

**Professor John Waterlow CMG FRCP FRS in interview with Dr Max Blythe  
Oxford, 9 June 1997, Part Two**

MB John, in our whirlwind efforts to get you to Jamaica and the start of the big metabolic work in Jamaica, we may have missed a critical step I think in the, in the later forties when you went to The Gambia. While you were working for Ben Platt he set up a unit in The Gambia. Perhaps you could tell us about the unit he set up, how that came about and then about how you became involved?

JW Yes, I should have said something about that before we get on to Jamaica. Platt had set up this unit after the war with the backing I think of Sir Edward Mellanby, at Fajara, which is near the capital Bathurst on the coast. And he had out-stations, I think more than one, in the interior where they did particularly crop research. And...

MB This was quite an investment, quite an MRC investment?

JW Oh yes, I think it was quite a big investment. Whether it, how far it was MRC and how far it was the Colonial Office I don't know, I think they worked very closely together. But there were buildings there in Fajara based on an old German rest-house for Lufthansa airways from before the war, and [in] other buildings wards were put up and labs, and living accommodation. It was quite a major enterprise.

MB And quite early on I think Ben Platt kind of suggested that you would go there, and this was of some real excitement to you, I mean given the dullness of the lab work?

JW Yes. I, this must have been somewhere around 1947 I suppose that he went out there to see how things were going on and getting them organised, telling me before he went that he wanted me to be his clinical assistant, looking after the wards. And I was delighted by this idea. When he came back he never said anything to me about it for several weeks and...

MB He just left you wondering what was happening?

JW Yes. I was, I was disappointed, disappointed, but never mind. And after a while he did arrange for me and my family to go out there, it must have been about '48, I'm very bad on dates...

MB 1948/49 I think that was...

JW Yes.

MB ...as far as I can trace John.

JW And we looked forward to that very much. And the work there, I was really under John Walters, who was in charge of the station, who was an ex-colonel of the Indian Medical Service, and he was the senior person doing all the clinical work. He was ... I was more, had a more decisive voice in the research side.

MB Right. But he was a well-tutored kind of tropical medicine figure, a lot of experience?

JW Oh yes, he was a great man for tropical medicine. A very, very nice man, absolutely sincere and honest. He was very helpful to me over the liver biopsies. He was very accustomed to exploring the liver with needles for ... for abscesses, and so he was quite happy with me doing all these biopsies. We even did some on chimpanzees and so on too, and...

MB You had a terrific collaboration with Walters?

JW We got on extraordinarily well and it continued after I came back to the UK many years later. And he was not only a very good doctor indeed, but a very decent, honest, upstanding man. So we were very happy there with him and his family.

MB And you spent close to a year there?

JW Yes.

MB With the, with the children?

JW A bit more than a year, I think. And the only problem was that there was nowhere to educate the children; my wife had to look after our own children, educating them. But it was a nice place, interesting place, and...

MB And you did critical work with the diver there?

JW Yes, there I started, and I... Yes, I, the first thing I tested in the diver was the enzyme pseudocholinesterase, which was rather sensitive to protein nutritional status, and that was interesting. I also did work with Walters on the pathology of the liver and the development of fibrosis of the liver which is extremely common in The Gambia, and we thought that it started perhaps with the fatty infiltration and so on. And that was all written up in an MRC special report series.<sup>1</sup>

MB This included kind of cirrhosis studies in a, in a large way?

JW Yes. So we had a, we had a fruitful time in The Gambia. I also used the first version of the quartz-fibre microbalance, which I had made to weigh biopsies.

MB Did you make that there, while you were there?

JW No, I made it in the UK.

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<sup>1</sup> JH Walters, JC Waterlow, *Fibrosis of the Liver in West African Children*, MRC Special Report No. 285, London:HMSO, 1954.

MB Oh right. And took it out with you?

JW And the incredible thing was that it went out by sea and it came back by sea and it was intact, it wasn't broken, although these fibres are very, very delicate. And that was amazing.

MB How were these balances made actually, John? Can you, can you just tell me?

JW Well, they're made, they're made of molten quartz pulled out.

MB That's it? Just pulled out?

JW Very ... I mean, you have a very hot flame and you pull it out as fast as you can and then you look at it under the microscope to see if it's the right size, and you go on pulling fibres until you've got one the right size.

MB So, the tension and the balance is established by, by this means?

JW Well, the tension... The way that the thing works is that there is a beam, a quartz beam fixed onto the fibre in the middle. When the, when the beam tilts, of course, the fibre is twisted and you (?) ... hence you bring it back with the dial to the original position, and that's... The problem was to seal the beam to the fibre. I did not succeed in doing that with any kind of a flame – the fibre would just fizzle up. But when I went to see my uncle – Bryan Matthews FRS, physiologist in Cambridge – and he said 'Why don't you use araldite?' which was the stuff which had recently been developed by de Bruyne<sup>2</sup> in Trinity for aeroplane work and was a marvellous glue. That solved the problem for me.

MB You couldn't buy, I think that was important(?), you couldn't buy balances like that in the shop?

JW No, you couldn't buy them, no, you couldn't buy them. Later, when I was in Jamaica, I made one for a friend of mine in New York and took it up to him. You couldn't ... no, they were not available.

MB John, I was going to ask about, one more thing about Platt. I think that when he came out there when you were there he was the one person who kind of set a slight tension in that unit that wasn't all that comfortable. And, you know, Platt wasn't in certain circumstances the most comfortable person to work with?

