The Royal College of Physicians and Oxford Brookes University
Medical Sciences Video Archive
Biographical interview MSVA 037

Professor Dorothy Crowfoot Hodgkin OM FRS in interview with Max Blythe
(The second interview in a series of four)

Oxford, U.K. March 1988

MB Professor Hodgkin, in an earlier interview with Sir Gordon Wolstenholme you discussed your early life, undergraduate days in Oxford and the beginnings of a research career and arrived at the point where you went to Cambridge because opportunities there were much better for work in x-ray crystallography which you had chosen to pursue.

DH Yes, at Oxford we were just two of us, beginning almost together with very limited x-ray equipment and no experience and in Cambridge, again, the group was relatively young and recently set up, but at least they had had three of four years ahead of us. And Bernal who was the lecturer in crystallography had very wide interests and had begun to pass x-rays through crystals of all sorts of different materials, including very important biochemical molecules, the sterols. And his first photographs with x-rays, passed through crystals of vitamin D, calciferol and various other sterols, showed him that the formulae that the chemists had reached were almost certainly wrong. Now the observations depended upon the characteristics of x-rays, that they have wave character, that in passing over the electrons in atoms and crystals they generate new waves which interfere with one another, because in crystals the atoms are arranged in regular arrays repeated in three dimensions and the diffraction effects can formally be recombined to show the structure, just through the same physical effects as we operate when we see objects at a larger scale altogether. The problem is that the x-rays cannot be refocused by lenses in the same way that light waves can, but it is possible to calculate the waves that will be generated by a particular array of atoms and from this array of waves form the recombined electron density pattern. If one has got the calculations correct the experimental intensities will correspond to the calculated intensities and the atoms will look like balls of electron density, of different density depending upon their chemical character. Now Bernal had not gone as far as that with the sterols. He had been able to show from the diffraction patterns what was the actual size of the unit cell within which the molecules were arranged, and the size and dimensions suggested long thin molecules not corresponding in shape to those required by the then chemical formula. But, of course, the photographs that he got, which showed an array of diffracted spectra of varying intensity, held all the information on what the molecules actually were, how the atoms were arranged within the molecules. Only at that moment we hadn't really time to settle down to work them out, but we began to know how they could be worked out by introducing heavy atoms into the crystals, which should be easily found by a modified form of calculation from the spectra and then calculating the phase angles imposed by the heavy atoms.

MB These (heavy atoms)were the great markers.

DH These were either single heavy atoms or a variety that should form an isomorphous series within the crystals. The way we could find the heavy atoms to begin with was sometimes obvious, as in copper sulphate, which was the first crystal solved in this kind of way by Beavers and Lipson in Manchester, or by a calculation due to Patterson, and both of these methods evolved during the time I was at Cambridge in about1935. So this was a moment in which one could see that this was a way to go forward and to be sure what the sterols were or anything else that turned up. And because of Bernal's experience with the sterols and the fact that this made the chemists rethink their evidence and suggest the correct structure, while I was in Cambridge we were sent a very large number of different very interesting crystals, vitamin B12 for example and also the first protein crystals, of pepsin, which we were able to show would also give diffraction effects. I think I told this story before didn't I, that Bernal discovered that pepsin crystals if kept within their mothor liquor would remain perfectly crystalline with regular arrays of molecules within them and therefore capable of giving diffraction effects, which showed that the unit cells were very large and the molecules correspondingly very large, much larger....

MB Than had been predicted?

DH Not than had been predicted. It was known they were about that size from Svedberg's ultracentrifuge measurements. Everything came together. But when we looked then at the working out of the position of thousands of atoms in space it seemed far beyond us, so I put the problem of working on proteins to one side in the last few weeks I was in Cambridge and tried to tidy up some of the other areas of investigation and particularly to think how to go further in checking on the sterols when I went over to Oxford. And Bernal advised me 'The thing to do now is to choose just one of these very interesting problems and settle down to work on it seriously in Oxford. However, actually I was defeated because the same situation happened in Oxford as had happened in Cambridge. Many crystals came in and amongst them the most important and serious was insulin. I couldn't resist trying to grow crystals of insulin suitable for x-ray analysis and then to take x-ray photographs and try to find what the distances between the spectra showed about the size of the molecule of insulin. And the asymmetric unit had of the order of a thousand atoms within it, so I had to put it on one side from the point of view of a serious solution, but I thought I must go on to find out how to carry out this serious solution and so turned first to one of the sterols and got a heavy atom derivative, cholesteryl iodide, and with Harry Carlisle we were able to show by somewhat slow and painful calculations how the atoms were distributed in this molecule, which did of course correspond with the chemists, Veland and Vendisis's, revised formula, and also the stereochemical distribution of the atoms in the whole molecule, which was done by one of my first D.Phil students, Harry Carlisle, during the first years of the(1939-45) war.

