Wellcome Film Project

Hypertension

The Scientific Basis of Medicine

Presented by Dr A F Lever, Western Infirmary, Glasgow.

University of London Audio-Visual Centre, 1973.

Introduced by Dr Ian Gilliland.

Produced by David Sharp.

Made for British Postgraduate Medical Federation.

Black and White
Duration: 00:43:55:06

00:00:00:00

<**Opening credits**>

<**Dr Ian Gilliland to camera**>

Dr Lever is Director of the Medical Research Centre's Blood Pressure Unit at the Western Infirmary of Glasgow. Prior to that, he was a Lecturer in Medicine at St Mary's Hospital Medical School of London and before that in the National Heart Hospital. He is very well known for his work on the renin-aldosterone mechanism and, of course, on hypertension which is the subject of the following discourse. Dr Lever.

<**Dr A F Lever to camera, then over slide showing 3 main parts of lecture**>

Well as you've just heard, my talk today is concerned with hypertension or high blood pressure as some people care to call it. And I've divided the talk into three main parts.

Could we have this first slide which shows you … initially we'll deal with the question of epidemiology of hypertension: it's the distribution of blood pressure, normal and abnormal in the community as a whole. And then we'll pass on to consider the investigation of the single hypertensive patient in a typical outpatient department and the investigations that can lead on from this and we'll concern ourselves also here with the renin-angiotensin system and aldosterone over-secretion. And thirdly, finally and fairly briefly, we'll discuss the question of treatment; treatment by tablets and treatment by surgery.

<**Lever, seated, refers to graph showing blood pressure results of normal population, then to camera**>

Now, perhaps the best way of considering the definition of what hypertension is in the first place is to show graphically, as here, and schematically I may add too, the distribution of blood pressure results from a typical screening survey of an allegedly normal population. Here, plotted on this axis, we have the number of individuals and on this axis there, diastolic blood pressure. And as you can see, most people have the expected normal blood pressure, a few in this top right-hand triangle here have distinctly increased blood pressures with diastolic levels above 110 mm of mercury and there's no doubt, I think, in anybody's mind, in any physician's mind, that these are undoubtedly hypertensive people. The difficulties arise with this borderline group between 90 and 110, some people would regard them, arbitrarily, as hypertensives, others would contest this and we'll come back later to exactly what this controversy means.

Now the important point or the second point to emerge from population studies of this sort is that there is no kink on the down stroke of this curve; there is no evidence, in other words, that the population of normotensives as divided, in a frequency distribution sense, from the hypertensives by a kink and two humps. The right-hand

hump being the hypertensives, the left-hand hump being the normotensives. And it was evidence such as this that led Pickering, and subsequently many others, to suggest that hypertension was not a disease entity, in the normally accepted meaning of the word, but a state of graded risk, rather like accident proneness. Some individuals, the very hypertensive, would be markedly at risk. Others with lower levels of blood pressure would be less at risk but the point that he was trying to make is that all of them would be at some risk.

<**Lever, seated, refers to graph showing blood pressure results of normal population, then to camera**>

Now this can be shown schematically in this next diagram here. We have data from the Framingham study of hypertension, coronary thrombosis and other illnesses, Framingham being in the United States. And they had first of all measured the blood pressure in their apparently normal population, plotted it out in different categories here for each individual, and then related it to the subsequent risk of developing a coronary thrombosis or myocardial infarction and as you can see, there's a very clear correlation between the two. It bears out, in other words, Pickering's contention that hypertension is, as stated, is a state of graded risk, certainly as far as coronary thrombosis goes, I think there's very little doubt about it.

00:05:06:00

<**Lever over table listing risks of hypertension, then to camera**>

Now, the other risks of hypertension are shown in this next transparency if we could have that, please?

Ischemic heart disease we've already touched on. Cerebrovascular accidents, CVA, also very much commoner, particularly cerebral haemorrhage. Thirdly, renal failure, particularly a consequence of malignant phase hypertension, is singularly deadly although not as common as the first two complications. And fourthly, cardiac failure, left ventricular failure particularly, may result from severe hypertension.