JW No, I think that's a good phrase. It wasn't, it wasn't comfortable. He after all had been in England, and it's very different from being in [England] and coming out for a couple of weeks or something, and working there and living there. On the other hand of course he felt that it was his place and he'd started it, but he sort of turned everything upside down, and didn't get on with John Walters, and it really became a rather miserable place to be. And so after about a year we came back. And when John had gone I didn't see what future there was.

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<sup>2</sup> Norman Adrian de Bruyne.

MB John Walters, I think his going had a little bit to do with that period of Platt's interference?

JW Oh yes, absolutely, I mean he...

MB He was a sad loss.

JW Platt accused him of various things, unjustly I think, and I mean he couldn't stay. He'd lost Platt's confidence, and there it was. And I left also. That left only McGregor, Ian McGregor, who was a young fellow who'd come, who'd just about come out. He was interested in malaria. He became acting director when the rest of us had gone, and eventually director.

MB And I think... If I can just trace that unit, because it had a long, it's had a long history and it's still going; and it's now run by Cambridge, I believe. Is it Cambridge University now?

JW Oh no, it's still the MRC.

MB It's still MRC?

JW It's still MRC and it's ... recently its director has left, come back to the London School [of Hygiene and Tropical Medicine], and his successor is the former professor of clinical tropical medicine at the London school. No, it's an out, the out-station which Platt had started in a place called Keneba always kept on doing nutrition work, even ... and was taken over by Roger Whitehead, who had been director of the new, the unit in Uganda when Roger was expelled by Idi Amin. When he came to Cambridge, he also took over this camp.

MB Right. That was the Cambridge link?

JW Yes, yes. That was the Cambridge link.

MB And Platt essentially lost that unit at some time though? He, he lost it?

JW He lost it after, I think after Walters and I left. Mellanby had retired and Himsworth<sup>3</sup> didn't get on with Platt and that was that...

MB So, that's how, that's how it came about, it was...

JW ...and I don't think he ever had anything more to do with it. Rather sad, rather sad. Anyway, we came back...

MB You had an accident on that return trip?

JW ...and we returned by car, shipped from Dacca to Casablanca, and then by road from, through Morocco to Spain, and in southern Spain we had a bad accident and all except my wife were injured. I had my leg crushed and my ankle crushed.

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<sup>3</sup> Sir Harold Himsworth.

And that has, although it worked very well for a large amount of, a long time, eventually it's caught up with me and now gives me quite a bit of trouble.

MB John, I'm not wanting to dwell on that tragedy because you did have a, have a bad time, a serious injury, but I think we ought to put on record that the service you received in Spain and the care you received in was quite, quite exemplary?

JW Yes, we were in hospital, in an old military hospital which was a square building with a tower at each corner, no lifts, circular staircase, so we had to be carried up and down on mens' shoulders. I, the operation on my ankle, which was putting a pin through the calcaneus in traction, was absolutely correct. The Spanish surgeons knew precisely what to do – of course they'd been well-trained in their civil war by Trueta<sup>4</sup> and others – but it was, the anaesthetic didn't work, very painful. And anyway, the Spanish authorities were ashamed at this accident which had been caused by two psychiatrists driving out of a lunatic asylum just in front of our car, and so they were very decent to us. Paid my wife – she wasn't injured – paid all her hotel expenses, came to see us, the Governor came to see us in hospital to apologise.

MB So, you were treated right royally?

JW We were, very royally. But of course it was very, the facilities were very primitive, which I didn't mind. In fact, I found it very interesting.

MB A fascinating time. John, when you came back, it wasn't long after you came back – we're really catching back with our story again – it wasn't long after that that you were propelled in the direction of that Brazil Conference, and then you went, on the way back, to Jamaica?

JW Yes, I...

MB And Tommy Taylor, that...

JW That's right. I went...

MB ...fateful meeting.

JW I went to Brazil in plaster up to above the thigh.

MB So you were still in plaster?

JW I was still in plaster up to above the thigh, which I was in for three months. And so I was a rather strange figure, I had a beard in those days, limping up to shake hands with the President of Brazil. But Tommy Taylor wasn't put off by this but agreed to the arrangement I've said, and so after about six months when I'd recovered from this accident we went out to Jamaica, and...

MB I was just going to ask you about Tommy Taylor if I may at this moment. He was, he had an impressive academic record and I just wondered, you know, how

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<sup>4</sup> Joseph Trueta.

you'd come across him to actually call in. And you spent some days with him on that, on that return journey. How did that link come about?

JW Well, I think it came about simply because I wrote to him as the principal of the university saying I wanted to come and look ... look at it

MB Have a look at the place, right.

JW I hadn't been there since it had been planned and he said 'Sure, come and stay with me.' He was that kind of man.

MB Yes, and it all took place. Let's take you there now, the family ... and you go there in '51, take residence in the university, in the university park?

JW In the university campus, which was nice houses, twenty or thirty of them, well laid-out.

MB This was the new campus at Mona?

JW The new campus at Mona. We had a garden to set up and so on, it was very agreeable. And I of course was fascinated by the countryside, the mountains.

MB You walked out there regularly?

JW I walked a lot. And there's, there's such a variety in the different parts of the island. The most beautiful place, particularly in those days before it was rather over-run with tourists.

MB Yes, it must have been very beautiful in '51.

JW And I did feel that this was the best way forward, that the problems of these third world countries were enormous, and it was really only by the people who ... came from there, we had to rely on them to solve these problems. We couldn't, you couldn't imagine there being enough expatriates and adequate training and so on to do these jobs. And I think that was the right view.

