Conference on Mechanism of Protective Action of Kidney and Relation of Renoprival to Chronic Renal Hypertension

Led by E. Braun-Menéndez, M.D.

Dr. Braun-Menéndez: According to the agenda for this conference, we will have to answer some very difficult questions. I think it would be convenient to say something about what is meant by the "protective action of the normal kidney." The term was first coined by Dr. Fasciolo who, while repeating Dr. Goldblatt's experiments on renal hypertension, studied the effect of the removal of the intact kidney in dogs with unilateral renal artery clamp. As you all know, after unilateral renal ischemia, the blood pressure goes up and remains high for only a few weeks, then it returns to normal. If the intact kidney is then removed, the blood pressure rises and stays high permanently. Evidently this normal kidney is doing something that brings the blood pressure back to normal levels and keeps it there. This is what Fasciolo called the "protective action of the normal kidney."

Now what is this action? Pickering and Prinzmetal working on the rabbit also observed that after putting a clamp on one of the renal arteries the blood pressure increase lasted only a couple of weeks. At this time the clamped kidney was reduced in size and the contralateral intact kidney was enlarged. This hypertrophied kidney had taken over the work that the ischemic kidney was unable to perform. If you then remove this hypertrophied kidney the work demanded of the sole remaining atrophic and ischemic kidney increases enormously. The kidney cannot increase in size and function because it has a clamped artery and permanent hypertension results. The protective action of the normal kidney led us to the renotrophin hypothesis. According to it, the removal of both kidneys should cause hypertension. Many experiments, including those mentioned by Dr. Goldblatt, showed that no hypertension developed in animals after removal of both kidneys. With von Euler,3 we experimented on nephrectomized rats, a good number of which were kept alive for 48 or even 60 hours. Hypertension developed in about 30 per cent. We then thought that perhaps hypertension wasn't present in the other 70 per cent because the urea was too high and the toxic effects of the removal of the kidney prevented the hypertension from developing. Some of our rats were treated by peritoneal dialysis which prolonged their life for 1 to 2 days more and hypertension appeared very readily. This was the first demonstration of the production of renoprival hypertension. After that Dr. Grollman4 developed his method of peritoneal dialysis and made an excellent study of renoprival hypertension in the dog. Now, may I challenge Dr. Grollman's statement that it is very unphysiologic and unbiological to load animals with salt and to give them other kinds of things? May I say that the removal of both kidneys is also unphysiologic? I have no great experience with the dog, but the nephrectomized rats I have seen are very miserable animals in spite of their acceptable external appearance. They have hypertension, but on top of that they have many other things, so I don't think this is real hypertensive disease as you see it in man.

Let us return to the questions. Can the mechanism of renoprival hypertension be demonstrated? Well, it has been shown by Dr. Rondell that some constrictor substance...
may appear in the blood of renoprival rats. Can you tell us something more about it, Dr. Rondell?

Dr. Rondell: A constrictor principle is demonstrable in the blood as we have obtained it. The best guess currently is that this is an artifact of the bleeding procedure and does not represent the circulating pressor material responsible for the hypertension. There needs to be clarification, of this, however. The techniques that we have used to conclude that the constrictor we observed is epinephrine are certainly not unequivocal.

Dr. Braun-Menéndez: Could it be norepinephrine?

Dr. Rondell: Yes. Aortic contractions to norepinephrine are quite parallel to those of epinephrine, though we have not studied this drug so extensively. The responses of renoprival rats injected with these materials are very comparable also; in vivo infusions of epinephrine and norepinephrine produce very similar responses at the same dosages.

Dr. Braun-Menéndez: The first question continues: 'Do the following appear to be more or less likely as the cause of renoprival hypertension: A. Extrarenal sources of 'renin'? B. Maldistribution of salt and water? C. Adrenal hormones? D. Pituitary hormones?'

What would you say, Dr. Grollman, about the maldistribution of salt and water?