At that time we were using rather simple methods. First we had to have a single crystal and mount this and take x-ray photographs of it, a full series that would show the spectra in three dimensions, and we took the photographs on special Eisenberg cameras and we measured all of the intensities of the x-ray reflections by eye. An eye is a very good measure of different intensity. Eyes are surprisingly accurate. It is all done by measuring reflections on the photograph against a standard set that we had made of corresponding reflections of which we knew the relative intensities. The whole method had been worked out by J.M. Robertson, who was by

then professor of chemistry in Glasgow. And once given all the intensities, we had to break the calculations up into small parts because we had no computing apparatus beyond a small adding machine and various ingenious devices such as strips containing the wave pattern corresponding to individual reflections to help in the calculation. Harry Carlisle did quite a lot of the sums required in the train going backwards and forwards between Oxford and a war job at Aylesbury

MB This was an enormous field of calculations. You did have so much to calculate to get the patterns.

DH But the structure came out quite nicely, as I say, through somewhat limited exploration of the three dimensional electron density, first of all projections of the atomic positions which were easier to calculate and then in cholesteryl iodide we explored the three dimensional electron density along lines perpendicular to our main projection. And so it slowly came out and emerged as expected. But by then I was anxious to try the method as a whole on something of which I didn't know the structure at all and by luck for me at that moment it became possible to work on penicillin.

The work on penicillin began in Oxford just before the war. Chain and Florey set out to explore antibiotic molecules occurring in nature and came upon Fleming's original observations and started attempting to isolate penicillin, which was clearly a very unstable molecule, for further investigation. The medical work ran ahead of the chemical work as might be expected and they had material which they thought pure enough to try out on patients, and in fact saved lives, before they had isolated really pure penicillin.

MB I think there was a very exciting day when you met Ernst Chain when some experiments had just been completed on mice, and he said penicillin would be coming your way?

DH Yes. This was just before they tried the first experiments on human beings. Ernst Chain I had known slightly in Cambridge. He came over to work with Florey at much the same time that I came back to Oxford and we met one morning in South Parks Road, with Ernst obviously in a very excited state because the night before they had shown that their most pure preparation was very highly biologically active. They had tried it on mice, four to whom they had given a haemolytic streptococcus and no penicillin and another four that they had given the same streptococcus plus penicillin, and the first lot all died while the second lot lived.(**1**)

MB All survivors.

DH Yes, all survivors. So they were sure they had found something useful and it was after this that they began the first experiments in the Radcliffe Infirmary at Oxford, which were very moving because they first tried it out naturally on individuals who were expected to die, mostly from blood poisoning. And in the first experiment on a Boars Hill policeman they found he was recovering and then ran out of the material, so they had to stop clinical experiments and collect a lot more penicillin.(**2**)

MB But that experiment was sufficiently prophetic to enthuse everyone. When did you first get crystals of penicillin to research, Dorothy?

DH Oh, that's much later. You see the material they were using at that time had been precipitated as a barium salt and while this was very attractive in theory to us and we tried to crystallise it, we got no crystals. They in the meantime naturally tried degradation experiments to see if they could find out how the atoms were put together in the molecule from chemical evidence, and we helped with these experiments because when they obtained crystals of the degradation products we took x-ray photographs of them and at least found their molecular weights. And this very often shortened the discovery of what they were, so that they fairly soon began to write a possible formula for penicillin. It was of course very good news, though I felt rather foolish about it when the news was brought back by Robinson from a visit to America that the chemists there at Squib Laboratories had obtained crystals of the sodium salt and I said to Edward Abraham, who was on the work on penicillin, "Do make me some sodium salt as soon as possible" and he said "Oh, we've got plenty of it, we keep it in a desiccator". So he brought his desiccator over and we took a little sodium salt on a slide and before our eyes it crystallised on the slide, picking up water of crystallization from the atmosphere. So, really, Oxford might have had it a long time back. But it was also fortunate because we discovered fairly soon, and I had indeed evidence before this from different degradation products, that the American chemists were not working on the same penicillin as the Oxford chemists. There was a difference in structure. The American chemists had started working with some, I believe, quite early on, but the main collaboration began after Florey and Hugh Cairns had been on the African front during the war and shown that penicillin was extremely useful in dealing with war wounds. This made the production of more of it important and Florey and Norman Heatley went over to America to persuade the big chemical firms there to take up the production because the war effort was already stretching English firms too far.

