

Sir,

We read with interest the report by Dr Funck-Brentano and colleagues (1986;55:596-8) on reversible renal failure after combined treatment with enalapril and frusemide in a patient with congestive heart failure. We agree that sodium depletion is a crucial factor in determining the ability of angiotensin converting enzyme inhibitors to induce acute renal insufficiency. We would add, however, that this complication can also occur in patients without cardiac failure and may arise after salt and water depletion from causes other than diuretics.

We have now seen three patients with severe hypovolaemia, hypotension, and transient renal failure after the development of diarrhoea while they were on treatment with captopril (two cases) or enalapril. One 66 year old patient was on captopril 25 mg twice a day for treatment of essential hypertension; he was otherwise fit and was on no additional medication. Both other patients had impaired left ventricular function (one because of myocardial infarction and the other after mitral valve replacement) and they were also receiving diuretics for their myocardial failure. All three patients recovered fully after intravenous fluid volume replacement.

These agents undoubtedly impair the homeostatic responses to fluid loss,<sup>1-3</sup> and renal impairment further exacerbates matters because both drugs are to some extent excreted by the kidney.<sup>4</sup> The potentially serious consequences of intercurrent salt and water loss in patients receiving angiotensin converting enzyme inhibitors need to be stressed.

John McMurray,  
David M Matthews,  
The Royal Infirmary,  
Edinburgh EH3 9YW.

#### References

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- 2 Blythe WB. Captopril and renal autoregulation. *N Engl J Med* 1983;308:390-1.
- 3 Hall JE, Guyton AC, Smith MJ Jr, Coleman TG. Chronic blockade of angiotensin II formation during sodium deprivation. *Am J Physiol* 1979;237:F424-32.
- 4 ACE inhibitors: enalapril and captopril compared. *Drug Ther Bull* 1985;23:89-91.

This letter was shown to the authors, who reply as follows:

Sir,

We thank Dr McMurray and Dr Matthews for their comments on the role of sodium depletion in the tendency for angiotensin converting enzyme inhibitors to induce renal failure. We agree that, whatever the cause, sodium depletion threatens renal function in patients treated with angiotensin converting enzyme inhibitors. McMurray and Matthews have reported on this effect elsewhere.<sup>1</sup>

More generally, glomerular filtration rate depends critically on angiotensin II mediated constriction of glomerular efferent arterioles when renal perfusion pressure is low. This is particularly true when several factors that reduce renal perfusion pressure are combined: It is worth stressing that two of McMurray and Matthews' patients had impaired left ventricular function as had our patient. We believe that patients receiving both diuretics and angiotensin converting enzyme inhibitors should be instructed to stop their diuretics when there is intercurrent salt loss (from diarrhoea or excessive sweating, for example).

The short and medium term renal effects induced by the combination of diuretics and angiotensin converting enzyme inhibitors depend on which of the two drugs is administered first.<sup>2</sup> It remains to be determined whether diuretics or angiotensin converting enzyme inhibitors should be given first to reduce the risk of renal insufficiency when these drugs have to be given in combination.

Christian Funck-Brentano,  
Gilles Chatellier,  
Jean-Michel Alexandre,  
Service d'Hypertension Arterielle et Medecine Interne,  
Hôpital Broussais,  
96 rue Didot,  
75674 Paris Cédex 14,  
France.

#### References

- 1 McMurray J, Matthews DM. Effect of diarrhoea on a patient taking captopril. *Lancet* 1985;i:581.
- 2 Mimram A, Jover B, Casellas D. Renal adaptation to sodium deprivation. Effect of captopril in the rat. *Am J Med* 1984;76(suppl 5B):14-21.