MB There's been an accusation occasionally voiced by people who say that at that time people who were second-rate in Britain and the first world went out there to take jobs in the third world because they couldn't make it here. That clearly wasn't the case in your story, but...

JW Well, it was, it was to some extent the case. I think, I think that did happen and some of the West Indians felt it was happening, whether truly or not.

MB I get an impression though, that looking at the medical side, that the actual exodus of doctors going to Mona and actually setting up that medical school, I get a ... looking at the list it was a very impressive record. And I just wanted to, it may have been weak on some wings in the academic field, but I didn't think medicine was short-changed out there by second-raters from here?

JW No, I think medicine was very good. Medicine was basically people...

MB I'm thinking of people like Cruickshank<sup>5</sup>, and a range of people who went out there?

JW Cruickshank, Bras(?) the pathologist from Indonesia and so on, they were really people who were pretty dedicated I think. This, this did apply to some extent perhaps to faculties like English and history and so on, but it was a passing phase.

MB John, just take me through that first few months you have there. What was the state of the university? I mean, had much building taken place? What was the state of play there? Was there a medical school on the campus by then?

JW Well, there was the beginnings of a medical school. The first buildings were the pre-clinical ones – anatomy and physiology – and those labs were just beginning to be set up, and physics and chemistry. The first, almost the first thing they had was the accommodation for people in houses and flats, and then the hospital was being built, so that when I went to...

MB That had just started, that had just started when you arrived?

JW Well, it had started but it hadn't, it wasn't finished. And so when I first went there there wasn't very much room in the physiology building – I can't even remember whether it was quite ready. So I worked in a wooden hut which was part of the old Gibraltar Camp, we were on that site, where there were a lot of these huts which had been built for prisoners of war. And for patients I used the Kingston Public Hospital, where of course I'd been before in 1949.

MB Just staying with the students on the campus though, John, you hadn't done much teaching before. This is early days teaching for you. We'd said when we talked about you applying for the professorship of physiology that that might have been a good job to avoid given the teaching experience you had. How did you find the teaching when you actually got led into it? I mean, was that good?

JW Oh yes, I enjoyed it enormously. The first year, and second year too I think, we had only between twelve and twenty students a year, and...

MB These were West Indian students?

JW These were West Indian, and I think there were one or two Americans but basically West Indian. And I was allotted, as the most junior person I was allotted those students who were considered to be weakest, about four of them. And I found this actually extremely stimulating, trying to figure out how to explain in the simplest and most effective way physiological principles. It did me a lot of good and they enjoyed it I think, and we became very friendly. We had a party every summer for all the students and so on, and I've never forgotten those early students of the early years.

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<sup>5</sup> Eric Kennedy Cruickshank.

MB Did any of those early students go on to be research students of yours, I'm wondering?

JW Yes, two of them did.

MB Two of them. They did PhDs with you?

JW Well, one of them ... Alleyne took a PhD with us. Yes, several of them, several of them.

MB Right. So, that was an exciting start.

JW Yes, it was a good start.

MB Some of these less, less impressive students did quite well in due course?

JW Very well.

MB John, bringing you back to that Kingston General Hospital now, what was the scene there? You were looking at babies again, you were still the kwashiorkor story...

JW More or less.

MB ...still following up the fate of the liver and protein metabolism?

JW Yes, that was it. Measuring various enzymes, liver biopsies, enzymes...

MB The diver still being...

JW ...the diver and the microbalance and so on, yes. And also I measured the nucleic acid content of these liver samples, in order to get...

MB That came very early, didn't it, looking at nucleic acids? I mean, that must have been very early?

JW That was in ... yes, that was the first year I was there. It was very early.

MB Because nucleic acids weren't as big on the map as they are today. I mean that was, that was...

JW No, but I was looking at them quantitatively, not qualitatively. I mean, the point being that the cell of course consists of a protein, a pool of protein surrounding a nucleus of nucleic acid, and in malnutrition the nucleus is not affected, the nucleic acid content doesn't fall whereas the protein of the cytoplasm does.

MB So you're looking at that ratio.

N/DNA (N over DNA)

JW So the liver DNA is a, gives you a measure of the degree of fullness or emptiness of nitrogen in the cell. And that is really the only measure of protein depletion which we have.

MB And you were very quickly beginning to demonstrate that, that it was protein that, all that had been said it was deficiency that you were looking at in a big way? That was the kwashiorkor base?

JW Yes, but the same would happen in marasmus too. I mean, it's also deprived of protein.

MB But more generally...

JW It didn't, it didn't really solve the question of what is the difference. The difference between the two is the presence or absence of oedema. That's the essential difference. And this didn't tell us the cause of the oedema. But I didn't solve any of this quickly because I had an awful lot of difficulty with the methodology of measuring DNA in these small samples. It wasn't a thing that anybody much was doing, and...

MB So, it was little by little, trial and error processing, working with the divers, getting some, getting some radioactive labelling in?

JW No, not at that time. No, not as early as that. But I think I was really one of the first to use this liver DNA as a measure of the protein ... deficiency or otherwise. McCance<sup>6</sup> later did, I think. N/DNA (ratio)

MB John, I just wanted to come to the diver. We've drawn a, a diver here and for anyone who's taking a look at this life-story of yours it would be absolutely unforgivable not to give them an opportunity of seeing you just explain, if they've not come across a Cartesian diver system before. Would you, would you just go through that with me?

JW Will we have a, will we have a picture?

MB Yes indeed, if you could just point it out on here that would be rather good.