So Robinson brought a little of the American penicillin over and we could check that the crystals were not identical with the Oxford ones and that, in fact, the unit cell was probably smaller than that shown by the Oxford penicillin. So I asked for some more and Sir Henry Dale, who was a particular friend of some of the American chemists, went and got a small sample from Merck for me, ten milligrams, and this was sent over by air to him in the war in London and he sent it up to Oxford by hand by Kathleen Lonsdale. And Kathleen and I looked at it and the crystals were microcrystalline but they had sent a cable of directions on how to recrystallise it, emphasising that it had to be dissolved in a minimum of one solvent, with the second solvent added dropwise. So I took a little tube and weighed out three milligrams in the little tube and added one or two drops to dissolve this portion of the sodium salt and we left it standing in a little test tube rack, a hole in a cork as a matter of fact, as it was that sort of size, while we were talking about it. And then when we looked at it we could see the crystals growing, long and lath-like needles in the body of the fluid. So when they seemed to have ceased to grow I picked out one on a needle and took an x-ray photograph of it and it gave good diffraction patterns showing a quite manageable unit cell. And the following day we started collecting the three dimensional intensities. I also asked Abraham and Chain to make the other salts, the potassium and rubidium salts, so that I could have an isomorphous series to help with the phase determination and the calculation of the electron density in the crystals.

And in fact I got these a couple of months later. I think Edward(Abraham)made small samples and then got more, from which the actual data was collected, from ICI, who by that time were working on the isolation of penicillin themselves.

MB What date was that? About 1943?

DH Yes, 1943.

MB Penicillin then really was the centre of the work for a year or two....

DH And by that time the decision about the formula had become somewhat restricted by the organic chemists, with two formulae very much preferred by sort of rival interests. One, the oxacelone, in which the penicillin molecule had a thiazolidine ring attached to an oxacelone ring, and the other was a b-lactam in which the second group of atoms was differently arranged. And in the Oxford penicillin there was a further amide attached, in which the residue group was 2-pentenyl, which in the American penicillin was a benzyl group. And we worked wholly on the benzyl penicillins.

MB The three salts?

DH The three salts. From the sodium salt we collected the data first and then followed during that year with the remaining data. And in the spring of that year, just after we had got the first salts, there was a meeting at Oxford of x-ray crystallographers. It was really an interesting and extremely good meeting and we showed how far we had got with penicillin and of course everybody was extremely anxious to help us. And both Kathleen Lonsdale at the Royal Institution and Charles Bunn at ICI Northwich suggested we should use a device of W.L. Bragg's, an x-ray microscope to try to help in the solution. This was a device in which the diffraction of the atoms in the crystal was simulated optically by representing the atomic distribution by little repeated patterns of the proposed structure by holes in black paper that represented individual atoms, and this was photographed through what is known as the fly's eye, which was again a square distrtibution of pin holes to give the repeated pattern. Charles Bunn at ICI had carried the actual study of the patterns produced in this way further than anybody else and it so happened that where he worked was rather near to where my husband worked, so it became rather convenient to take the children in the vacation up to a farmhouse mid-way between them and go over and work with Charles Bunn at Northwich on the study of diffraction effects in relation to the proposed structure of penicillin. It was clear that the sodium salt would be the best structure to use for these experiments because the size of the unit cell was half that of the potassium and rubidium salts, so that only one model had to be printed out each time to get the model for the diffraction experiments. On the other hand, the other two potassium and rubidium salts were actually isomorphous and therefore exteremely attractive for the direct analysis and I had one research student then, Barbara Lowe, who had started by studying penicillin degradation products and now took up the analysis of the potassium and rubidium salts while, because we had too much to do in Oxford, I encouraged Charles Bunn on his own to carry on on the sodium salt. He was beginning to work on it after hours at ICI. It wasn't his formal work there, but luckily for him in the autumn when he began to take the structural analysis seriously, Lord Melchett passed through the laboratory and saw the penicillin

