

**Sir David Weatherall FRS in interview with Sir Gordon Wolstenholme
Oxford, 10 November, 1986**

GW David, from my point of view, you're still a young man, and you've already been an occupant of this Nuffield Clinical Chair at Oxford¹ - very distinguished Chair - for a dozen years or so. And you've established a world reputation in regard to genetic factors in disease. What age were you when all this began? When did you first think of entering into a medical career?

DW Oh, I think, for some bizarre reason, probably about the age of five, as soon as I decided not to be a plumber, I think! I've no idea why, but I don't remember doing anything, wanting to do anything else, really, over the years.

GW Was there any model figure? Local doctor or something?

DW No. No, nobody in the family. My father was an industrial chemist in Liverpool, and I spent quite a lot of my childhood pottering around the lab, but there were no medical people in the family.

GW His lab, in the...

DW Yes.

GW So there was a chemical sort of element to your early days?

DW Well, a bit of chemistry, yes. I think my father's first love was music, actually, and he'd arranged his laboratory to be near the parish church in Liverpool, so he could spend about fifty per cent of his time on the organ, and fifty per cent in the lab!

GW You've inherited some of that, haven't you? I think the music...

DW Oh yes.

GW Are you, yourself, a player?

DW I'm a kind of... I play the piano in the bath, as it were. I mean, I wouldn't like anybody else to listen, but I get tremendous pleasure out of it, yes.

GW And then your school, did your school offer you opportunities to go into medicine?

DW Yes, I went to a school called Calday [Grange] Grammar School, which was a very good old grammar school, outside Liverpool, on the Wirral. We suffered a little

¹ Sir David Weatherall was Nuffield Professor of Clinical Medicine from 1974 to October 1992.

bit because, of course, it was in the war, and the best of the kind of teachers were away, really, the younger teachers. Science was a little bit thin, but we had a biology department, with a rather stimulating chap who ran it. And certainly, a number of people did go from there to do medicine, yes.

GW So you weren't alone, you weren't a freak, so to speak!

DW Not... no, no, not in... No, I think, in fact, in my own kind of contemporary sixth form, at least about half a dozen of us did medicine.

GW And you went straight from there to Liverpool University?

DW Yes, I went to Liverpool. In those days, there was... I mean, nobody went from there to Oxbridge. There was a chance of staying on for an extra year to do the Oxbridge entrance, but I was terribly fed up with school by about seventeen, and went for an interview to Liverpool, which was a slightly bizarre interview! I mean, it just... the entire thing, actually, were the novels of Thomas Hardy, because I was fortunate enough to do English as well as the sciences, and the dean thought he knew something about Thomas Hardy, so we had an hour on Thomas Hardy, and then they let me in!

GW You had done some written papers, I presume, before that?

DW I'd just done the ordinary - whatever it was those days - higher school certificate, and got a local scholarship. That's right, yes.

GW Who was the dean at that time, do you remember?

DW No, I've forgotten. I've repressed his name, actually. I had a violent argument with him. I mean, I didn't think that I would be getting into Liverpool to do medicine.

GW He obviously thought you had some endurance, which they look for, I think, in these interviews.

DW Yes, maybe, yes.

GW Well, when you went into the Medical School, well, Liverpool was already beginning to be on the national... have a high profile, wasn't it.

DW Yes.

GW Where was Cyril Clarke in those days, when you were in the School? I mean, was he already a... I can't remember the dates. Now, you qualified in '55, so in the early fifties you were...

DW Yes. The chaps that I remember well from the Liverpool School, in the Pre-Clinical School, we had one teacher who probably had more of an impression on me than anybody since, and that was Sir Rod Gregory. He was professor of physiology. And he... it was just the excitement of listening to him lecture, because he used to lecture in a filthy white coat, and it was quite clear he'd come straight out of the research lab, and one had the feeling that this chap wasn't just talking about

physiology, he was making it happen. And then in the Clinical School, I think the chap who impressed me most, initially anyway, was Harry Sheehan, who was the professor of pathology, who used to kind of lecture on pathology, with his kind of pipe dripping into the kind of corpses, and was a very amusing character, but a superb teacher. Cyril, actually, Cyril Clarke was... we didn't know much about Cyril, because when I was a medical student, Cyril hadn't made any kind of academic impact. I mean, he was doing... he had a big private practice, he looked after asthmatics, with his wife, in her odd bizarre kind of highly idiosyncratic clinic in Liverpool, and it was just when I was... I did locums as a student, and realised that he was an interesting chap, and managed to get his house job. And it was just that time, I think, when, because of his interest in butterflies and butterfly genetics, he'd taken an interest in some of the work of Ian (?) at the Hammersmith, on blood groups and disease. And I seem to remember, when I was doing his first house jobs, they were just thinking about looking at the blood group/duodenal ulcer relationship. So I think that's what started Cyril off, actually. It was about mid-fifties. It's an amazing story because, I mean, he'd never done any research before that, and I don't think had any pretensions to being an academic clinician.