JW Well, the key thing about the diver is that it depends upon, it's a volumetric apparatus just like a Warburg apparatus, and it is a capillary about 1½-2 centimetres long, 1 to 1.2 millimetres diameter. You know what you want to put in the diver for any given reaction. If for example it is oxygen uptake, you load it with a little sodium hydroxide in the bottom, then you can put against the wall of the diver which has previously been coated with silicon a tiny drop, a quarter of a microlitre say, of some substrate, supposing you want to measure succinate oxydation, say. Then you put in a ring, a layer across containing your homogenate or solution of active enzyme, then you have a seal of oil. And finally the mouth of the diver is sealed with a salt solution into which the diver is going to float. The vessel, it floats in a vessel containing...

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<sup>6</sup> Robert Alexander McCance.

MB A pressure-controlled system.

JW ...salts, yes, and the pressure in that flask is controlled. The point, now the point about the diver is when you know what you are going to put into it, all these things I've mentioned, you can, you can calculate its air volume and you can calculate the weight that it has to have for that air volume in order just to float in this floatation vessel. And so you make it with the tail, which you adjust the weight until it's exactly right.

MB A glass tail that you build up until it's exactly...

JW You build it up, yes.

MB ...balanced right in the water?

JW Precisely.

MB Or in the, in the ... and then it balances...

JW And then you put it into the floatation vessel where it balances just a little, plus or minus a few centimetres of water. You can pull it, if it's a little too heavy you apply a negative pressure and pull it up to the mid-point, the reference point which you look at through a microscope with a graticule on it. Then you maybe, you take a reading, then maybe you mix your substrate, your homogenate with the substrate, oxygen is taken up, the pressure becomes more and more negative and you get a linear plot of pressure against time. And it's perfectly simple. It's of course just the principle of Boyle's Law. It's a thousand times more sensitive than the Warburg and all it takes is, you know, a certain amount of manual dexterity to make the apparatus, make the pipettes and work it, make it work.

MB John, I think you were saying at one time that you had a look at Krebs<sup>7</sup> at work on Warburgs. He was really, it was really bucket methods, wasn't it?

JW Yes, it was.

MB By comparison with this?

JW Yes. Well, what I liked about this was actually it's, it is a very accurate method. One got beautiful linear plots, and it was perfectly versatile for different enzymes if you used different substrates or what not. It's of course now been overtaken by spectroscopic methods and polarometric methods and so on and so forth, I've never ever met anyone who uses the diver any more. But it served my purpose very well both for this, and as we shall see later on for measurements of lysine content.

MB John, you got out numerous publications based on diver work, it must have popularised the diver, it must have given it a new life?

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<sup>7</sup> Sir Hans Adolf Krebs.

JW Well, I'm not so sure. The work I did in Jamaica which finished, I mean [it] was of quite a few enzymes, but it finished with the measurement of oxidative phosphorylation in the liver biopsies, was published through the help of McCance in the *Proceedings of the Royal Society B*. And I only know one person who's ever read that paper.

MB Really?

JW Yes, Mike Golden.

MB But that was a major...

JW Well, I never had any reaction to it.

MB Was that kind of '57/'58ish?

JW I think it was before that. I think it was before that.

MB Mid-fifties?

JW Yes. '54, something like that.

MB We shall put it on the record anyway, and maybe people will start looking at it. So, I shall find a reference for that.

JW Yes. I'm sorry I haven't brought all this data with me. I don't remember these things very easily...

MB John, what I would like...

JW ...but it had no, it had no influence, none.

MB I'd just like to summarise this. You've talked about finishing up looking at oxidative phosphorylation. Perhaps we could go through the journey to that because you looked at a number of enzymes as you've said; the performance in the liver, under the conditions of post-mortem kind of liver being examined from victims of kwashiorkor?

JW Well, it wasn't post-mortem, I mean it was biopsy...

MB And these were biopsies as well?

JW Biopsies, yes. And of course we had the great advantage of being able to do biopsies initially and after treatment, after several weeks' treatment. Well I ... the sort of enzymes I measured were things like malate dehydrogenase, succinate dehydrogenase, succinate oxidase. I can't really remember them all.

MB Right, so you were looking at kind of citric acid cycle metabolism and that kind of thing?

JW Yes, some of those, some of those were...

MB And then onto oxidative phosphorylation?

JW And they didn't really, these earlier enzymes didn't really show any interesting differences.

MB Right. The same in healthy livers as those in victims of kwashiorkor?

JW Yes. They were very, very much the same. I mean I had been hoping, following some of the experimental work during the war in America, that protein deficiency would lead to a destruction of these enzymes and hence a considerable sort of, have an impact on the function of the cell. Not a bit of it. Some were a bit, some not. So I thought well then, the oxidative phosphorylation relies on a structure in the cell and arrangement of the enzymes in relation to each other and so on, and perhaps this is what goes on compared with single enzymes. And so I really concentrated on doing that.

MB And that bore all results?

JW Well, yes. I think, I mean we did a lot of work...

MB And we're talking about the late fifties now?

JW Yes. We're talking about a lot of careful experiments trying to rule out our defects and so on. I think it did bear results. But the problem, I mean... Oh, and that was the first time also I'd used radioactivity, I think, for merging the phosphate...

MB These were  $^{32}\text{P}$ ?

JW Yes, the phosphorylation side of it. The problem was that the kwashiorkor biopsies contained an excess of fat, and they were not very stable. I mean, if you left them lying around for half an hour they performed less well than when they were entirely fresh and so on, which all suggests that the fat may have been disturbing the membranes. And it was a ... how can I say ... a physical effect rather than a functional biochemical effect, but that I think, that was the point at which I left it.