papers lying about and said "I'm so glad you're working on this". So then he was allowed to give it a job number and have an assistant working on it, Ann Turner-Jones, which speeded everything up, so that he, in fact, produced a trial electron density map of the sodium salt at about the same time that we produced a trial electron density map of the potassium and rubidium salts. And these were curiously different. They involved different errors and different ways of thinking about the structure and yet I had a feeling that they were both right if we could see what was wrong. And this is one of the first little pictures in the book...this one. This is the electron density map of the potassium and rubidium salts. I think it is the rubidium salt, in fact, but they are both very similar. And this is the one that Charles Bunn produced. And this one, as you might say, has no atoms attached to it because the only ones we knew were these which the rubidium had, these very heavy ones. This one had a postulated structure attached to it and the first thing about it was that the positions of the sodium atoms suggested in the proposed structure were nothing like the arrangement we saw and yet we absolutely knew that this part was correct. So we had to think what about these two structures was the same, and we picked up the fact that there was a little curled up object in one and another little curled up object in the other structure that were effectively the same and each involved one heavy peak which must be the sulphur in the penicillin, though here the electron density nicely corresponded to an aromatic ring on edge. Here it was very weak but there was at least some electron density that might correspond. So in both cases we then went on to take a new arrangement of the atoms that was the same in each molecule essentially as a guide and did maps in which we calculated phases just for this limited set of atoms. And in our case, looking at the potassium and rubidium salts, when we did this here is the aromatic ring beginning to come out, and a group in between which we thought we still could make the oxacelone ring. We added in atoms corresponding to this but they didn't come out corresponding at all. The phase relations carried them into quite different positions corresponding with the b-lactam structure. And the same sort of thing happened to Charles Bunn, so that by the beginning of the following year...

MB Which was 1944?

DH Actually, I must have got it a year wrong because it was 1945. We had both come to the conclusion that it was almost certainly the b-lactam structure. This is the sodium benzyl penicillin and rubidium penicillin compared. This is two dimensional, a map, a projection of atomic positions and we were building models to get a third dimension. But of course we can also calculate electron density in the other two dimensions, and because of the complexity of the crystal structure the individual atomic positions are not as clear in these other projections, but they are seen here in the potassium salt.

See now, this is a little bit of the crystal structure. The potassium ion is projecting there and there in this structure and this is the carboxyl group of the formula, connected with the iron. And these two atoms are also in contact with potassium ions or the yellow atoms, which are oxygen in this model are connected together. And you can see most clearly the force of the structure in this projection with the sulphur projecting here and the aromatic ring projecting there. And the amide group is very obvious with all the atoms separated in the other direction. They just fuse together and form a straight line here. And here again we get the sulphur atoms which should

project here if this model was correctly set at right angles onto this sulphur atom. So we could set it up in three dimensions from the projections. Now of course we had realised that a lot of our trouble was due to other particular positions of the heavy atoms which didn't give us the full phase pattern and the fact that it was simpler for us, with our very limited computing, to calculate just the projections rather than the three dimensional structure. But at this Oxford meeting a comrade who was a professional mathematician and computing person had suggested we should do our calculations in three dimensions and had offered to put the whole calculation on punched card machines. And so I got a grant from the MRC(Medical Research Council)to get the cards made, necessary for calculating the three dimensional phase series on a punched card machine.

MB So that was a massive step forward.

DH A massive step forward, but the structure came out before it was done and so we had to somehow make good this operation and show what was the power of the three-dimensional method. And by the time that Conway had the cards ready to calculate the three dimensional electron density series we had atomic positions in three dimensions close enough to calculate the near correct phase constants. So we got him to do this for the three-dimensional calculation and this particular photograph is of the model we set up in the three-dimensional calculation. The electron density is calculated at intervals through the body of the unit cell, in fact 0.3 of an Ångström interval in each of these dimensions. And we drew it out on sheets, and the calculation comes off in figures round which we draw circles at equal intervals of electron density. And when we put the sheets together we get this three-dimensional representation of the molecule and this is the first one we ever did. It is in the Museum of the History of Science and it is just held by these pillars, with the intervals grooved in them. And you just slip in one layer of plastic after another with the structure drawn on it. I must say I found it very exciting just showing W.L. Bragg how putting these sheets together you'd gradually build up this great molecule.

MB It is most remarkable, like a distant galaxy. Apart from it being intense science there is something quite beautiful about it. Artistically there is something quite satisfying about the whole process. Did you find that?

DH Yes, although the first model we made didn't cover even quite the whole of one molecule, as you can see, in the model making. We had it all, of course. It is, as I said, down in the History of Science Museum. The only thing I should say about it, which I again feel a certain guilt about, is that it is on the wrong hand. Natural penicillin is the mirror image of that representation there, and that was due to a certain casualness on my part. It was discovered, I mean our structure was plotted out before the correct hand was discovered crystallographically by J.N. Byfoot. But if I had stuck to the chemists' convention I would have been alright, but I was not really bothering about conventions. I just took them(the patterns) off the maps as they came off.