GW No. I think, in many ways, he doesn't claim to be one now, although he's made such extraordinary contributions.

DW Yes. He's the kind of archetypal talented amateur. I don't think he would feel badly if he heard me say that.

GW Was your own interest in genetics awakened by that, or had it arisen separately?

DW No, no. We had no... I mean, I don't think we even heard the word 'genetics' in the clinical course in Liverpool. I mean, thinking back, I mean, the Watson/Crick model for DNA was published in '53, when I was half way through the clinical course. I don't think anybody mentioned it. And, no, what happened, I did his house jobs, and thought that genetics might be quite interesting. And then I did an extra year after the house jobs, and did the MRCP, and then I had to do my military service. And, being a kind of nervous chap, I didn't want to go abroad, so I made big efforts to stay in the UK, so they sent me to Singapore. And it was actually in the first... because I had the membership, they put me in charge of the children's ward in Singapore Military Hospital for a year. And quite early on, we had a child, a Ghurka baby, who had been the rounds of all the military hospitals in Malaya and Singapore, with a refractory anaemia, and it just... I got interested in this baby, and it turned out that there was a chap called Frank Vella working in the Biochemistry Department in the University, and I used to go down there once a week to do rounds, and was chatting to him about this, and he was interested in the haemoglobin disorders in South-East Asia, just getting started. So we worked at this baby, and discovered that it had thalassaemia, and we wrote a little paper on this for the *BMJ*, because nobody really realised that that disease occurred outside the Mediterranean at that time. And I got into great trouble over that paper, because I didn't clear it with the War Office. Apparently, you're supposed to get the War Office involved in anything published from military hospitals. I nearly got court martialled over that! But that was what stimulated the interest, really.

GW Yes, yes. And when you came out of your military service, you got a research fellowship to Johns Hopkins?

DW Yes.

GW And, if I may just jump ahead a little, I mean, after coming back to Liverpool for a time, you again went to Johns Hopkins.

DW Yes.

GW It occupied a... it must have been a very substantial formative experience?

DW Oh, it was enormously important to me, yes. I went out there straight from the Army, really, which was a bit of a culture shock, and went to work with Victor McKusick for a while, and learnt a bit of genetics. And then it became obvious that my research interests were really in genetic blood diseases. So I switched from Victor to a chap called Lockard Conley, who is head of haematology at Hopkins - not really a very well known character over here, but a very fine haematologist, and a remarkable man, really. And I spent a year with him and started some research on the very simple kind of characterisation of some of the genetic anaemias and thalassaemias in the Baltimore Negro population. And then the fellowship came to an end, and I went back to Liverpool as a locum senior registrar for a year, but the Hopkins people wrote and offered me a kind of faculty post, as soon as I got back to Liverpool. And everybody in Liverpool, except Cyril, said, 'You'd be crazy to go back. You'll ruin your career. You'll get off the standard British career ladder,' usual stuff! And Cyril wasn't kind of given to career advice, just said, 'Well, if you want to go, go.' So I went. And I spent two more years back there, and that's when we really got some serious research started. If I hadn't really had the time and facilities that the Americans offered at that critical time and had spent it in a more conventional kind of British training programme, I don't think I'd ever really have got anything off the ground.

GW No. That's right. A very unusual story, isn't it, really, at that stage of your career. I mean, many people who achieve distinction, have some spell in the States.

DW Yes.

GW But yours was at such a formative stage.

DW Yes. And I'd realised, I think, by the early sixties, that this group of disorders was probably the one that was going to, perhaps, open up the opportunity for applying the techniques of molecular biology to clinical problems, and obviously one had to go to a place where one could get properly trained. So, although I was in the Haematology Department at Hopkins, I had a kind of... not a formal appointment, but a joint position in the Biophysics Department, there with an extraordinary man called Howard Dintzis, who, I think, was probably the cleverest man I've ever worked with. And there, there were people who talked protein chemistry and talked protein synthesis, and you could kind of try your crude ideas out on. And that environment was invaluable, actually.

GW This was very much a research job, was it? I mean, did you have any tie up with the Paediatric Department; Wilkins, I presume, at that time?