MB But you did, when you started to use radioactive phosphate, begin to show a difference in the oxidative phosphorylation levels in the liver. Certainly you showed that.

JW Yes we did, yes we did, and the uptake into phosphatides, of  $\text{PO}_4$  into phosphatides. Yes we did show differences, and these differences could have existed *in vivo*. I can't be certain that they did, but they might have.

MB Do you think that this blocking and this damage to one end of what was an exciting respiratory opportunity towards oxidative phosphorylation and the Krebs cycle or whatever, do you think it drove things in the direction that the actual cause of the fat accumulation was accentuating(?) kind of fatty acids synthesis? I mean, is that what we were looking at?

JW Well I don't actually think, I think the defect if any in oxidative phosphorylation is a consequence of the fatty infiltration rather than a cause of it. But on the other hand if such a defect existed more generally in cells it would surely affect for example the sodium pump and the electrolyte distributions and so on. I mean, it would be a very important discovery, and I feel very sorry that as far as I know nobody's followed it up.

MB But these were exciting ... exciting developments in a field where there'd been so much confusion for many years about kwashiorkor. All of a sudden you begin to chart the inside story of what was happening.

JW Yes, but I should say that I don't think we could make a clear difference between kwashiorkor and marasmus in this. You see the ... in, a little later on there was so much confusion about the definition of kwashiorkor and marasmus, and what was the essential feature of kwashiorkor, that the Wellcome Trust very kindly organised or allowed us to organise a workshop in Jamaica for, international workshop, where this was thrashed out. And the only consistent difference was that it demarked, that kwashiorkor cases are oedematous, and therefore you can really call them oedematous and non-oedematous malnutrition. Two conditions. And I don't know whether the, there is a theory that the oedematous kwashiorkor is due to a failure of reabsorption of sodium and water in the renal tubule because perhaps of this energy deficiency.

MB The jury's not in on that either?

JW No.

MB It's still a colossal problem, isn't it?

JW Well, it is, the detailed pathogenesis is still a problem.

MB But of course the disease internationally has declined as a result of more and more concern on the ground about the nutrition of children.

JW Yes, quite.

MB So, you drew attention to that?

JW The prevalence of the disease has declined. And from the practical point of view I mean I believe still that the protein deficiency plays a very important role, perhaps not the only role but a very important role, and that if you pay attention to the quality of the children's diet as well as its quantity you probably provide protein, potassium and all these trace elements which are needed.

MB John, just looking at that, you mentioned that one wing of the work that was to grow was the idea of the treatment of the children who suffer this disease, finding out more. No one really knew how to handle it effectively, I think, when you went out to Jamaica?

JW No.

MB You know, one knew what it was, one had ideas about what the causes underlying it were, but no one was actually treating it well with any real strategy. And I think sometime in this period in the fifties you began to pick up a pattern that one had to provide the right calorific background for the protein status of the individual to be restored. Not just ~~being~~ protein. <sup>pour in protein</sup> ①

JW That's absolutely right.

MB Whose work was that? I mean, you collaborated with another...

JW Well I think that was our work and particularly Ann Hill. The point was that people were treating kwashiorkor with absurdly high protein intakes. And when we looked at it and did some calculations about the energy cost of growth and that sort of thing, it became clear that the limiting factor in actual treatments was the energy intake, because with ordinary sort of food like milk and porridges you could not get enough energy into these children. So we, I think we were really the first...

MB You were.

JW ...to promote the idea of giving them extra calories in the form of oil, which actually reduces the viscosity of the mixture and makes it much easier to eat and so on. And so we would propose 150 calories per kilo, 200 calories per kilo even, for the treatment, the recuperation phase of the treatment, and this shortens the period of weight gain very much. Later it became apparent to us that if you give this treatment, high energy treatment too early, you can, you can run into difficulties. But that's a different question.

MB Just thinking of the time-scale and what was happening; you got out there, you researched using the hospital initially before you created the unit, you started to research the children, you continued the diver work to learn more about the enzyme changes that might be occurring. This was what you were looking at. You're also looking about the restoration of children to health. What I would like to ask at this stage, John, is how much were you driven by that social conscience that had ... about the welfare of children and about the families out there in the backwoods of Jamaica at that time? Or was it a pure research kind of drive that drove you?

JW Well, I have to say that I hardly was driven at all by concern for the families and social welfare. I left that to the Jamaicans or some of my colleagues who were much more interested in that, and I was simply concerned with the sort of intellectual problems, as you might call them.

MB Right. You were absolutely focussed on the metabolic story there?

JW Exactly, yes, and I sometimes feel rather ashamed about that.

MB In '54 you set up a unit – the Tropical Metabolism Research Unit – that still goes. You and I had the pleasure of spending time there this April. Tell me about the origins of that unit, John.

JW Well, I think it was in the beginning of '54. I'd done three years in Jamaica, entirely on my own apart from a technician, and I was due for leave, and I came back on leave. And I was supposed then to be rejoining Platt's unit. But as I have said I was not very happy with, in that unit in the time I was there before the war, and I didn't quite see what I was going to do in that unit away from the clinical material.

MB You'd have moved heaven and earth to prevent yourself going back there wouldn't you?