The point to make, I think, about all of these is not that hypertension is a disease in its own right but it predisposes to a whole series of complications, which do occur in other situations, but are much commoner in hypertension. Some of these, renal failure and coronaries, for example, are quite deadly and therefore it is an important thing to detect hypertension if it is curable.

<**Lever over graph showing how treatment for high blood pressure reduces the risk of medical complications, then to camera**>

Now that brings us back to another point which I can best illustrate by this graph here – remember this is our frequency distribution curve and I posed the question of whether or not, having detected blood pressure there's any point in, hypertension, whether there's any point in reducing it [*tape jumps*] are there benefits from treating it [*tape jumps*].

Well, if you take individuals in this top right-hand category, with diastolic blood pressures above 110, I think there's no doubt at all, from quite a few trials, some of them poor, but most of them reasonably good, in which reduction of blood pressure is associated with quite definite reduction in the risk from complications, particularly the cerebrovascular accidents and renal failure, there's still a question mark hanging over the myocardial infarcts.

Well so much for the undoubted hypertensives, what about the borderliners, if you like? Well, here there is no doubt about the risk again and maybe 3, 4 or even 5 times more likely to die from a coronary thrombosis, but it doesn't follow from this that they're necessarily going to benefit from reduction of blood pressure. And such trials as have been organised so far are rather inconclusive, not because the problem is inconclusive but because the number of people required for such trials is so enormous that the economic considerations alone in running trials of this nature are almost prohibitive. Anyway, they are being run and hopefully there will be an answer.

<**Lever over table showing summary of epidemiological evidence, then to camera**>

Now, if we could have an interim summary of the epidemiological evidence. Firstly, hypertension seems to be more a disease of risks rather than a disease entity in its own right. Secondly, a point that I should have made earlier but didn't, it's often symptomless. In the survey we ran in Renfrew, for example, in 65% of the people detected with hypertension, didn't know they'd got it and nor did there general practitioner. Thirdly, there is no doubt about the benefits of treatment in the severe case but you remember that these are relatively rare as compared with the moderate to mild case where benefit has yet to be demonstrated. But if it is demonstrated, I suggest that there will be a major need to organise screening surveys since for every hundred people that you pass on the street, there may be 5, 6 or 10 or even 15 with undetected, symptomless hypertension at risk from this hypertension and presumably capable of benefiting from reduction of blood pressure. So this is the picture, then, raised by the epidemiological work. Most of it's fairly recent and it's obviously going to influence developments in the field very considerably.

Now, the next thing I would like to do would be to pass on to, from the field survey type of work to the actual clinic and consider what happens to an average out patient with hypertension as he passes through a general medical clinic – most patients, of course, will be seen in outpatient departments when they have hypertension, they won't be admitted to the ward.

Now, the first thing to bear in mind is that, as with any general medical case, they will have a full medical history taken but, over and above this, there will be particular medical points that the physician will be on the lookout for and these points are shown in our next slide.

<**Lever over table showing points in medical history a physician will look for in a patient with hypertension**>

Well, first of all, he'll be looking for a history of vascular disease and by that I mean angina or possibly a past myocardial infarct which give fairly characteristic symptoms, looking for intermittent claudication in the history, for example. Heart failure, represented by a fairly characteristic set of symptoms – dyspnoea, paroxysmal nocturnal dyspnoea particularly, may be present in severe hypertension. But perhaps more important, I think, because it occurs in the very severely hypertensive, usually particularly in the malignant phase hypertensive, are the tell-tale visual symptoms – sudden loss of vision in one eye, for example, in a patient who has hypertension means a lot more than symptomless hypertension. And the fourth point I've put down here because it's so easy for people to forget, and certainly we've forgotten it on several occasions in the past, is the question of whether or not a woman is taking oral contraceptives at the time she comes up for the consultation because there's no doubt whatever that these can rarely, it's not a common complication, but rarely raise blood pressure very considerably and occasionally raise it slightly and they can also worsen pre-existing hypertension.