DW Yes. Well, the research fellows at Hopkins were given a lot of time for research, but they also... that's one of the good things about Conley, because he was a superb clinician as well, and he insisted that, for several months of the year, we actually did clinical work, and we did our clinics right through the whole time. And for two or three months of the year, we did consultations on the wards in blood diseases and read all the marrows for the hospital. So, as well as getting a research training, there was... you got a bit of clinical experience as well. Again, it was rather unique. It would have been very difficult, I think, in the UK, to have got that kind of mix, and being given that amount of free time. I mean, the problems we were tackling then were difficult, and needed time, and I don't think I could have got that at... I mean, one might now, occasionally, in the UK, but even then, we are so rigid about our training, and young men mustn't, you know, deviate from the standard path too much. So I was very lucky.

GW I think that Johns Hopkins, of course, had extraordinary individuals. Did you meet Kurt Richter at all there? I mean, a real natural scientist of a man, whose horizons were limitless.

DW No, I didn't. The... I think the... it was an interesting School, perhaps a little bit inward looking at the time, perhaps past its greatest. The professor of medicine, [A McGehee] 'Mac' Harvey, was an interesting man. He, of course, had been a good clinical scientist himself, and had done an enormous amount in the kind of early days in the lupus field. Victor McKusick was extraordinary. I mean, in a sense, a bit like Cyril Clarke. I mean, a chap who started out as a cardiologist, was one of the kind of first people in phonocardiography. In fact, when I got there, he was still half cardiologist/half geneticist, and then moved from cardiology, through the inherited connective tissue disorders, into genetics. And again, a tremendous breadth. Now, in the basic sciences there, I saw something of the Biophysics Department, and a little bit of Lehninger, which is another extraordinary man. And a little bit of (?). I didn't really get much time in the Genetics Department there. But it was really this very stimulating group of young people in Biophysics. And then I met up, in my last year at Hopkins, with a young English protein chemist, called John Clegg, who has been my kind of research partner ever since, kind of Gilbert and Sullivan act! He... that was another interesting chance event, really, because John is a fairly forthright character, and he had done his PhD with Fred Sanger in Cambridge, and gone out to do a post-doc on the west coast with Hans Neurath at Seattle. And Neurath was a brilliant chemist, but he ran his department in a fairly rigorous Teutonic style.

GW Teutonic style.

DW This wasn't John, and he was not going to appear at eight o'clock in the morning for a journal club three days a week. So, after three months, he got a note on his desk from Neurath, saying he was disrupting the department, and he had to go. So he made his way to Johns Hopkins, because there was an Irishman there, Mike Norton, who'd also been with Fred Sanger, in Dintzis's lab, and John arrived at Hopkins, and we were both working on extremely difficult problems, actually. He was trying to pulse label insulin, that he'd learn how the insulin molecules kind of assembled, and I was trying to do the same with haemoglobin, and we used to talk over tea. And I couldn't get the two halves of the haemoglobin molecule separated, and John couldn't get insulin pulse labelled. So he said, 'Let's try a technique I've been using for my thesis in Cambridge.' So he was able to get the chain separated, and I was able to get

the kind of label, labelling of haemoglobin. So the two fell together. So when we wrote our first paper together, in the *Journal of Molecular Biology*², John, unbeknown to me, insisted on putting a little piece in at the end, thanking Hans Neurath, without whose help this work would never have been done! I don't think Neurath was amused by that.

GW Was it through John that... did you have steady contact with people like Max Perutz and so on, at Cambridge?

DW Yes. When, in '66, when we both came back, John went back to Cambridge, and worked, I think, for a couple of years there. And I went back to Liverpool. And the... we'd kept quite a good contact with the Laboratory for Molecular Biology, and we got to know Perutz around about that time, and Fred Sanger to some degree. And then John, actually, worked on sequencing immunoglobulin molecules with César Milstein, who... they were just really working out the basic structure of the immunoglobulins, in the mid-sixties. And... but John had kept, really, very interested in the haemoglobin problem, and so we decided to team up together in the late sixties. And I think it was the Wellcome who really made that possible, by giving us the senior lectureship in protein chemistry for John, and we set up a small team in Liverpool. And that was the time when Cyril Clarke had got the money for the Nuffield Institute in Liverpool. And so we had a small floor, or part of a floor of that, so we were able to start to build up some kind of research team in the late sixties.

GW When you came back from Johns Hopkins, you had no difficulty in getting a lectureship at Liverpool, and consultant...?

