Talk with Sir Henry Dale

British Medical Association and British Life Assurance Trust for Health Education, 1960.

The British Medical Association presents Medical History in the Making, May 1960.
With Sir Henry Dale, OM, GBE, FRS, MD, FRCP, Chairman, The Wellcome Trust and Dr R Prosper Liston, Chairman of the BMA Film Committee.

Produced by Dr Brian Stanford.

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Duration: 00:14:46:24

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<**Opening credits**>

<Liston and Dale remain seated throughout, in face to face discussion>

<**Liston**>
And am I correct in saying that you are 85 years of age?

<**Dale**>
Yes, that's true, or to be more precise, I shall be if I live for another few weeks.

<**Liston**>
And since your retirement from the Medical Research Council, you've found other interests as Chairman of the Wellcome Trust?

<**Dale**>

Yes, that is so. But your mention of that now reminds me that it is more than 55 years since in 1904, as then still a youngish physiologist, I began to get my first experience of research in pharmacology in the Wellcome laboratories, where I remained for the next 10 years. And that led directly to my major research opportunity in my service with the Medical Research Council for the next 28 years. But my research is in that main period, about some of which I expect you're going to ask me questions, was largely derived from clues which I'd picked up in those earlier 10 years.

<**Liston**>
And now in our retirement?

<**Dale**>
Well, as you've already said I'm finding a new kind of opportunity in bringing help to the researches of other people as Chairman of the Trustees, appointed with the will of the late Sir Henry Wellcome. These trustees draw their income, you know, from the pharmaceutical business which belonged to Henry Wellcome himself when he lived. And they use that income for the support of research and historical scholarship in the field of general medicine anywhere in the world.

<**Liston**>
And in 1936, Sir Henry, you were awarded the Nobel Prize for Medicine jointly with Otto Loewi.

<**Dale**>
Yes, that was so. And may I say that it gave me an additional pleasure in that the award was made jointly with my old friend Professor Loewi who I've known for, I suppose, about 60 years – since he worked in London for the first time, and in Cambridge. Near the beginning of this century.

<**Liston**>
And that award was given for the work that you did on the chemical transition of the effects on nerve impulses.

<**Dale**>
That's true, yes. But we ought to remember, you know, that 32 years earlier in 1904, the idea of such a chemical transmission of the effects of nerve impulses was actually proposed by another friend of mine, Professor TR Elliott, while he was still working as a research student in Cambridge. He put it forward to explain what he was then working on – the remarkable correspondence between the effects of injecting adrenaline and those of stimulating nerves of the true sympathetic system. And it wasn't until 10 years later in 1914 that I came across acetylcholine in a peculiar ergot extract, and was helped in identifying it by remembering that Professor Reid Hunt of Harvard, some years earlier, had had that substance made for him artificially and found that it had an extremely potent inhibitory effect on the action of the heart.

<**Liston**>
Was that the only effect there?

<**Dale**>
No, when I came to examine the effects of acetylcholine on the internal organs in general, first I found that these corresponded in a most remarkable and significant manner with the effects of stimulating their nerve supplies through the parasympathetic nerve system, and just as Elliott had found, that the effects of adrenaline corresponded with the effects of stimulating the true sympathetic nerve supplies. But beyond all that, I found also what was perhaps more significant, that acetylcholine stimulated all the cells in autonomic ganglia and the motor endplates of voluntary muscle fibres. And then to jump some 20 years ahead, later with a series of distinguished co-workers, we succeeded in demonstrating that acetylcholine was actually liberated at these synaptic junctions in ganglia and at the endings of voluntary motor nerves to transmit the effects of the impulse to the motor endplate of muscle fibre.

00:05:17:05

<**Liston**>

And where does Otto Loewi come in?

<**Dale**>
Ah, earlier. Because Elliott's work with adrenaline in 1904, my own with acetylcholine in 1914, had as it were I think prepared the way for what was to come in 1921 when Otto Loewi gave the first and beautifully simple demonstration of such a transmission of nervous effects by liberation of chemical stimulators, when he stimulated the two nerve supplies to the isolated heart of a frog.

<**Liston**>
And what then was the practical consequence of this work?

<**Dale**>
Well, I'm always a bit shy, quite frankly, of seeming to claim practical consequences in medicine, for findings with which I had been concerned in the laboratory, but since you put the question, I think it is a fact that this discovery of this chemical mechanism for the transmission of effects at nerve junctions has had at least some effect on clinical conceptions of nerve functions in general, and of course upon the disorders of those functions, and that in particular the application in treatment of now a whole long list of drugs; some of them natural, some of them artificial – most of them artificial, which either antagonise or directly accentuate the effects of one or another of these transmitters when they are liberated, or the other hand, hinder the actual liberation of one or the other of them.