MB Dorothy, you complete this incredible challenge. You get a shape for this molecule, a three dimensional shape, by 1945, which is pretty good going.

DH The whole of the structure was determined and it was early in May that I went up to break it to Sir Robert Robinson that this was the structure.

MB This wasn't an easy task, was it?

DH No, he was very devoted to the other(structural interpretation)...

MB He was in the "other team"....

DH To the other view. He had himself thought of the thiazolidine oxacelone structure and he thought the b-lactam structure was very unlikely because penicillin was so unstable and most b-lactams were rather stable. And this is still something of a mystery, why it should be very unstable.

MB But you never did persuade him fully...

DH Well, I did persuade him in the sense that he wrote it in the book that this was the structure all right, but at the very end, when we were talking together a short time before his death he said "And really the positions of the atoms in space are very close to one another in these two molecules, aren't they?" And so they are in a sense, you see, as we had shown because we had placed them in this region in the lower ring, but they have moved remorselessly into the positions that made the structure b-lactam, but obviously could move back again in certain kinds of breakdowns. This little model is one that was made by Frank Welsh, our technician in the laboratory, and there isn't any one like it in the world. I've promised to give it to the Museum of the History of Science, but it will have to be left in my will because I find it too useful to keep it about to show at the moment.

MB Dorothy, just keeping up the momentum of our talk, given the time-span we have today, after penicillin was there an aftermath or did you move quickly on to another problem?

DH Moved quickly on. The whole of the penicillin research was published for everybody who had worked on the subject in this book.

MB In this volume?

DH This volume by Princeton University Press. I went over to the USA to talk about it in 1947. It was early in 1948 when I was back at home again that Lester Smith brought into the laboratory little red crystals which he had just got of vitamin B12, and they were very remarkable little crystals and nothing was known about their chemistry at all for certain.

MB So you had another great problem.

DH So I started while he was still visiting. He had come up for a Biochemical Society meeting to report on the progress on this antipernicious anaemia factor. I took the first x-ray photographs, one overnight, the other the next morning, and was able to give him a rough molecular weight of about 1,500, which was half what he thought it was, which was rather cheering, but a large molecule of 1500mw didn't seem

immediately practical to work on. However, a few weeks later I was rung up by Glaxo who had isolated the material to say "this vitamin has got cobalt in it. One atom per molecular weight. There's a heavy atom for you".

MB Terrific. What great news.

DH Yes, so that of course led to the beginning of serious work on that still larger molecule and a dropping of various other ploys that were going on.

MB And you went on and got increased support for this. It was a time when you built up your unit.

DH I could see that I really had to have at least one stable helper because I had up to then been living on chance comers, actually one very good post-doctoral fellow, Jack Dunnets, but he wanted to go off and have other experience, and of course, the Somerville line of Part II Chemistry (students) and perhaps D.Phils if they were good enough. And naturally they didn't stay for ever. Barbara Lowe, when she got her D.Phil, went to America on a postdoctoral fellowship and one knew that this was going to happen, so Dr Janet Vaughan, who had an earlier life that I didn't know anything about, working on vitamin B12 herself, on the anti-pernicious anaemia factor**(3)**, got a grant for me from the Nuffield Foundation to give me both access to the old punched card machine for computing and a very good, already experienced postdoctoral fellow, June Broomhead, from Cambridge. And gradually, as the project took many years, we accumulated other supporters.

MB It was a large team enterprise, taking a long time.

(***Due to a technical problem, filming continued from this point in black and white.***)

DH With B12 we realised that we had to go into three dimensions(from the start) and so we collected the three dimensional data, which June Broomhead did, and then sent it to Betty Gittas, who had calculated penicillin, to calculate on the same machine, the Pierce-Alpha, which was at that time at Liverpool where she had a computing job. So she did the three dimensional Patterson computation and from the three dimensional Patterson itself we were able to see quite a bit about the molecule. We were able to see that there was something like a planar group, with four or five membered rings attached to a central cobalt atom, and then on one side of it a cyanide group and on another side a trail of atoms which gradually over the years emerged from the mist looking like this.

If you'll hold this, I think you can see this part of the molecule is the chain coming out from the planar group, the planar group is lying this way on, and the aromatic ring, this one is that seen on edge, and there is a phosphate we can see up here...