DW It wasn't all that easy, actually. I came back, and they had a lectureship, which I applied for from the States, and got, and then dashed back to Liverpool to take it on. I think it was... I was in that for a few years actually, and there was some difficulties about knowing whether to stay in Liverpool at the time. I think there are two or three people who suggested moving to London. I think John Dacie was very persuasive. The Hammersmith was very exciting in the late sixties, early... well, it still is, but, I mean, haematology at the Hammersmith was very exciting, it was the kind of era of John Dacie at his peak. And David Mollin had just left to go to Bart's as professor of haematology, and I think John thought I might take his place, which was very tempting, really. And then, even Sheila Sherlock had a kind of brief wooing, because they had a readership at the Royal Free, around that time. But I was very fond of Liverpool, and the... I think some kind of senior lectureship and consultant post was kind of put together in the latter half of the sixties, which meant one... well, one has to have that, really, to have the stability to raise money, basically, and so I stayed on, yes.

GW But was there a professor of haematology then?

DW No. There wasn't any haematology. So I started to build up a Haematology Department in Liverpool, when I got back, which was very tough, actually, because it was... I guess just at the time when people were starting to do serious things about leukaemia treatment, and although it wasn't my major research interest at all, I mean, one felt duty bound to try to set up some kind of clinical programme in Liverpool. And

² Clegg, J.B., Naughton, M.A., and Weatherall, D.J. (1966) *J.Mol. Biol.*, **19**, 91.

so I got a... well, a curious kind of arrangement. I shared the tropical ward in the Royal Infirmary with Herbert Gilles, because there wasn't much in-patient tropical medicine in Liverpool, so I took it over eventually. And we had about twelve beds, and rapidly became full of very difficult malignant haematology. And the problem was, I was the only consultant, and didn't have much... any back-up, really, no senior registrar-like figure really, just eventually some kind of pre-registration houseman, and a share in a senior house officer. It was a very difficult few years that, because I was trying to build up the lab programme, and at the same time, getting more and more of these kind of very sick people to look after, because Manchester had rather declined after Martin Israels and Wilkinson, and so a lot of the stuff came down the other end of East Lancashire.

GW Yes. That happened in several places. I mean, I was with Rigby and so on, and again, the whole thing totally collapsed and disappeared.

DW That's right. So we got a fairly enormous kind of practice, and I think, in retrospect, I mean, it was probably the toughest time of my life, because the research was going better and better at that time, and one had this enormous clinical load, without any help. So ridiculous things would happen. I mean, you'd try and go away on a couple of weeks' holiday, and you'd be on the telephone all the holiday. So that... I mean, I don't think it was anybody's fault, really, I don't think anybody had anticipated that the load would grow at that rate. But it was round about the early seventies when I was in the midst of all this, when this rather bizarre phone call came from Oxford.

GW Well, I think most of us weren't surprised. But just before you leave Liverpool, amongst this clinical load, there would be a fair number of cases of... valuable for your research, were there not?

DW Well, there were, yes. But I think...well, I realised first... in the States, actually, because I was interested in, particularly in thalassaemia, because I always thought that held the key to understanding of normal gene action. When I got to Baltimore, much to my horror, I discovered that there were no thalassaemics. So I think I really learnt that one had to collaborate with people afar, if one was going to do this kind of work. In fact, most of the early work on protein synthesis I did by going up to New York in the morning, and taking blood from the enormous number of thalassaemics in New York, and incubating the blood cells with radioactive amino acids and then coming back on the train to Baltimore, and working them up in the evening. And, I mean, I was carrying this enormous kind of wad of highly radioactive material up and down the east coast on the train. I shudder to think what would have happened if there'd been a train crash! But, so we learnt, very early on, to collaborate. And we developed some excellent collaborations in the late sixties. I did a WHO trip for... to really look at the problems of genetic anaemia in India and Pakistan, and throughout South-East Asia, and built up a lot of contacts, particularly in Thailand.

GW That was in the late sixties?

DW Yes. So although we had patients in Liverpool, we... the bulk of our material came from overseas collaboration, and we were able to do, I think, some of our most interesting work, in collaboration with the Thais and people in Singapore.

GW And does that still continue?

DW Oh yes, very much so, yes.

GW The difference between New York and Baltimore was an ethnic settlement?

DW Yes, it's interesting. It was... I mean, there were very few Greeks in Baltimore, but there were Italians, but mainly from Central Italy and the north. And the genetic anaemias, the thalassaemias, particularly, are rather restricted in Italy, they're particularly common in the south and in Sicily, and then up in the north in the Po Valley. But central Italy, there was much less. So, for some odd reason, I think the kind of ...it must have been a kind of ethnic clustering, if you like, in the States ... enormous numbers of patients in... mainly attending Cornell, but very few in Baltimore. Some in Washington. I mean, I used to go down to Washington as well.