<**Liston**>
And while it was engaged in this series, which I think you call the sympathomimetic amines, that you devoted your attention to noradrenaline?

<**Dale**>
Yes, remember 50 years ago, at that time noradrenaline was still a new synthetic curiosity. It had been made by one of the big German firms and it had been made independently in this country by a man who was then a young research chemist who was to become another of my closest friends, Henry Deakin.

What I found about noradrenaline was that it not only, as perhaps was to be expected, reproduced effects of sympathetic nerve stimulation as adrenaline itself did, but it did so with a much closer accuracy of detail than adrenaline did.

<**Liston**>
And what did that lead to?

<**Dale**>
Well, oh, after many years to the recent discoveries that noradrenaline after all is not merely a synthetic curiosity but is an actual constituent of the living body, and particularly of the sympathetic nervous system. And that in many species, including our own human species, it does act as the principle transmitter of the effects of sympathetic nerve impulses. Those discoveries have been made largely by men who at one time or another have worked in my own laboratory, but they've made them long after I myself retired, now 18 years ago.

<**Liston**>
And what about the old liquid extract of ergot in whose value the general practitioners have great belief? Although I think that belief was challenged by the pharmacologists and indeed by yourself?

<**Dale**>
Yes, well of course that's another story and one in which I had the privilege of being an interested spectator and perhaps to some extent a consultant rather than an active participant. What happened was that the Medical Research Council had been asked to get an accurate clinical comparison between two well-known alkaloids of ergot for which rival claims were being made to be the essential obstetric constituent. And they'd invited Dr Chassar Moir, who was then a keen young obstetrical registrar, to undertake the comparison and he consulted with me and I perhaps helped him to obtain a suitable apparatus which he used to obtain objective records of the contractions of the human puerperal[?] human uterus. And with that he very soon settled the matter because he found no difference whatever between the actions on

the human uterus of these two well-known alkaloids. But he also found that neither of them had any distinct activity of that kind when it was given by the mouth.

00:10:05:03

<**Liston**>
But where does the old liquid extract of ergot come in?

<**Dale**>
Oh, in both ways because that was always given by the mouth and also it contained no recognisable traces of either of those alkaloids so that if the general practitioners and the obstetricians who used it had any good ground for their belief in its activity, it must be due to something else. Well now Chassar Moir had at his disposal an ideal technique for putting that to the test and he very soon got the result which was to show that the old liquid extract administered in the conventional way by the mouth had a very potent and very valuable action on the activity of the human uterus. And then the way was clear for him to operate with my late chemical colleague Dr Harold Dudley and they were at work for nearly three years until finally from the old liquid extract Dudley succeeded in isolating a hitherto unknown alkaloid, now known as ergometrine and recognised everywhere I think as the essential obstetrical invaluable constituent of ergot, which I among others had been looking for in vain for many years by laboratory methods.

<**Liston**>
Am I correct in supposing that your work on ergot, indeed, led to many important further discoveries?

<**Dale**>
Yes, a number of discoveries of quite different kind. For example, some of my early experiments with ergot, I came across quite by accident, evidence for the presence in the pituitary posterior lobe of a very potent oxytocic hormone now known as oxytocin. And then histamine came to my notice through its occurrence in a peculiar extract of ergot, and Barger[?] and I soon found that it was a natural constituent of

the tissues of the body. And then when we came to examine its activities in detail these showed a most remarkable correspondence to the chief features in different animal species of the then recently discovered and described anaphylactic reaction. And now in recent years, the generation after mine has been discovering that histamine is actually released in the anaphylactic reaction and all this evidence is naturally leading to an increasing application in therapeutics of substances which directly antagonise the actions of histamine.

<**Liston**>
And this work led to your interest in, and indeed influence on the biological standardisation such as insulin?

<**Dale**>
Well I suppose I did have some influence on that but chiefly I think by my insistence on the use of permanent, stable, standard substances, in terms of which generally accepted units had to be defined – a principle indeed which was already laid down as long ago as 1897 by the great Paul Erlich and his classical description of the standardisation of the diphtheria antitoxin.

<**Liston**>
And you were indeed a pupil of …

<**Dale**>
For a short time.

<**Liston**>
For a short time. What strikes one so forcibly Sir Henry is that your work has led to such important clinical results, both for the benefit of the doctor and the patient.

<**Dale**>
Oh well if that has happened, insofar as it has happened, of course it's been a stimulus and an encouragement to a laboratory worker. But I think I ought to say that except in response to some official prompting, I don't think I have ever worked with a

consciously clinical aim. It's just happened. The results which have fortunately been obtained in my laboratory, on one thing or another, have been recognised by other people as having useful clinical applications either for practise or theory.

And altogether you know I have the feeling that in more than one way I've had more than my fair share of the good luck.

<**End credits** >