Dr. Grollman: There is no question that a disequilibrium of salt and water will induce a change in the hemodynamics of the organism and that deviations from normal electrolyte and water metabolism occur in hypertension. I admit that nephrectomy is unphysiologic; even putting a dog in a cage is unphysiologic, as is also putting a clamp on the artery. I still insist that overloading a rat with salt and water and observing a rise in blood pressure does not mean that you have induced hypertensive disease. Bilateral nephrectomy, on the other hand, does reproduce a condition comparable to that encountered in the accelerated stage of human hypertension. One does not have to use complicated procedures to do so nor does one have to induce gross changes in salt and water metabolism, and the animal looks as normal as the patient with essential hypertension.

Dr. Braun-Menéndez: What about the hematocrit level of these animals?

Dr. Grollman: It is initially normal, but as in the human, renal failure ultimately results in marked anemia.

Dr. Braun-Menéndez: Dr. Kolff, would you like to comment on that?

Dr. Kolff: Do not I recall a paper by Dr. Grollman that overloading with saline and water makes no difference in the blood pressure?

Dr. Grollman: Yes, that is certainly true when the expansion of extracellular volume is not too great.

Dr. Kolff: Why are you suddenly so upset now?

Dr. Grollman: I am upset only by the consideration of obvious changes in blood pressure attributable to alterations in fluid volume as indicators of hypertensive disease.

Dr. Kolff: I think we agree about that.

Dr. Handler: May I ask how the first in that series of questions actually read?

Dr. Braun-Menéndez: 'Can the mechanism of renoprival hypertension be demonstrated and do the following causes appear to be more or less likely?'

Dr. Handler: What I am wondering now is, is this merely the other side of the coin? Is lack of the protective action of the kidney, which we were just discussing, by definition renoprival hypertension? If so, I wonder if the right set of questions has been posed?

Dr. Braun-Menéndez: Well, the right question appears afterwards. What evidence supports the view that unilateral renal hypertension in the rat or human occurs via the renoprival mechanisms? Would you like to comment on that?

Dr. Handler: Well, I would prefer a different set of questions. If one puts any credence in these notions, then you have to say that a healthy kidney does something useful for the animal. You said this yourself earlier. Now we may ask what are the possible useful things that it might be doing.
and list these. Simply as logical postulates, unrelated to anything one actually knows, one might say that this healthy kidney releases a depressor material which has an offsetting influence. There is, as I think Dr. Rodbard suggested, not only the possibility of renin coming from the bad kidney but another pressor material coming from somewhere else in the animal and if the healthy kidney can somehow relieve the animal of that burden, then this might also account for the protective influence. Finally, there is the possibility of excretion of something unknown. I would then ask if any of these 3 have been tested adequately experimentally. I suggest that the answer is "no" for all 3.

DR. GROLLMAN: There is a fourth factor which we must consider, namely that the kidney produces some product such as has been demonstrated in extracts from the kidney. One can lower the blood pressure in the hypertensive animal by many methods, some of which may prove fatal; with these extracts blood pressure can be reduced for a long time with no obvious detrimental effects.

DR. BRAUN-MENÉNDEZ: It may not be a substance secreted by the kidney, but some kidney enzyme which reduces the concentration of some special substance or affects some metabolic function.

DR. GROLLMAN: I do not think so, because enzymes would be ineffective when administered orally.

DR. HANDLER: There is a word of caution which I would like to insert here. The problem is whether or not the renin-hypertensin system exists, teleologically speaking, actually to regulate blood pressure. Any observed action depends on where one stands and looks at it. The group assembled here is concerned with materials which affect blood pressure, simply because they do affect blood pressure. It is entirely possible, however, that this entire machinery exists biologically for some other reason unknown to us. There is a series of incidents in the literature where the "right material has been isolated for the wrong reason." As a simple case in point, if we knew nothing about the mechanism of muscular contraction and set out to isolate adenosinetriphosphatase from muscle, one might isolate myosin in huge quantities and call it ATPase, thinking one knows what it is there for, and completely miss the fact that it relates to the contractile process as such. Similarly, I wonder whether renin and its substrate, under normal circumstances, have anything whatsoever to do with blood pressure mechanisms and whether they do not exist for some quite other reason, granting the possibility that if this normal machinery were disturbed it might result in an unphysiologic elevation of blood pressure.