GW Yes, some evidence of the fact that Italy, until recent years, didn't move at all, did it. I mean, it stayed... the south was the south.

DW Oh, very much so. And the south is the south in North America as well, yes.

GW And then the invitation to Oxford. This must have been really exciting, and what kind of an offer was it?

DW Well, probably a typical Oxford offer, really. There was a... there was a visitation from somebody to ask if there was any interest, and a suggestion I sent the CV in. And then not much happened. And then I was invited down to meet Richard Doll, and - I'm not sure whether I should give you the Oxford secret! Well, why not! We had a rather bizarre dinner at Jim Holt's, in which I was obviously being assessed by a number of the electors. I seem to remember John Ledingham and John Badenoch, and a couple of others. And poor old Jim's wife was kind of feeding us, and then was obviously told to get out, and we talked and that's all that happened. And then I went back to Liverpool, and I wasn't taking it too seriously, quite honestly, because I didn't know what was going on. And then the phone rang one afternoon, and a voice said, 'The electors met this morning and would like to offer you the Nuffield Chair. Would you let us know by tomorrow.' And then I realised I had to take this seriously! So I had a chat with my wife, and the research group, and the general consensus was that maybe we should go. So I wrote back and said, 'Yes,' with one or two kind of constraints to space and that.

GW And taking some of your people with you?

DW Yes, yes. But not many, actually. And everything seemed to be all right. But it was a very early appointment. I mean, I think they made the appointment in early '73, or mid '73. I think [Paul] Beeson had wanted his successor to be in early to do some of the planning for the new hospital. But nothing happened then, for ages. And it was about six months before I was due to leave Liverpool, I'd heard nothing from Oxford, so I thought I'd better do it right, because I'd never formally resigned, and I thought I'd better write to the Vice-Chancellor in Liverpool. So I rang up Oxford and said I thought they had appointed me Nuffield Professor last year, but I'd heard nothing, and

was it still on, as it were? And I rang up the Chest, and a rather kind of snooty voice said, 'Oh, just a minute.' And I heard some muttering and rustling of papers, and then this voice came back and said, 'Well, it was in *The Times*, wasn't it? What more do you want?' And, you know, there's no answer to that, really! But I never had anything on paper. I mean, never any contract or... I just went and... and they started paying me after a while, so I assumed that it wasn't all a great mistake! And, yes, we moved down in '75.

GW It was a very big responsibility to take, wasn't it. I mean, you're taking other people, moving house, new life for your wife.

DW Yes. I mean, a totally different world, really. I think I did, in retrospect, probably take it... well, I've never taken... now, this sounds very trite, I've never actually taken movements, career movements, too seriously. I think that's probably one of the good things I learnt off Cyril Clarke early on. I didn't go into it very carefully, I just thought I liked Oxford, and knew the science was good here, and knew the Clinical School was lively. I don't think, unless you're an Oxford graduate, you quite realised what you were taking on, because one's got this unique interaction, really, of the kind of... a rather over-heated, over-charged Clinical School with a... a... again, a very curious situation, where a very fine, now, Clinical School was grafted almost into a country hospital, really, with the Radcliffe. So enormous problems at that time. And then, of course, an ancient university, who are still, or certainly ten or fifteen years ago, I think, were still looking on science with a bit of suspicion. And then, of course, to add to that, the complexity of the college system.

GW You're in Magdalen, aren't you?

DW Yes. And I must confess, when I first went to Magdalen, I found it extremely difficult. I think it's easier if you've been an undergraduate here. And it was a bit stuffy those days. It's a very delightful college now, although I get very little time there. So you were plunged into a very bizarre world, and also a world where the... we were moving into the new teaching hospital and there were a lot of problems there. So I really didn't know what I was getting myself into.

GW How has been the balance between clinical, teaching and research?

DW Well, I... one of the first things that happened when I got to Oxford, I think I may have known this, but it was nice to have it confirmed. I think one of the people who was most helpful to me, initially, was George Pickering. He got me down, before I arrived, and gave me a kind of tea at Pembroke. Tea with George then, he was writing that book on... called *Creative Malady*,³ at the time. His thesis was that a lot of great men, like Darwin, and himself, had escaped into illness to get away from the world and do something interesting, was the basic thesis, which was, I think, okay for Darwin and Florence Nightingale, I think when it got to...

GW (??) I think, wasn't it?

³ Pickering, G.W., 1974. *Creative Malady: illness in the lives and minds of Charles Darwin...* London: Allen & Unwin..