JW Maybe, yes! And suddenly – we were on holiday in Italy – suddenly it occurred to me well why shouldn't I go on working on these children? How can I be expected to make fast progress when there's only me? Why don't we have a unit? And the unit was supposed to consist of four people, that really seemed to be quite enough – myself, a biochemist, a clinician, one other – and I put, with a building and with laboratories and wards under the same roof, that was very important. Himsworth, who was still secretary to the MRC, liked this idea. He liked the idea of...

MB Did you go to see him? You just went to see him?

JW I went to see him. I think he liked this idea of laboratories and wards joined together, and it wasn't very expensive in those days.

MB And this was right in the university park near to where the new medical school hospital was going to be?

JW Yes, it was exactly that. It was next to the department of paediatrics or the paediatric ward as it was then, bang in the middle of it. There was a bit of a problem about the running expenses because the treasury said that as it was for looking after Jamaican patients they should be paid by Jamaica. And Sir Hugh Foot who was governor then, when I went to see him, said 'Well if you expect to get anything out of us it's a non-starter.' I remember those particular words. So I then conceived the idea that we could say that a lot of the hospital services such as pathology, food, even drugs and so on could be made out to be part of the normal contribution of Jamaica; they were there and they were paying them, so that was their contribution. And we would contribute anything extra that was required by the research...

MB So you rigged it?

JW ...including a couple of nurses. Yes, we rigged it and we made a compromise, and that was all that was necessary. The treasury accepted it and Jamaica accepted it and so we were in business. And that's how it got going. It took about a year to build. We had in the starting period we had Roger Smith, Verity Wills, Joan Stephens ... and we began these...

MB Garrow, John Garrow?

JW Garrow came a little bit later ... a little bit later, I think. I'm rather, I'm still slightly, I'm afraid I'm slightly hazy about dates, but it doesn't matter really.

MB No, no, we've got the feel of the place. So it took about a year to put in place, and I think you once said to me that looking back it was pretty well planned, apart from the fact that you underdid the office accommodation. Is that right?

JW Yes, that's right. I considered that everybody's place was in the lab or the ward, and that only one office was necessary for the director in which to keep things.

MB But the ward was the nuclear area for the children, with a side area for some experimental work?

JW Yes. Well, it was quite a big side area; it was more than just a side ward.

MB I know that we're hoping to film some of the ward and the centre a little later this year, so it will be nice to actually put some of that material with this conversation.

JW Yes, there was quite a big... And of course since then there have been continual additions to the unit. It never seemed to be big enough, but then its staff increased rapidly and considerably. And so that takes us really to the first few years of the unit.

MB Yes, and these collaborators of yours, we might, we might take that in actually as it got going and put collaborators in place. Roger Smith, for example, we've mentioned, we might put his work ... he's Oxford based now, and we might put his work in Jamaica in perspective?

JW Yes. Well, of course it was always a problem recruiting these collaborators. Roger, I was put onto him by Max Rosenheim who was professor of medicine at UCH as a man who'd got a first-class in biochemistry at Cambridge - he was at my college, Trinity. And I don't think they had any particular job for him, he'd recently qualified, and he accepted it without any difficulty I think. Joan Stephens had been a, had a PhD in biochemistry and was working in MRC head office.

MB She'd been at UCL. Is that right?

JW She had been at UCL...

MB Trained there?

JW ...yes, and she was working in MRC head office. She had been in the publications section, so she'd been responsible for my two reports, which were MRC special reports series reports, so she, and she became rather keen on this work and was glad to come out and resume biochemistry, and...

MB So you'd met her on visits to the UK and in dealing with this reports. I mean, that's how it came about. It was a homespun industry bit that you were creating, John. I mean, you were meeting people over here, inviting them back. It was a very gentlemanly, caring business of inviting people and getting their collaboration?

JW Yes. Well, it went on like that to the end and Verity ... Verity was out there as a registrar, and I met her of course and I thought well, she was ideally suited to this work and so I recruited her on the spot. Yes, well it's always been like that. I mean, many of these things have been pure chance, many of the appointments, and I think they've been much better...

MB Twenty years of very happy appointments generally?

JW Very, I think very much better than the sort of advertising and all the rest of it.

MB Appointment committees and all that. You didn't need any of that?

JW Yes, I think, I think I was quite good at picking people, and very few failures.

MB Joan Stephens, a remarkable biochemist – you once said to me you wouldn't have managed without her?

JW No, I couldn't, I wouldn't have had the techniques. I had enough, I had a sufficient knowledge perhaps of biochemistry but I wouldn't have known how to go about some of these separations and columns and all that sort of thing.

MB But you were a good pair of hands at the bench, and so together you must have done rather a good job?

JW Yes, when we went to, when we were... After the initial four years of the unit, I went back to London for two years I think with Joan Stephens to work in Neuberger's<sup>8</sup> lab...

MB At [St] Mary's?

JW At Mary's, and I'll come back to that a little bit later, but we were complimentary in our skills.

MB And so Joan and yourself, you concentrate on the divers, the liver biopsies, some of the RA work, radioactive work as it came on board. And you got people like Roger Smith very interested in...

JW Well Roger Smith...

MB ...potassium and...

JW Roger Smith in a sense initiated the radioactive era, apart from a little bit of phosphate, <sup>32</sup>P, that was used in the diver, because he did two things. He worked on whole body potassium in the children, and that required using in those days <sup>42</sup>K, which has a life of about thirteen hours. So we had a hell of a time going down the airport in the middle of the night and collecting it and getting it up and getting it into the children and calibrating it and so on, but it could be done.

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<sup>8</sup> Albert Neuberger CBE.

MB Were you bringing that in from the States?

JW Oh no, the States didn't ... Amersham, Amersham...