DR. BRAUN-MENÉNDEZ: I think that is a very important statement. Now I would like to comment on an experiment that I think Dr. Grollman has also made. If you leave one kidney in situ with its ureter connected with the vena cava, the blood pressure does not rise. Is this so?

DR. GROLLMAN: Yes, in these experiments, one induces excretory failure but no rise in the blood pressure nor other concomitants of hypertensive disease. I think that is a crucial experiment.

DR. BRAUN-MENÉNDEZ: That is a crucial experiment in that it shows that the kidney is doing something aside from its excretory function which keeps the blood pressure normal.

DR. GROLLMAN: Why say it is doing something? Why not say it is essential for the maintenance of the normotensive state?

DR. BRAUN-MENÉNDEZ: There is time to hear some comment from the audience.

DR. GOLDBLATT: I would like to hear the answer to question no. 2. If Dr. Grollman admits that the relief of the hypertension associated with unilateral renal disease, in man or animal, can be explained only on the basis of the elimination of something which was coming from the diseased kidney and which was elevating the blood pressure, then why bring in the renoprival theory? I do not follow the logic of such an argument. What evidence supports the view that hypertension associated with unilateral renal disease is renoprival?
DR. GROLLMAN: In the first place, Dr. Goldblatt, removal of one kidney does not often induce hypertension. The animal species and conditions under which you work will determine how often you observe it. In the case of the dog, for example, I only recall 2 instances where unilateral nephrectomy resulted in hypertension. In one dog worms had destroyed most of the other kidney, and in the second dog a stone had formed in the kidney. In the case of the rat, as shown by my colleague, Dr. Bela Halpert, who did this study with me some years ago, in every instance where unilateral nephrectomy or application of a figure-eight ligature induced hypertension, disease of the other kidney was always demonstrable.6

DR. GOLDBLATT: What you have just said about hypertension after unilateral nephrectomy is completely unrelated to my question. I did not mention the development of hypertension as a result of unilateral nephrectomy, and I do not believe that it ever occurs, if the other kidney is normal. I agree with you on that, but that does not answer my question. I am merely asking you to explain, on the basis of the renoprival theory, the return of the blood pressure to normal as a result of nephrectomy in an animal with hypertension due to constriction of one main renal artery.

DR. GROLLMAN: One cannot.

DR. GOLDBLATT: That is just what I wanted to hear you admit.

DR. GROLLMAN: But you will not get hypertension unless you reduce the blood flow markedly, will you Dr. Goldblatt? If you just clamp it slightly nothing happens.

DR. GOLDBLATT: The constriction of the artery does not have to be as great as you imply, but it is certainly true that if it is very slight then it may prove inadequate to bring about an elevation of the blood pressure. Your statement, however, that tying off the artery or sudden complete obstruction also results in elevation of the blood pressure is completely erroneous.

DR. GROLLMAN: You will not get hypertension temporarily?

DR. GOLDBLATT: No, that is an error; but again we are getting away from the original question. I hope that you will agree that if the hypertension associated with unilateral renal disease or constriction of 1 main renal artery is cured by the removal of the affected kidney then, since the removal of the kidney is even more renoprival, the blood pressure should go up even more instead of down, as it does.

DR. BRAUN-MENÉNDEZ: I think the only experiment that answers your question is the one done in human twins. There you have constricted kidneys causing hypertension and when a normal kidney was grafted the hypertension disappeared. But after a time the normal kidney did not function well and the blood pressure rose again. Something was happening to this normal kidney. It wasn’t able any more to neutralize the substance secreted by the diseased kidneys. On removal of the diseased kidneys the blood pressure then returned to normal.