Now if we can have the next transparency. A very rare condition, best detected probably at the initial visit because I think otherwise one tends to forget about it altogether, is the phaeochromocytoma and this could present from a symptom point of view with pounding palpitations in the chest associated quite often with pallor and sweating and these patients are often very anxious indeed, and combining these otherwise fairly common symptoms often leads to the penny dropping and the appropriate tests being organised to incriminate a phaeochromocytoma, but this is, nevertheless, a very, very rare association with hypertension. And sixthly, we have two important conditions which may crop up in the more distant history – glomerulonephritis with previous history of sore throat in a child often, followed by oedema and headaches and breathlessness on occasion, all subsiding and everybody feeling that everything thereafter was to be well until maybe 15, 20 years later the condition crops up again. Then there's pyelonephritis with a much more familiar pattern of recurrent urinary infections, dysuria and sometimes haematuria, a frequency in nocturia and even loin pain and fevers.

00:12:29:00

<**Lever to camera, then over table showing points to look for in examination of a patient presenting with hypertension**>

Well, so much for the symptoms. And there certainly can be quite a few symptoms in hypertension but I would guess that, by and large, they're not going to lead you to the diagnosis very often. Now what about the physical examination?

Now here we've put the main points out on a transparency for you. And again, I'd make the point that every hypertensive patient, like every general medical patient, should have a full physical examination. But particular things that you're interested in in the hypertensive patient is the question of whether or not they've got Cushing's syndrome and I'll show you a fairly spectacular example of this in a moment. Another thing which I think should be emphasised is that blood pressure is a very variable commodity and that it can be high when the patient walks through the door and perfectly normal 15 minutes later if anxiety was an associated feature. It's also an unfortunate fact of life that one person taking blood pressure will get quite different readings from another, the left arm might give you a different reading from the right and so on. And so all these sources of variation need to be borne in mind when assessing the severity of hypertension. Then thirdly, and extremely rarely, you will at physical examination pick up occasional cases of coarctation of the aorta by feeling the femoral pulses. I would guess this is very rare indeed as I say. And then finally, and I think importantly, the fundi are a source of considerable information to the doctor interested in hypertension.

<**Lever to camera, then over a slides showing a female patient with Cushing's syndrome, then back to camera**>

Now I would like to show you examples of the first, that's Cushing's syndrome, and the fifth of these important points and if we could turn our attention to this grossly obese, unfortunate lady, here. As you can see, she has a round Cushingoid type of face. She's also got acne, as you can probably see, on the right side of her face and probably not very well shown on this is the fact that she is hirsute, she has hair

around her jaw. But interestingly, I should think several of you could probably see from here, particularly when I lean back a bit, that she has some very distinct scars over her shoulders, like epaulets, and these are the characteristic striae of Cushing's syndrome, they occur quite commonly in Cushing's syndrome. Now, the next slide shows the lady in profile and as you can see, she is extremely fat with one proviso, and that is that although her body is plump and egg-like, her legs are relatively gaunt and this is a feature – the limbs do tend to waste, there is quite a considerable amount of muscular wasting associated with a lot of obesity. She also has, rather, the bent forward buffalo hump appearance of Cushing's syndrome. And then, finally in this series, we have a picture of the front wall of her belly which shows quite distinct striae, those are the vertical lines which in colour would look, of course, blue.

So much for Cushing's syndrome, I think it's the sort of diagnosis that you would make on the patient walking through the door. If you miss it then you're probably going to miss it for quite a while thereafter. It's an instant impression type of diagnosis.

<**Lever over slides showing different appearances of optic fundus in a hypertensive patients, then to camera**>

Now what about the optic fundus? Now, this next slide here shows you an example of a hypertensive patient's optic fundus and, by and large, it looks perfectly normal with the optic disc in the centre shown in white with the blood vessels radiating out across the retina to nourish the tissue. By and large, you can't see anything seriously wrong with it, particularly you don't see haemorrhages, you don't see exudates and you don't see the tell-tale papilloedema of malignant phase hypertension. Now these changes are those that you describe as benign phase hypertension, mainly because there's not a great deal to see. But in malignant phase hypertension there's a great deal and in this next slide you can see some of it.