MB Oh right, you were bringing it...

MB ...from the UK, yes. And that was one thing. The other thing was the total water content of the body, which he measured with a very ingenious homemade apparatus. That was based on a gas-flow counter developed at the National Institute of Medical Research by John Garrow.

MB Right.

JW No, by a man called Pucker(?).

MB A copper tube, long electrode business...

JW Yes, a copper tube into which the water vapour is, through which the water vapour is passed.

MB What did he find about this oedema and the water? I mean, it must be quite dramatic in kwashiorkor.

JW Well, you find a huge excess of body water which was far ... and the ratio of body water to deposit solids was far higher than it should be. Then he found, then he found that the body weight often in these children didn't change for a week or ten days, and the reason for this was that water was disappearing but solids were appearing, so these two balanced themselves out. So the weight didn't change, but the distribution of the weight was of course much more favourable. And that was interesting because people had worried, you know, are we treating these cases properly if they, if they don't change weight? Well they're losing oedemas, so that was good.

MB You spent, right through the fifties, you spent time looking at a range, nibbling away at a range of issues relating to kwashiorkor.

JW That's right, yes, yes.

MB Looking at magnesium, looking at phosphorus, looking at potassium, a range of things?

JW Yes. And I mean, we also, Verity Wills and I did a lot of balance(?) studies in order to see whether the system was so broken down that it couldn't absorb and utilise protein and that kind of thing. Simple ideas, but some such things had been done before. I mean, I don't want to give the impression that we were doing things which nobody had done before. Some of this, similar work had been done in Mexico where they had masses of kwashiorkor by an American group, I've forgotten the fellow's name now for the moment. But they had such complicated and obscure ideas that it was impossible to understand their papers, whereas we were working in very simple concepts.

MB I think it was said at one time by somebody that it was fascinating that some of the American universities picked up what you were doing, and some of the technology, some of the methods you employed?

JW Yes, that was later when we were doing the...

MB And there was this kind of remarkable comment that how exciting that the third world, a third world area was actually exporting to the USA?

JW Yes, that was, that was the turnover stuff.

MB Right, which was to come in the sixties. We're talking about amino acid turnover rates, that used to be in the sixties. We'll keep away from that at present. I wanted to come back to Verity Wills and you actually on the kind of balance work that you did. Could you just describe that very, very simply? What actually took place in that work, John?

JW Well, the children ... these were children who were past the acute phase and were beginning to recover, and therefore I suppose in a sense we weren't quite asking the right question. But they, these children had a diet, I mean basically milk, which was very carefully measured and controlled. All their urine was collected, for this reason they were mainly boys, and their stools were collected and these measurements were made. And it was shown, it was shown that... First of all, let me see, we got a general picture of the efficiency of absorption and utilisation with one of the Jamaican PhD students. We continued that work and showed that in the recovering malnourished child the efficiency with which protein is utilised is virtually 100 per cent. The usual figure quoted for fat efficiency is 70 per cent. And so it would seem quite clear that the depleted child was doing much better than ... once as I say he'd got over the acute illness. And that was quite an important finding. Then we did some studies comparing cows' milk and breast milk by the balance method and found no difference, no difference. So, you know, there was quite a lot of team work of that sort.

MB A lot going on, a lot going on, for a small unit. I mean, you really were pitched into the problem in a big way, covering all the edges.

JW Yes, well we were covering all the...

MB When did John Garrow come out? You said he wasn't quite in the first flush of people?

JW No, John Garrow must have come out in about 1958 I should think.

MB Right. He was going to do the radioactive bit, I think, I got the impression?

JW Yes, we were beginning then to think about isotopes, both stable and radioactive. And I, there was a man in America called Allison<sup>9</sup> who was doing some

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<sup>9</sup> James Boyd Allison.

very nice work on protein depleted dogs and so on. And as we weren't quite ready yet with our wards and everything wasn't quite set up I suggested to John Garrow that – it must have been earlier than '58, but anyway – that he go out, he go up to Allison for three months and get some experience of handling Sulphur-35 and the labile proteins and that sort of thing, which he did.

MB Well that ... didn't work out all that well?

JW That unfortunately didn't lead to anything terribly interesting. I had hoped that John Garrow would sort of, being very good in a certain way at sort of maths and physics, at least he knew a lot more than I did, really take to this isotope work, but he didn't exactly take to it.

MB No, he didn't go for it.

JW He didn't go for it.

MB What did he go for, John?

JW Well, one of his main contributions ... well, he became particularly interested in body composition, and he did an incredible thing. He dissected and measured eight corpses of children who'd died – livers, all the organs, and the total corpse. So we had a picture of the total electrolyte and nitrogen content of the body which really more or less doubled the world literature on this subject, except that they weren't normal children.

MB He totally used up these bodies; he actually measured all the parts?

JW Yes. He measured all the parts and there was nothing left as it were.

MB Dissolved them away?

JW That's right. Dissolved in acid or alkali...

MB Amazing research.

JW ...and David Halliday came out and continued that. That was, that was very important. And John Garrow did a bit of work with me too on albumin turnover and things like that, but... And he was supposed also, after I'd, when the mass spectrometer – Wellcome first gave us the mass spectrometer – he was really going to be in charge of that and get it going, but he had an awful lot of difficulty because of variations in electricity supply.

MB Oh yes. It must have been a great problem?

JW It was a great problem.

MB But that was in the sixties, I think?

JW That was in the early sixties.

MB Yes. I'm going keep you to the fifties though actually, John, for the time being.

