was a question of clean water, clean sewage disposal and so on. Now, he says that probably the biggest advance in medicine in this century is the recognition that the chronic non-infective diseases are also due to factors in the environment that can be controlled. And this is gradually becoming generally accepted now. I mean this is far more important than the high technology medicine, which is brilliant but is not so important taking the population as a whole.

MB This environmental note, Denis, brings us to the end of this particular recording session. Many thanks for all your guidance through Africa and this new interest.