Now, down in the bottom left-hand corner, here, we have the optic disc which is pathologically swollen with papilloedema, and if you follow this blood vessel out here to the periphery, you can see a large haemorrhage – and if it's possible to focus

down on that a bit it would be very nice – a large haemorrhage out here and jammed in the space, the almost pear shape where … of the division of this vessel and we have quite a good specimen of an exudate. There's another one, of course, below here. These then the papilloedema, the retinal haemorrhages and the exudates are characteristic hallmarks of malignant phase hypertension and it's a serious condition and this would be something you'd have to act fairly promptly about.

00:17:25:00

Now, could we have the next transparency please?

<**Lever over tables showing what to expect at the end of a first visit of a hypertensive patient to a clinic and how to proceed according to the findings**>

So that at the end of our hypothetical patient's first visit, we'd be in a position, perhaps, to suspect that Cushing's syndrome may or may not be present, that phaeochromocytoma may or may not be present. We get some clues about the possibility of renal disease and we would certainly be in a fairly strong position to decide whether or not any of the more serious complications – ischemic heart disease, cerebrovascular accident or malignant phase hypertension had developed.

Now, what are we going to do? I think that's the next question. We've investigated the patient fairly fully, how are we going to decide one way or the other on treatment? Well, the big issue, I think, at this stage, is to decide whether to admit the patient for further investigation and I suggest these days is a very rare outcome, maybe 1 in 20 patients are needed to, need to be admitted straight away to a ward, whereas 19 or 20 or thereabouts can be perfectly adequately investigated and treated as an outpatient.

<**Lever over table listing investigations to be made on a patient with confirmed hypertension, then to camera**>

Now, I think the next thing to discuss would be investigations which should be organised as an outpatient, just willy-nilly of whether the patient goes into the ward. Now, blood counts are done partly because they are done in all medical outpatients or they should be in my view, they also occasionally reveal the anaemias which go with renal failure or with some of the collagenoses. The ESR is helpful, occasionally, because it shows up or gives you the first clue to the fact that the patient has a collagenosis. Blood urea is helpful in as much as it gives you the first clue, perhaps, to the existence of renal functional impairment and this can, of course, be a serious matter in hypertension. It can develop either because the hypertension has been there for so long that it has produced renal failure or because the patient has a renal condition which itself produces renal failure and, independently, hypertension.

Now the electrolytes I'll come back to in a minute because they're, in our view, extremely revealing and they've been the mainstay of much of our research interests. The mid-stream specimen of urine is important and worth doing because it can give you a clue to the existence of a urinary infection on culture, and on microscopy it can show you whether or not there is evidence, perhaps, of old glomerulonephritis or of current urinary infection. Chest X-ray, again, is done as a routine, or should be in medical outpatients, and in particular in the hypertensive patient it may give you a clue as to the existence of coarctation or left ventricular enlargement or even cardiac failure. Now I should there have put in a note about the electrocardiogram which is obviously a very important routine and that would give you evidence of ischemic heart disease.

<**Lever to camera, then over an intravenous pyelogram of patient with severe hypertension**>

Now, the intravenous pyelogram is done in these patients because it may give you a first clue to some renal disease which is underlying the hypertension and in this next transparency, here, we have an intravenous pyelogram of a patient who had really very severe hypertension indeed, and I think the important point about it is that the two sides are showing in the renal pelves difference in size and difference in concentration. I think you'd agree, or perhaps with a bit of persuasion, that the left

side is slightly larger than the right, but I think you'd agree without any persuasion that the right side, this side, is distinctly more concentrated in its dye than in the left. Now this is the hallmark of renal artery stenosis and the reason why it's a hallmark of renal artery stenosis is quite interesting and we've illustrated it in this next transparency here, in this next chart I should say.