DR. GOLDBLATT: I have a very simple explanation for that, Dr. Braun-Menéndez. In the immediate postoperative period, and you must not forget that it is a considerable operative procedure to transplant a kidney, he had some fall in blood pressure, but finally the 2 diseased kidneys which were producing something that caused the elevated blood pressure, asserted themselves enough to cause again a rise in the blood pressure.

DR. BRAUN-MENÉNDEZ: Wouldn’t you agree with me, Dr. Goldblatt, that a double nephrectomy was also a hard operation for a man of 24 who already had a grafted kidney?

DR. GOLDBLATT: I think a nephrectomy is not child’s play. I would say it has its hazards.

DR. HANDLER: Dr. Goldblatt, what is your own explanation of the protective action of the normal kidney which was originally observed in your own experiment? What is your opinion of that?

DR. GOLDBLATT: Do you mean the return of the blood pressure to normal in the dog with unilateral renal artery constriction when the other kidney is normal?
Dr. Handler: Yes, and when you remove the good kidney of a dog with a clamp on the other renal artery the pressure goes up again. This is your own observation, but what is your explanation? This is where the story of renoprival hypertension really starts.

Dr. Goldblatt: Originally, when we observed the development of considerable accessory circulation to the cortex through the capsule of the ischemic kidney, we thought that perhaps this collateral circulation was responsible, at least in part, for the fall of the blood pressure by lessening the ischemia. I have many illustrations of large vessels entering the cortex of the kidney. Such vessels could be effective in bringing blood to a kidney, the intrarenal vessels of which are normal, but which were not getting an adequate supply of blood. You must not forget that the kidneys of the dog are always normal before the operation. From the very beginning, however, I recognized that the contralateral normal kidney might play a part in the fall of the blood pressure in the dog with hypertension on the basis of unilateral constriction of the main renal artery, but I did not have then, and I do not have now, a satisfactory explanation of how the normal kidney accomplishes this. I have no better explanation for this than anyone else. In fact, all that we have heard so far is just pure supposition.

Dr. Braun-Menéndez: Dr. Kolff, do you have a question?

Dr. Kolff: Yes. I would like to hear Dr. Goldblatt explain why the blood pressure does not come down if you take out both kidneys of a chronic renal hypertensive animal.

Dr. Goldblatt: That statement is not completely true. It does come down definitely in some animals, in some it does not. In these circumstances the renoprival hypertension of Dr. Grollman probably develops, if the animal is kept alive by special treatment. I do not see in that an inconsistency or a stumbling block to the acceptance of the renal pressor mechanism as the cause of the hypertension when the renal arteries are constricted. The greatest stumbling block to the renoprival theory, on the contrary, is that when one clamps a renal artery just moderately, not necessarily severely, so that the blood pressure goes up, and at a time when it would still stay up, you take out the kidney, the blood pressure falls to normal. You will have to admit that the removal of the entire kidney certainly is more renoprival than the effect of mere constriction of the main kidney and that, according to the renoprival theory, the blood pressure should go up, not down, as a result of the nephrectomy.

Dr. Grollman: I will admit that a pressor agent is involved in this reaction.

Dr. Goldblatt: That is all I wanted to hear you say. Why isn't it also involved when you constrict both main renal arteries?

Dr. Grollman: The time of the rise in blood pressure is important. It hasn't been considered in much of the literature, but is crucial in our interpretation of the phenomenon.