DW That's right, and Sigmund Freud. It may have been a little bit pushed. So he was in the middle of that, and I got a lot of that. But I also got an incredibly scurrilous history of the Oxford Clinical School. So I was in no doubts as to that it was a place with, certainly, an exciting past. And then he told me that the thing to do when I got here, was to do nothing about the teaching or the clinical work for six months, and get the research set up, because if I didn't, I never would. And it was very good advice.

GW Very. Typical George.

DW Yes. I mean... I mean, right from the beginning, I made some afternoons a week absolutely sacrosanct, there were going to be no committees or appointments or anything, and got some of the Liverpool team down. We had no space, really. And got one of my other very good Liverpool graduates back from Seattle, Bill Wood. So we formed a core of a team. And we were very fortunate right about that time, because just before I left Liverpool, the MRC had seemed to like the work, and had given us a unit. And that was a tremendous help, because we could actually start to get some permanent scientific posts. It would have been very difficult, I think, employing scientists full-time in the clinical departments in Oxford, for a whole variety of reasons. So that went well. And then I gradually started to pick up the clinical side and the teaching, which was, I think, very good... and an incredibly talented collection of physicians in Oxford. I mean, talent always breeds kind of difficult characters and problems. But, by and large, the quality of clinical work and teaching was very, very high when I got here. The School was being expanded, which made problems, and there was the move to the new hospital, and a big bed shortage. Those were the difficulties. And then I realised, early on, that we had to get into that new hospital because the old Radcliffe was really hopeless in terms of outpatient facilities, academic facilities. And then there was a financial catastrophe in the NHS, and they said they weren't going to open it. So, together with one of the consultant haematologists, Alan Sharp, I had to form what was called 'the Central Oxford Hospital Working Party', and really tell the NHS how to get into that hospital. That was very hard work.

GW It was really a different number of beds, anyway, wasn't it?

DW Yes. So the research built up really quite well. And then in the new hospital, the clinical side, having such good physicians, was not too difficult. I hadn't realised, I think, previously, how much a place would look to the professor of medicine for kind of leadership on the NHS front as well. It's... I don't know if it's everywhere in the UK, but there had been a strong feeling, I think probably stemming from Pickering and Beeson, that, in that sense, the professor of medicine in Oxford, would act as a kind of American chairman. So one had to take on some of that. And so we settled down, really, in the new hospital, with tremendous difficulties on the service side. But, I mean, the good things about the place have been the extraordinary talent of the physicians, and the friendliness of the place, really. I mean, there've been no very difficult characters, and a Faculty Board that's remarkably friendly and constructive. Having a professor of surgery arriving at the same time, Peter Morris, was very good, because we became very good friends, and one didn't have the usual kind of fighting between medicine and surgery. And we've developed a joint immunology research programme, so I think the thing's been quite good.

GW And this is the outside impression. But Oxford, altogether, of course, is very much on the heights. And... but you've kept your contacts with the States too, haven't you? Have you not? I note contacts with Yale, Harvard.

DW Yes. Yes. Yes, for a variety of reasons. We've done collaborative research with Harvard Medical School, particularly with Boston Children's Hospital. But, yes, I've been over and done a number of visiting professorships. I think the most terrifying was probably the one at Harvard, at the Peter Brent Brigham; they have a week each year, when they have an outside chap who takes over from the chairman. And the current chairman, of course, is Gene [Eugene] Braunwald, a rather terrifying figure of American medicine! So I did that for a week. That's been very useful, I think, in trying to assess our own kind of level, and try and... further kind of training programmes, and house staff and students with our own. I did the same at Yale, I did the Bondy professorship, a couple of years back. And then at the research level, yeah, I need to go to America once or twice a year. I mean, there's a kind of liveliness and belief that anything is possible, which is quite important, coming from this country now.

GW I suppose that as molecular biology has entered more and more into the genetics of blood disorders, that America has strengthened its lead, really.

DW Oh, yes. Well, I say sadly, the... I don't know why they've been able to take it in their stride so much better than we have. Obviously, it's partly money. It's partly an attitude, I think. I think British clinical departments have always been rather, if not suspicious, certainly frightened of the basic sciences, and the American... I think the way the American clinical schools are set up, really, I mean, there isn't this strict divide between pre-clinical and clinical, and in some ways, I think that's made it much easier for the clinical departments to take all this in their stride. And then, of course, in the last few years, one's had this enormous Howard Hughes development, which has been specifically pushed towards immunology and molecular biology. And so it's not just in the blood diseases, I mean, in everything... it's ...