<**Lever over chart showing how renal artery stenosis affects fluid output, then over slide showing arteriogram of renal artery stenosis, then to camera**>

This schematically shows you the nephron from the affected kidney, the one with the stenosis, and the nephron from the contralateral normal kidney, respectively right and left as in the intravenous pyelogram. Both the glomerular filtration rates on the two sides are quite normal, or relatively normal, and thus dye from the intravenous pyelogram material is passing through the glomerulus into the renal tubule in both cases. Now the difference lies in the fact that having got through into the renal tubule, the amount of water that is reabsorbed is very much greater on the stenosed side than it is on the normal and thus any dye that gets through will be more concentrated in a relatively small renal pelvis. The upshot is that if you measure the output of urine from this side, it is less and the concentration of some of the important solutes is considerably increased. And these, then, constitute an important indication for renal artery stenosis.

And in the next slide we've got a picture of an arteriogram in a patient with renal artery stenosis and I think you can see that the interesting thing here is that the artery comes out from the aorta, undergoes a sort of sausage-like constriction and passes out to the periphery and to the kidney, and it's this stenosis which is producing the trouble. And it's this stenosis which is the source of attraction for the surgeon and these days, by and large, the operation is relatively successful; the operation being removal of the kidney or correction of the stenosis by placing a plastic piece of vessel between the two ends.

00:23:34:00

Now, so much for the intravenous pyelogram, now what about other tests that we can organise in these hypertensive patients? One important one, as I said, are the plasma electrolytes since they are relatively easy to do and they are often a source of quite considerable excitement, particularly around our laboratory.

<**Lever over table showing electrolyte patterns in a patient with primary and secondary hypertensive conditions**>

And our next slide will show you an electrolyte pattern in a patient, and I think you could probably guess the diagnosis here and it's chronic renal failure; at the bottom of the slide blood urea pathologically raised at 156, and to go with it a metabolic acidosis – bicarbonate of 10. A rather low plasma sodium concentration and a potassium at the lower end of the normal range. That's a fairly typical pattern for chronic renal failure and these patients would be hypertensive when they present in the clinic quite commonly. So there would be no problem, I think, about the diagnosis here but the important thing to determine next is whether or not they have a treatable cause for it; most often, unfortunately, they don't.

Now the next electrolyte pattern is shown … could we have the next transparency please? The next, oh here it is, and it shows a plasma sodium of 146 which is pathologically high in contrast to the previous patient, a plasma potassium which is distinctly low at 2.2, a bicarbonate which is high, 33 – the hallmark of metabolic alkalosis, in contrast to the previous patient, and a perfectly normal blood urea. Now this, as you might guess, happened to come from a patient with primary hyperaldosteronism or Conn's syndrome and I'll say a bit more about this, but meanwhile, I should perhaps emphasise that hypokalaemia and hypertension is extremely common and this particular pattern is not the commonest cause of it.

<**Lever over table showing causes of hypokalaemia in hypertension**>

And the next slide will show you some of the more important alternatives. Well, first and foremost we have the thiazides which are often given these days, sometimes without monitoring of the plasma potassium and these, as you know, produce, as an

almost necessary bi-product of their effect, a depression of the plasma potassium concentration. The alternatives are mineralocorticoid excess just generally, and the specific example I showed you was from a case of primary hyperaldosteronism which is synonymous with Conn's syndrome when it is produced by a tumour of the adrenal cortex. It's also possible to get exactly the same electrolyte abnormality in DOC excess, that's deoxycorticosterone secreted, sometimes by a tumour, perhaps, and certainly by hyperplasia of the adrenal gland. Then, as we'll come to in a minute, we should contrast the so-called primary hyperaldosteronism with secondary hyperaldosteronism where an excess of aldosterone is due to an excess of renin.

<**Lever to camera, then walks to magnetic board with movable pieces and describes the mechanism of primary aldosteronism**>

I think, perhaps, the best way of illustrating the differences is to use our magnetic board and try and sketch for you the important points.