Dr. Goldblatt: What you have just said may well apply to the figure-eight method you use, but not to the constriction of the main renal artery. I can show you the charts of many animals in which constriction of the renal artery by means of the clamp resulted in an elevation of the blood pressure within 24 to 48 hours, which gradually increased, it is true, and then persisted. What you have said, therefore, about your method may apply to hypertension in the rat, but it does not apply to the method of constriction of the artery in the dog by means of a clamp. By the figure-eight method you are evidently taking the long way around to produce the effect of the clamp, which is very prompt. Your method acts like the perinephritis method of Page who uses a silk or cellophane bag around the kidney. By this method also an animal may take weeks or months before showing a significant rise in blood pressure. I would say that by your method you depend on the formation of scar and produce renal ischemia in that way. For that reason the method is not as good as constriction of the renal artery.
DR. GROLLMAN: Why not? You get just as good hypertension!

DR. GOLDBLATT: Yes, that is probably true and the pathogenesis is probably the same, but it is not as immediate or as dependable, and it certainly does not simulate the pathologic state of the kidney in human essential hypertension.

DR. BRAUN-MENÉNDEZ: This same discussion has been going on for about 20 years. I believe Dr. Helmer would have something to say.

DR. HELMER: In chronic renal hypertension in dogs, if you can develop a good antirenin titer, a lowering of blood pressure is obtained. How do you explain that?

DR. GROLLMAN: Well, if you would feel better, I would even go so far as to admit that you can have some renin for a long time . . .

DR. BRAUN-MENÉNDEZ: That’s right.

DR. SANCETTA: I would like to pose a question to Dr. Kolff in regard to renoprival hypertension. One of the “Merrill” twins underwent a transient decrease in blood pressure following introduction of a donor kidney. It is common knowledge, and I think you will agree with this, that in many individuals with elevation of diastolic pressure general anesthesia followed by a major surgical procedure will result postoperatively in lowered diastolic pressure for a number of weeks; but then a gradual rise occurs, even though the patient is kept inactive in bed. How can you state that the lowering of blood pressure in the patient was not due to this simple nonspecific effect rather than to any beneficial effect on the part of the normal donor kidney?

DR. KOLFF: So far we have not one transplanted kidney in 1 pair of identical twins, but Dr. Merrill now has 3 similar events. I think that the answer to your question, whether this is due to a more specific effect, will come when you find us more twins.

I also have an answer to Dr. Helmer’s question. Antirenin does not seem to work if there is no renal tissue in the body. We showed, with the help of Dr. Wakerlin and Dr. Haas, that renoprival hypertension cannot be reduced or cured by the administration of adequate doses of antirenin.7 Shipley made a very crucial experiment.8 He had a dog with chronic renal hypertension, gave it antirenin and then removed kidneys. The antirenin caused no alleviation of the hypertension. To develop its antihypertensive effect, this antirenin needs renal tissue in the body.

DR. HELMER: That is right, Dr. Shipley gave antirenin intravenously to a dog with chronic renal hypertension that had been bilaterally nephrectomized and got no lowering of pressure. The antirenin used was from human hypertensive subjects treated with hog kidney extracts. It had a high titer against dog renin. Wakerlin9 has shown that antirenin has lowered the blood pressure of such dogs by passive transfer and it was assumed this serum would behave similarly. The antiserum was given after the bilateral nephrectomy when the dog’s pressure was still at hypertensive levels. There was no fall in pressure.

DR. GOLDBLATT: I think that much which has been said during the past 5 minutes is completely non sequitur and has absolutely nothing to do with the problem under discussion. On what basis would anyone ever think that antirenin might cure renoprival hypertension?

DR. KOLFF: You get renoprival hypertension some time after you take the kidneys out. Dr. Shipley’s dog could not have had renoprival hypertension. It still had a Goldblatt hypertension which could not be cured with antirenin in the absence of renal tissue. Renoprival hypertension never develops immediately but takes several days, but in the animals with renal hypertension the blood pressure remains high immediately after bilateral nephrectomy. The fact that the blood pressure is not reduced even for a few days after bilateral nephrectomy suggests that the underlying mechanism for renal and renoprival hypertension may be the same.