MB The camera probably can't take that all in very well(*Professor Hodgkin has taken up a second model and placed it adjacent to the glass profile)*but possibly can take in that second model very well. It is in fact lined up with the structure we can see illustrated in the glass profile. So that gives us an idea and we can take a look at this separately, later.

DH And if we look at this small model, on a smaller scale altogether, we see the form of the planar group which is in that kind of direction.

MB I don't know whether the camera can quite see that. It can possibly make out the pattern against my shirt.

DH It is there that though we see there are four five-membered rings, they are not arranged exactly as in porphyrins which at first we thought, but in a new pattern of rings which we called the corrin ring system

MB Initially, you thought it might be a porphyrin ring structure?

DH Initially, we did our best to make the electron density map into a porphyrin, but some of the other objects I show show what happens if you do this. And it doesn't look as good as it does if you let it go the way it wants to go. This is one of the tests you always have. And this just illustrates the effectiveness of the calculation that we plot out in two dimensions and then stack together, one above the other, giving you the full three-dimensional arrangement with the right calculated intervals between the sheets. In fact, I'm afraid this is some arbitrary scale done to suit the thickness of the slides.

MB So that's the building up of them....although that's just three of them...

DH. Yes. If you want to go further back you look at the one on the side which shows at this time what we were given by the computing machines. I really want the other one first. The one with the red atoms.

Here's the cobalt in the middle, which we haven't bothered to draw all the contours out It is obviously extremely heavy as you can see. You can see that the figures which are the figures that come out of the computing of the punch card machine. All are the actual figures for the electron density according to the formula for any Fullerian series that you use. And we just draw circles round at equal intervals of electron density to map out the individual atoms. And the red in these maps is a stage of the calculations, the areas we knew at the time the calculations were done and put into the sum. And the grey areas are the ones that have come out as a consequence of our getting the phases of the atoms correct, so that we gradually repeat the calculation. We start first with just cobalt phases and what we think we can see round it.

MB So, you relate it all to the initial (cobalt) "anchor"?

DH Yes. I should point out at least that the figures seen here are rather beautifully printed out, if you can see them closely,. They are actually done by my nephew, Sebastian, as a job from school, during the vacations to earn some money. I used to make these children plot out the maps for me because it was necessary for scale.

MB Professor Hodgkin, we are rapidly running against the clock and in the three minutes remaining I don't want to lose anything you would like to (include)...

DH I'm going to finish the story. The other maps there, which haven't yet got their drawings of the atoms in much, were actually due to a very clever American who for

the first time made our then computing machine that we had in Oxford, the Mercury, print out the intervals.

MB That was a marvellous step forward.

DH A marvellous step forward.

MB What year would that be?

DH That must have occurred about 1960. And this is the model of a very wonderful molecule which is the real vitamin B12 in which there is attached to the central cobalt not a cyanide group but a deoxyadenosine. And this is known as the cofactor and was discovered by Professor Barker in California as a coenzyme involved in the growth of certain bacteria and is what is really involved in our growth too and is the real molecule present in liver and elsewhere, which is broken off when chemists use cyanide as a means of isolating it. I haven't the full three-dimensional model of that drawn out owing to the fact that crystallographers now tend to skip these stages because it is very easy, and just go for the centre of the atom and draw and calculate out the molecular dimensions.

MB Everything is so swift now. You really have been tracing the path of a very interesting science that has escalated in all its paces.

DH Well, while the B12 work started with the punched card machines that we'd used at the end of the penicillin work, it really got well away when electronic computers were introduced, at first very casually by an American crystallographer, Ken Trueblood, visiting Oxford and offering to put our calculations through on his experimental programmes because he had nothing large enough to test them on. So we provided the material and we had a very happy six months on that.

MB Professor Hodgkin, we'll take up the final story, on insulin, in another interview. It has been marvellous for me to hear of these developments today. Thank you.

DH Thank you. Of course, I can tell you a lot more.

Other interviews in the Royal College of Physicians and Oxford Brookes University Medical Sciences Videoarchive relating to this interview and referenced in the text:

(1) Interview MSVA 013, Dr Norman Heatley in interview with Max Blythe, 1987. **continued...**
(2) Interview MSVA 001, Professor Charles Fletcher in interview with Max Blythe, 1986.
(3) Interview MSVA 026, 1988, Dame Janet Vaughan in interview with Max Blythe1987.

(Transcript by Dr M Blythe, Oxford Brookes University)