GW There is an advantage of scale. I mean, it's a continent, people know exactly where the main work is being done over a wide range, don't they. I'd always hoped that Europe might develop in this way, but it isn't, or, at least, it's terribly slow.

DW There are signs. I mean, the EMBO - the European Molecular Biology Organisation - I think, has been a success in some ways. I mean, it's brought molecular biology in Europe together. Sadly, EMBO has very little kind of clinical input. And there is... I think people are gradually getting off the ground in this country, but just at the time when people started to realise its importance, we hit the kind of cut-backs. So it was a very bad time to get going.

GW How do you see things going? I mean, it's so exciting at the moment, there's so much movement.

DW Yes.

GW But it's hard to hold back at all, isn't it, and look to the next ten years or so.

DW Yes. I think may be the... may be the case has been a bit overstated. I think that there are two areas that one might think about. One area is where is the field going, in relationship to the practical fallout, for clinical medicine? Well, I think we know where that's going in human genetics, clinical genetics. I mean, one is probably from the work in the thalassaemias, got a fair old idea now about the repertoire of things that can go wrong with genes. And it's turning out that the same things are going wrong with the genes in other genetic disorders, and one can use that information for very accurate diagnosis, for pre-natal detection of these diseases. And it looks to me as though, although there are very great difficulties at the moment, that one will come round to some form of gene replacement therapy, maybe limited to a small number of diseases for a very long time. And then if you take the broader view of the bigger clinical problems, it's looking very much as though the cancer field is bursting open in a number of directions, based on the use of molecular biological techniques. Hard to see, at the moment, where the practical fallout will be, except in the kind of rare familial cancers, but one could imagine being much more specific in terms of interfering with abnormally activated genes, once one knows what they're doing. I think one has to believe now that the oncogene business, if not causally related to cancer, in terms of a secondary event, may be critical in the kind of normal machinery of the cell. One already knows enough to say that, for the kind of pharmaceutical industry, in the broadest sense. I mean, it's extraordinary to think that, what, it's only about six years since the first human genes were isolated, and yet in the last three months, I mean, erythropoietin produced by a human gene, *in vitro*, has been used to treat patients with renal disease. I mean, that's pretty good going.

GW None of us remotely anticipated this speed.

DW No, no. That's right. And I think, of course, if you take an even broader view, because we have a particular interest, of course, in tropical disease and in the third world, that from the point of view of... well, I'd better be careful about malaria vaccines, since there's been a catastrophic failure, recently, with the first lot. But I think that, ultimately, it will lead the way to some important vaccines. But much more importantly, I mean, the effects on agriculture should be enormous, since we're all going to be starving, anyway, by the end of the century!

GW I was amused to see in the paper - was it yesterday - somebody has put the gene from fireflies into some plant, so that it now glows. A nice bit of trans-specific..!

DW Yes. So I think that agriculture is enormously exciting. I think, on the other hand, I've just been reviewing a book for *Nature*, on the kind of pastoral and ethical problems of some of these things, and I think everything has happened too fast for us.

GW Yes, we've tried, some of us, to make people look at the possibilities of these things, and be ethically, or morally, prepared for them. But still, we're overtaken by events. What do you think about the early diagnosis in the foetus, of the chorionic villus, of the genetic disorders? I mean, there are ethical problems there, of course for the parents mainly, but...

DW Yes. I think there's been a lot of confusion in the discussions, and it's not surprising, really, if you... I mean, modern, high-tech medicine was getting a very bad press two or three years ago, wasn't it. I mean, it was just the time when people were

getting a bit disillusioned with it, and looking for alternative medicine. And then suddenly the newspapers started to be filled with things like genetic engineering, and surrogacy, and test-tube babies. And I think the... it caused a mass reaction, which we've not see the end of. A lot of those procedures, the one you've just mentioned, I mean, early pre-natal diagnosis, even somatic gene therapy, are really not a new departure. I mean, we've been doing pre-natal diagnosis of... for Mongolism, for what, twenty years now. And they don't open any new moral questions. What does, of course, would open a completely new kind of question, would be the whole question of interfering with the fertilised egg, and doing a kind of... what's done in mice now, the transgenic experiment, where you would be putting in genes which would be expressed in future generations. Then one is kind of altering the genome of society. Whereas if I take one of your genes and replace it now, it's no different to having a blood transfusion, or a bone marrow graft. So those are serious problems, and I think some of the problems in reproductive physiology are what I... the thing that worries me, really, is how to develop a sensible debate in a society which is so miserably kind of educated in science.