DR. GOLDBLATT: The animal develops renoprival hypertension, for the kidneys are out, and the animal is being treated, so that the hypertension which was previously on
the basis of a humoral pressor mechanism, due to constriction of both main renal arteries, has progressed into the other type (renoprival) as a result of the bilateral nephrectomy. Perhaps the baroceptor mechanism described by Dr. McCubbin plays a part.

Dr. Tobian: There is one interesting thing in regard to the theory that renin can somehow inhibit the antihypertensive mechanism of the kidney. It is in relation to observations on the renal transplantation in the twins. The first twin had malignant renal hypertension; generally a patient with malignant hypertension who undergoes an operation of medium severity will have his malignant hypertension back in good measure within 2 weeks. In those I have seen this usually turns out to be true. The hypertensive twin, however, had a drop of blood pressure of 2 months’ duration following renal transplantation. Renin should have been pouring from his diseased kidneys during this time and yet it was not sufficient to prevent the normal kidney from lowering the blood pressure during these 2 months. How can you reconcile this with the renin inhibition theory?

Dr. Goldblatt: I think there is one error involved here. I have a letter from Dr. Merrill in regard to this. In the case of the twin with malignant hypertension the diagnosis was glomerulonephritis.

Dr. Tobian: Dr. Joseph Murray told me that papilledema was present, indicating a malignant phase in the hypertension.

Dr. Goldblatt: Is papilledema an extraordinary occurrence in glomerulonephritis?

Dr. Kolff: He had diffuse chronic glomerulonephritis, according to the report. He had pyelonephritis. He had long-standing hypertension, several years over 200 mm. Hg, and finally, he had signs of malignant hypertension and chronic renal insufficiency.

Dr. Lichton: I understand that the 2 forms of hypertension are produced by different technics, one of which involves abolition of excretory function while the other ideally involves no disturbance of excretory function. In one form of hypertension the renin and antirenin mechanism is apparently clearly implicated and in the other it is not. Dr. Grollman told us that in renoprival hypertension it is possible to have elevated blood pressure without changes in electrolytes, but in experimental renal hypertension electrolyte disturbances are known to occur. The question I would like to ask is this: Is there any real evidence to show that there is a relationship between renoprival hypertension and Dr. Goldblatt’s form of experimental renal hypertension?

Dr. Kolff: Dr. Floyer has done some experiments which may help to answer your question. In normal rats the blood pressure does not begin to rise until 48 hours after total nephrectomy. In unilateral renal hypertension removing the clip from the renal artery results in a fall in blood pressure within a few hours. Consequently, if the 2 forms of hypertension had different mechanisms of action, one would expect removal of the sole remaining clipped kidney in a hypertensive rat to cause a fall in blood pressure for the first 48 hours before the renoprival mechanism took over and started the blood pressure going up again. Actually, Floyer found that the blood pressure did not fall to normal after removing the sole remaining clipped kidney, so he argued that the renoprival mechanism must have been already in effect in the renal hypertensive animal before the nephrectomy.

Another argument used by Floyer to show the identity of the 2 types of hypertension is based on the following further experiment. In a group of hypertensive rats unclipping of the single remaining kidney was followed by a fall in blood pressure. A nephrectomy, done 3 days later, was followed by a more rapid rise than if the nephrectomy was delayed 7 to 28 days after the unclipping. Thus, even after apparent cure of renal hypertension in the unclipped rat, the “mechanism” was still operative for a time as shown by the more rapid rise in blood pressure following early total nephrectomy.

Dr. Helmer: As I remember it, Floyer was showing that in the course of hypertension produced by renal artery constriction,
extrarenal factors are also operating—both renal and extrarenal mechanisms play a role. The extrarenal mechanism might be an electrolyte shift, as suggested by Tobian’s work.  

Dr. BRAUN-MENÉNDEZ: What about Dr. McCubbin’s work?  

Dr. HELMER: Dr. McCubbin’s work on the carotid sinus may have an important bearing. In all probability there are more than 2 factors. However, 1 of the factors is renin, as shown by the antirenin work in acute and chronic experimental hypertension in dogs.