Now, aldosterone is, as we said, a mineralocorticoid. It comes from the adrenal cortex, it's secreted into blood and it circulates through the blood to act on the kidney where, in the distal tubule, it promotes sodium gain at the expense of potassium loss. Now this is a perfectly normal function going on all the time and it's one of the mechanisms by which the body prevents itself losing its natural sodium content. Now, if aldosterone is produced to an excess there can be excessive sodium retention with excessive sodium and potassium loss and this can produce the disease we've just been talking about. But more instructive than just to put it that way, I think, would be to build up a feedback mechanism which controls the aldosterone secretion.

Now, most hormones, cortisol for example, have trophic hormones governing their output and aldosterone's no exception. Several influences are brought to bear on its secretion and one of these is certainly the angiotensin mechanism. Now, angiotensin II is responsible for stimulating aldosterone and it seems that the angiotensin II is produced in blood as it circulates through the lungs, particularly by the action of a so-called converting enzyme from an inert precursor called angiotensin I. Now, angiotensin I itself is produced by that famous enzyme renin which is released from

the kidney and is known to be released from the kidney a long time ago, at the end of the reign of Queen Victoria in fact, where it acts on a substrate to produce angiotensin I. Now, much more recently the problem about what controls the secretion of renin has been partially sorted out and it now seems likely that the stimulus to renin is sodium loss. So that we have a so-called negative feedback mechanism in which sodium loss, which can be produced in a whole variety of ways, pathologically and physiologically, can lead to an increase in the circulating level of renin which will correspondingly produce an increase in circulating angiotensin I and angiotensin II. This will stimulate aldosterone production to promote sodium gain which would then bring to a halt the sodium loss which had led to the stimulation of the feedback mechanism in the first place. So a sequence of changes follow a stimulus which is, in fact, arrested at the end of the sequence of changes – typical feedback mechanism.

Now, that's a perfectly normal state of affairs with the renin-angiotensin system and one wonders how it is deranged in primary hyperaldosteronism. Now, you'll remember that the abnormality there usually is a tumour which produces an excess of aldosterone. This produces excessive sodium gain which negates, as it were, the sodium loss, and the excess sodium gain tends to suppress renin. As a result of the suppression of renin, angiotensin blood levels will also decrease. Now the important point is that if the patient was perfectly normal and hadn't got a tumour in the adrenal cortex, a suppression of plasma angiotensin concentration would be followed automatically by a suppression of aldosterone. But the tumour is, in fact, behaving like a, well, an ill-behaved factory, out of control from its managers and its staff and it's producing aldosterone in excess, willy-nilly of the commands that it's receiving from the outside world. It's autonomous, if you like. So that autonomous over-production of aldosterone by a tumour produces the hallmarks of this condition, primary aldosteronism, and these hallmarks just to summarise are: an excess secretion excretion or plasma level of aldosterone, hypokalaemia with evidence of potassium loss, sodium retention, suppression of renin and suppression of angiotensin I and angiotensin II. And you can find all these results if you look for them hard enough in the blood of a patient with primary hyperaldosteronism. Well, that's how to diagnose it and usually it's a fairly relatively easy matter.

Well the next question is what we do about it having diagnosed it. Well, there are several lines open and one possibility is shown in the next transparency if we could have this please.

00:31:37:00

<**Lever over table showing treatment options for hyperaldosteronism, then to camera**>

And that is surgery. Now, for a tumorous type of hyperaldosteronism I think there would be no doubt that surgery would be the most sensible thing unless the patient had some contra-indication to surgery. But for hyperplasia, obviously, rather like hyperplasia with Cushing's, there is a problem because one does not wish to normally remove most of both of a patient's adrenal glands and this is what is necessary if blood pressure is to be controlled. And therefore the tendency is these days to consider as an alternative, number 2 here, spironolactone which is a competitive antagonist of aldosterone, which acts by blocking the effect of aldosterone on the renal tubule and thereby liberating the sodium that would be retained by the aldosterone and retaining the potassium that would otherwise be excreted.