GW Yes. I think this is a tremendous problem. I got involved myself, a few years ago, unexpectedly, in a big meeting in France, on the prevention of congenital abnormalities. And, of course, eventually coming only down to better education in human biology, which... and then when you look at it, there's incredibly little. Even in good schools, there's still incredibly little in the...

DW Yes. Yes, I took a fairly active interest in that with my own son, and discovered that the... certainly in a lot of the local schools, if the chaps are going to do a kind of non-science 'A' level, that's the last they ever hear of biology. And many of them don't even do the 'O' level biology. So that this idea that there's good all-round general scientific education in the sixth form, and in the universities for the non-scientists, is probably rubbish, actually.

GW Up in Maine, they started taking weekend courses for zoological teachers, and botany teachers, and giving them a sort of crash course in human biology, with a fantastic success. These people lapped it up, and got very, very excited. And that was quickly communicated to the next generation.

DW But there's something basically wrong, I mean, our media is very poor. I mean, I think the BBC do a good job, but, I mean, if you consider the average kind of news coverage, I mean, going over to the States and looking at the high quality east coast newspapers, of which there aren't many, but, I mean, the *New York Times*, *Washington Post*, are incredibly good on science. And yet *The Times* has a miserable few inches every day, and our serious weaker newspapers very rarely make...

GW Yes, it affects the whole attitude of our public doesn't it - our politicians, our government, everything.

DW That's right. That's right.

GW And just where it begins to turn the other way.

DW That's our biggest problem, I think, is education. I'm not absolutely sure what we do about that.

GW Are there any other problems that you would like to mention whilst we're talking?

DW You mean problems that I perceive for medicine?

GW Yes.

DW Yes, I do, actually. I think, in fact... of course, I think one always feels one's own generation is the generation with all the problems, and it may be a little bit middle-aged to kind of go out looking for them, but I think the biggest difficulty I foresee at the moment, is for British academic medicine, really. And it's not just one of money. There's no doubt that we have fallen behind. I mean, there's been a recent Royal Society and ABRC [Advisory Board for the Research Councils] surveys, but they were only in physics and in molecular genetics, but I'm sure if we did the same in high quality medical journals, we will find the same. It's partly time and money, but I think it goes back much deeper than that. I'm not absolutely sure that our whole kind of system of medical education, really, is not geared to what I would call modern kind of medicine. I think the idea that... well, first of all, in the clinical schools, and certainly in many universities, there's still an extraordinary division between the pre-clinical and clinical sciences, and certainly there is in Oxford. I think when the young men get beyond their kind of first few years qualification, they perceive a cutting back in academic future. Very few of them, therefore, have the courage to say, 'Well, I'm going to make an academic career, come what may.' Therefore, they feel, then, they've got to be trained as though they were going to be both, kind of academics and NHS consultants. Our colleges are now producing the most demanding training programmes on all these people, and what we're really trying to do is to have a totally uniform product at the end.

GW And that uniformity is at a level at which we don't want it replicated.

DW Well, I think so, yes. I mean, it is just crazy to expect a young man to be, who's going out to be a consultant in a district general hospital, perhaps, and a young man who wants an academic career and to push along, you know, some of the extraordinary advances in basic sciences, to have an identical training. But I hear, at the College, last week, people proudly saying, 'There's no difference between my lecturers and my senior registrars,' and that is a British attitude. That's where we fall behind with the Americans. The Americans are willing to look at a number of their young faculty people and say, 'Right, we will accept this man is never going to be... such a superbly rounded clinician as some of the people who do it full-time, but we're going to give him a flexible kind of training programme,' and that's what we lack. And I'm not even sure that our undergraduate programmes are geared up to the requirements of modern medicine. I was just... I was very depressed this year, after our final exams, and watching the MRCP exams in Oxford. I mean, we're still going round, you know, sticking stethoscopes on the short cases, and giving our kind of instant answers, and bringing out all our old kind of rarities. And I'm not absolutely sure that our final qualifying exams, or our MRCP examinations, have got any kind of relevance to modern medicine. I think that the... the kind of American Board System, with a much

more of an apprenticeship approach, and a much less kind of emphasis on these very formalised, stylised exams. I think a lot of our kids are training themselves to do examinations, not for the real world. It sounds a bit gloomy, but it was what I felt after the finals this year, anyway.

GW Well, I think we ought to be listening to you. And I'm very grateful to you, David, for submitting to this ordeal. I'm glad I asked you that last question. I think it's very important that more people realise how the comparison with the States and some other countries, isn't so favourable, and we really ought to do something about it.

DW I think we ought.

GW Thank you very much indeed.

DW It was very nice.