Discussion

Chairman: PROFESSOR H. E. DE WARDENER

PROFESSOR W. ANDREWS (London): I'm going to toss in a few more pieces of jig-saw and hope that the speakers will be able to fit things into this fascinating picture. For instance, volume receptors have been found in both the mesenteric vein and the liver. Recently—though not yet published—it has been shown that some hepatic nerves are susceptible to changes in osmotic pressure (large molecules only) within the physiological range, although they are not affected by changes in ionic pressure. Some other receptors, reported by certain authors to be osmoreceptors, are in fact specific sodium receptors and are only stimulated by changes in sodium concentration relative to other ions present.

DR R. BRANCH (Bristol): In support of a control between the liver and renal blood flow, recently we did some work on the effects of phenobarbitone administration to the Rhesus primate. After 2 weeks of treatment the size of the liver and its blood flow increased. We also noted a 25% increase in renal blood flow.

CHAIRMAN: But if the liver is being exposed to phenobarbitone then so is the kidney.

DR P. VESIN (Paris): In relation to the retention of salt and water in cirrhosis, which has been so interestingly discussed by Dr Wilkinson, I would both agree and disagree with him for the following reasons. We have described three stages with reference to fluid retention in cirrhosis. In the first stage, i.e. the patient without ascites and oedema, there is a moderate and fluctuating retention of sodium. Aldosterone secretion, at this stage, is normal but plasma and urinary levels may be elevated because of impaired hepatic metabolism. The second stage is characterized by ascites and we all agree that such patients have hypersecretion of aldosterone. Dr Wilkinson suggested that total renal perfusion is normal at this stage, even though there may be an outer cortical hypoperfusion. In our experience both GFR and RPF are moderately depressed in these patients even though they do not have azotaemia. But of course we agree that hyperaldosteronism is important in the pathogenesis of sodium retention in these patients and that spironolactone is highly effective

in reversing it. Then we agree again in the third stage, i.e. when there is functional renal failure, since although hyperaldosteronism is observed the sodium is resorbed in the proximal tubule so that in these patients hyperaldosteronism is not important.

CHAIRMAN: Weren't you studying patients who did not have a reduced renal perfusion, Dr Wilkinson?

DR S. P. WILKINSON (London): Yes. In fact we studied many more patients than I presented. We were particularly interested in those patients with a normal total perfusion of the kidney for good reason. Of course what one sees in cirrhosis is a complete spectrum of normal or even increased perfusion at one end and markedly reduced at the other, and I would agree with Dr Vesin that the patient with ascites often has a reduced perfusion. However, we wanted to look at the end of the spectrum, the patients with normal total perfusion in whom hyper-reninism and hyperaldosteronism could not be accounted for by reduced perfusion. Only by looking at the ends of the spectrum can we gain an insight into what is going on within the kidney and it is because previous authors have not considered the different levels of renal perfusion that there has been so much confusion about the significance of hyperaldosteronism in liver disease. I do not entirely agree with Dr Vesin's comments about aldosterone secretion and metabolism. Work from Laragh's group in New York has shown that an increased aldosterone secretion rate is far more important than impaired metabolism.

DR J. LEDINGHAM (Oxford): Dr Wilkinson produced a rather idealized situation in his last diagram. He suggested, I think, that renin went up as a result of a redistribution of blood flow within the kidney. It could, of course, be the other way around, the redistribution being induced by changes in local renin and angiotensin concentrations. Finally, J. O. Davis has shown, in the chronic caval dog preparation, that administration of the specific angiotensin II antagonist, 1-sarcosine 8-alanine angiotensin II, induces an increase in renal blood flow even though arterial blood pressure falls.