Now, so much for primary hyperaldosteronism. Now the … superficially, a condition with which it's commonly confused is secondary hyperaldosteronism, which occurs perhaps almost as commonly, has a very different course indeed and is certainly much more serious from the patient's point of view.

<**Lever over table showing main features of secondary hyperaldosteronism**>

And in the next transparency, we have the main features of secondary hyperaldosteronism with hypertension, I should have put there. The hypertension, firstly, is often severe, it's in the malignant phase which, quite frequently, not invariably but quite frequently, and you remember that malignant phase hypertension,

clinically, was characterised by that rather unpleasant looking retinopathy with haemorrhages, exudates and sometimes with papilloedema. But also quite common in malignant phase hypertension is renal failure and a rarer occurrence, fits of the so-called hypertensive encephalopathy type. And if you then come to look at biopsy material or even autopsy material in these patients, they have a curious lesion in their small blood vessels and their small arterioles which are called fibrinoid necrosis and this can be a characteristic, almost hallmark, of the malignant phase hypertensive.

<**Lever to camera, then walks to earlier magnetic board with movable pieces showing the mechanism, now, of secondary aldosteronism**>

Now anyway, secondary hyperaldosteronism does occur in severe hypertension and I'll show you now how it could be related to our magnetic blackboard diagram.

Now, the problem here is that, first and foremost, is that renin, instead of being depressed, is abnormally high. And we're not certain why it's abnormally high but it's likely that an excess sodium loss is partly responsible for it. Now, as a consequence of the excess renin, angiotensin II and angiotensin I are also quite markedly increased. And as there is no tumour here in this case, there's nothing to interrupt the signal from the shop floor to the factory and the response of aldosterone is perfectly appropriate to the very high level of angiotensin, and aldosterone, likewise, is markedly increased. This produces the potassium loss.

So, to summarise the situation with secondary hyperaldosteronism, we've got almost the exact opposite of primary hyperaldosteronism, with the only difference being that both have an excess of aldosterone and a deficiency of potassium. It starts off in some way with an excess of renin, possibly because sodium is depleted. It's associated with high levels of angiotensin, high levels of aldosterone and with, generally speaking, a rather poor prognosis unless something could be done about it either by tablets or by surgery.

<**Lever over chart showing details of a case of a man with severe secondary hyperaldosteronism, then to camera**>

Now, this next graph, this next chart of ours will show us something of a patient who had secondary hyperaldosteronism, very badly indeed. This was a man with malignant phase hypertension who presented at this point in time with extremely severe hypertension which was resisting all the conventional forms of treatment and I'll tell you a bit more about these subsequently.

His plasma levels of renin, of angiotensin and aldosterone, which you'll remember from our magnetic chart, were all increased markedly. And as the disease progressed without evident improvement in his blood pressure, we decided to begin regular dialysis because his blood pressure was so difficult to control. Regular dialysis, unfortunately as it sometimes is, was associated with a further rise of blood pressure and a worsening of the situation. Now we therefore made the rather heroic decision in this man's case to remove both his kidneys, not one, but both of them, and as the kidneys are the source of the renin and, as we hypothesised, the renin was the source of the aldosterone stimulation, as you might expect, the renin, the angiotensin and the aldosterone all decreased after the operation. But more important from a practical point of view, his blood pressure also became perfectly normal after the operation and has remained normal thereafter – regular dialysis treatment obviously being needed and he is a very good candidate for a renal transplant at a later date. He's not had one yet but I guess he probably will because he's a young man, supports a fairly active family, he's about 40 years old and I guess that he will do very well in the long run. But there's no doubt whatever that had we not operated at this point that he would now not be with us.

00:37:30:00

Now, so much for secondary hyperaldosteronism. Now, just to contrast the two states, I've put them here on a chart for you.