Dr. HOODLER: I would like to bring out 2 points. The first is that with any kind of hypertension if you insert a kidney into the circulation you get a dramatic improvement, whether it be the renopril hypertension of Dr. Grollman, or the unilateral renal hypertension of Dr. Goldblatt. This protective function is enormously important, whether it is primary with the kidney or acting secondarily on general vascular reactivity. The second point is that the renoprivalists seem to me to have 1 difficult problem to explain. It is posed by the experiments of Byrom and Dodson in which the unilaterally clamped kidney in the rat leads to permanent hypertension. I would like to know why this unilaterally clamped animal is more apt to become hypertensive than a uninephrectomized rat. This seems to be a crucial question for those who believe that renal hypertension is caused by a renoprival mechanism.

Dr. BRAUN-MENÉNDEZ: I think that we can conclude that renoprival hypertension is a different thing from renal hypertension. That is, when the kidney is constricted it is doing something; probably it is pouring out renin, as I think the antirenin experiments show very clearly. What is the protective action of the normal kidney? We don’t really know. Probably the normal kidney can take over the work that the ischemic kidney is unable to do, thus relieving the latter from some stimulus which would otherwise cause it to secrete renin. Dr. Goldblatt says that in some of the experiments he could see some collateral circulation in his ischemic kidney. Are you quite positive, Dr. Goldblatt, that in all of the experiments this was the cause of the fall in blood pressure?

Dr. GOLDBLATT: Dr. Braun-Menéndez knows that I was thinking of the possible part played by the normal kidney very early in our investigations. I can show you that even before we published about the successful production of hypertension I was already transplanting normal kidneys, or trying to, to the neck and the groin with the idea of relieving the hypertension. I was thinking even of the possible effect of giving normal kidneys to human beings with hypertension and bilateral disease. It was the obvious thing to think of, so I expect no special credit for it. The fact that I cannot explain how the normal kidney acts, any more than you can, does not have any direct bearing upon the fact that the kidney with its main renal artery constricted is the cause of the hypertension probably because it is the source of a pressor substance which causes the elevation of the blood pressure.

Dr. BRAUN-MENÉNDEZ: I think that is a very good conclusion. The normal kidney acts; we do not know how.

Summary

This conference opened with an elaboration of the concept of the protective action of the normal kidney (Dr. Braun-Menéndez). After initiation of unilateral renal ischemia, the elevated blood pressure is reduced as the intact normal kidney hypertrophies to take over the work of the ischemic kidney. Removal of this intact kidney causes hypertension because the ischemic kidney cannot increase in size or function. As the protective action of the kidney is also lacking following bilateral nephrectomy, renoprival hypertension develops, providing the animals are kept alive long enough.

The cause of renoprival hypertension remains obscure. Gross changes in salt and water metabolism do not have to be present (Dr. Grollman). The normal kidney may produce some material which lowers the blood pressure, or it may destroy or excrete a
pressor substance (Dr. Handler). Excretory removal is not so likely as a cause, since the production of simple excretory failure by diverting urine back into the blood stream does not result in hypertension (Dr. Grollman). According to some participants, renoprival and chronic renal hypertension are not identical: Removal of a unilateral ischemic kidney causes the blood pressure to return to normal. This does not fit with the renoprival hypertension theory and is evidence that a pressor agent must be involved (Dr. Goldblatt). A further difference is that whereas antirenin lowers the blood pressure in chronic renal hypertension, it will not lower the blood pressure in renoprival hypertension (Dr. Helmer). Dr. Kolff, however cites reports, such as that of the failure of bilateral nephrectomy to cure renal hypertension, which favor the view that the mechanism of production is the same in both forms of hypertension. Both groups finally agreed that some cases of renal and of renoprival hypertension could not be explained by assuming a single mechanism of action.

REFERENCES


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