JW Yes, yes. So I think that's, that really covers what John Garrow did in the fifties.

MB In the late fifties, just coming to one of the really seminal events, it was quite important to you ... I think one of the great events for you was the first opportunity to appoint West Indians to posts in your unit, '59ish.

JW After it had been going three or four years, yes.

MB That was very satisfying to you?

JW It was very satisfying. I mean we ... we were beginning to appoint them as soon as we could. We had this fellow Chan, Chinese fellow, who did the nitrogen balance work, and then George Alleyne and Dave Picou. Alleyne continued the interest in electrolytes; he did a good deal of experimental work. He, and when we got a whole body counter he rather took charge of that for a while and did a beautiful series of studies.

MB But that was in the sixties as well.

JW I suppose it was.

MB Keeping to the point, this was Dave Picou and George Alleyne.

JW I really, I really should have brought the list, shouldn't I?

MB No, I think this, they came on board about '59.

JW I can send you the list some time.

MB They came on board in '59, as I say... But it wasn't all that easy with the MRC because they weren't typical staff, and I think you had your hands full giving them a reasonable deal?

JW Yes. Well the MRC's attitude, of course, for the first three years there was no problem about hiring these people and we had to see whether they turned out well or not or wanted to stay. When they did turn out very well and they did want to stay, then the problems arose, because in those days after three years satisfactory [work]...

MB You were permanent.

JW ...you became permanent staff. And that's when the MRC said 'No, we can't do this.' And the treasury said 'They can't have a foreign service allowance,' because Jamaica, all those places are in the same, are counted as the Caribbean even though parts of them are two thousand miles away. And, well this really was an impossible situation. They had...

MB They could get overseas pay when they came to England?

JW Yes, which they did for a month or two, a couple of months perhaps even every year, but it wasn't the same thing, it wasn't...

MB No, incredible anomalies.

JW Yes, it was an incredible anomaly actually.

MB And you weren't happy with that, I know.

JW Well, we couldn't, I couldn't do anything about it. They accepted it in a way very well and that situation persisted till I left in 1970. But one or two people of that period I've omitted to mention. Montgomery came in the late fifties.

MB Robert Montgomery.

JW Montgomery, Montgomery who... And he, I suggested to him that he should look into this question of magnesium deficiency, and he did a very good job on that, working out the methods. He also took a great interest in plasma albumin, which was well known to be low, and showed that the lower it was the greater the mortality, which is an important point. And he made a good contribution. He went back after the usual two years to become a consultant in Birmingham. And of course that was another problem for me, to try and make sure that everybody who worked with us and didn't want to stay could get back to a job. On the whole that worked. Roger Smith had a hard time, as you probably know. He did, he got a Fellowship to America, then he was in bad shape after that. He was on the dole for a time until the question of his appointment at the Nuffield, the orthopaedic place, came up and he said 'Well, you know, they, people say it's absolutely, it would be absolutely suicide for a physician to go there. It's a place only for surgeons.' I said 'I don't agree at all. I think you'll have a marvellous opportunity for work on collagen.'

MB Yes. And so it turned out?

JW So it turned out, yes. He was very good about it, but he really ... I remember going to see him, and he really had a hard time for a while.

MB John, did the hypothermia work come in the fifties or was that the sixties?

JW I think that was the sixties.

MB Right. John, at this stage, we've really gone through the [fifties], we've had a long day together and I'm thinking that if you want to just recall anything else that we might have missed from the story then please do, but otherwise I'm going to wind down for today. And then next time when we meet we'll start at the beginning of the, the beginning of the sixties – we've done the, right up to the sixties today – and we can go through the sixties and into the seventies and approach a second phase of your career. But for today we've got you well established, with a new unit.

JW Well the only thing I would say is that I was beginning at the end of the fifties to think about this problem, this question of whole body protein turnover, and...

MB Yes. That was really beginning to bite, that idea that you had to look at protein turnover?

JW I went, I had to go on some, I was an adviser of some sort to Brazil, and I remember very well... It was Easter and nobody was doing, no work was possible, and I was sitting in my hotel trying to read and understand the recognised textbook on pool analysis, compartmental analysis, which is quite complicated. And I did succeed in mastering it, or mastering both of them. And I then began to think well how can I use this information to do the kind of experiments which will answer the questions. So, that really was the starting point.

MB Of what were terrific studies on lysine?

JW Yes, well they of course were in the seventies. No, no, sixties. Sorry, the sixties, yes of course.

MB Which we shall take in in our next talk. And so that really set the scene for the next phase?

JW Well, what happened after that was that I then, '61 I think it was, I went back to the UK, you see, with Joan Stephens to do work, and start to develop this isotope work. So, this is a natural time to stop.

MB John, one final thought I'd like to offer. In the whole of your training and the preparation for this you never had a really great mentor. You were almost an amateur, you found out things virtually all for yourself?

JW I was an amateur. Yes, I was.

MB You were really a classical nineteenth century amateur scientist?

JW Well, I was badly trained. I mean, I didn't know enough maths and I didn't know enough paediatrics. Those were my two...

MB But you were bringing it off...

JW Well, I mean, in the beginning of the...

MB ...just by sheer pursuit?

JW Because I never had anybody who, as I say, I could look up to as the leader until I met Neuberger.

MB Neuberger was a big influence.

JW Neuberger was a big influence, yes.

MB And we'll take him into the story, in the next time.

JW In the next interview. Yes, Neuberger was a big influence, but he's the only one I've ever had.

MB John, for today, thank you.

JW Thank you.