<**Lever over chart showing diagrammatic comparisons between primary and secondary hyperaldosteronism, then to camera**>

Primary hyperaldosteronism, the patients with Conn's syndrome characterised by the aldosterone excess, by excess sodium, depression of renin, depression of angiotensin and the interruption between the trophic hormone and its site of production. Removal of the tumour corrects everything. Secondary hyperaldosteronism associated with sodium depletion, high renin in contrast to low renin there, high angiotensin and high aldosterone. Our treatment here is either by tablets or by surgery. And in some cases drastic surgery, removal of both kidneys, is needed and, as you can see from this particular case I showed you, seem to be fairly successful.

Now, drug treatment. So much for the investigation of individual cases that may crop up in an outpatient clinic, now how are we going to control them?

<**Lever over tables showing different drug treatments available for hypertension**>

If we could have the next transparency, please. Most patients, as we've seen, have got mild to moderate hypertension and for most of these a fairly simple therapy is perfectly adequate to control blood pressure. And probably the most widely used would be the thiazide group of drugs, although we're not particularly keen on them ourselves, I think most people or many centres dealing with hypertension are, and it would be fair to say that they're an extremely effective, fairly bland, form of treatment for mild hypertension. Beta-blockers, propranolol, for example, have come onto the scene more recently, and they do very well indeed, by and large, in the milder moderate type of case. Alpha methyldopa also successful, dose around about 250mg 3 times a day to start off with, would usually control the average case.

Moving onto the more severe, severely afflicted patients. Methyldopa again could be very useful even in severe hypertension but in this category we would be beginning to think about the sympathetic blockers – bethanidine being an example, which are probably the most potent available form of hypertensive treatment. They have the disadvantage that they tend to produce rather more marked side effects than the others, but the side effects are not as bad as they were with the earlier hypertensive

drugs. Then one can use combinations of drugs – methyldopa with a sympathetic blocker, for example, that can be quite effective.

Then, finally, if we could have the next transparency, there will be the cases of intractable hypertension, not responding to any of these therapies. And here, in desperation, perhaps one might think about diazoxide which is useful in those cases of intractable hypertension who've gone on to chronic renal failure. The drug is extremely effective by and large, but it does carry with it some unpleasant side effects such as the tendency to produce severe and very acute, fulminating almost, diabetes. And finally, one would undertake bilateral nephrectomy in the patients who were uncontrollable by any of the other means, provided the physicians in the renal units were prepared to take them onto their chronic dialysis programmes.

<**Lever to camera, then over tables summarising points of lecture**>

Now, I've talked about the epidemiology of hypertension. I've said a bit about the investigation of the individual patient, placing particular emphasis on our own interest – the renal-angiotensin and aldosterone mechanism and how it was deranged in primary and secondary hyperaldosteronism. I've talked a bit, and only superficially, about the drug treatment of hypertension, but because this is a rapidly moving field and, basically, an optimistic one in which one expects to control blood pressure in most, there's no point in dwelling in great detail on individual drugs and their dose schedules.

So, finally, if we could summarise on this last slide here, I've made 4 or 5 points. Firstly that hypertension in our view is a graded risk type of disease. Secondly that it's extremely common – if you pass 100 people in the street it's quite possible that 10 or 15, as I say, will have hypertension and not know that they have it. If you investigate these patients in some depth, you will not find a clear-cut cause for their hypertension except in a few instances – Conn's syndrome, renal artery stenosis, secondary hyperaldosteronism, Cushing's syndrome and so on. But these, by and large, are rare and you're not going to find a cause in more than, perhaps, 20%. Then, the control of blood pressure by tablets is, generally speaking, easy – if one

tablet doesn't work it's perfectly simple to substitute another which is likely to work. But more important, perhaps, than the control of the blood pressure is the question of whether or not there is benefit from reducing blood pressure. If patients start with severe hypertension, in this top right-hand part of the distribution curve, is there genuinely benefit from reducing their blood pressure into the middle of the distribution curve? Because if there is, there is going to be a major public health problem, in my view, from the screening and investigation of hypertensive patients.

<**Lever to camera**>

Thank you very much.

<**End credits**>