- McClellan KJ, Goa KL. Candesartan cilexetil—a review of its use in essential hypertension. *Drugs* 1998;56:847-69.
- 10 EUCLID study group. Randomised placebo-controlled trial of lisinopril in normotensive patients with insulin-dependent diabetes and normoalbuminuria or microalbuminuria. *Lancet* 1997;349:1787-92.
- 11 Begg C, Cho M, Eastwood S, Horton R, Moher D, Olkin I, et al. Improving the quality of reporting of randomized controlled trials. The CONSORT statement. *JAMA* 1996;276:637-9.
- 12 Badenhop RF, Wang XL, Wilcken DEL. Angiotensin-converting enzyme genotype in children and coronary events in their grandparents. *Circulation* 1995;91:1655-8.
- 13 Allen TJ, Cao Z, Youssef S, Hulthen UL, Cooper ME. The role of angiotensin II and bradykinin in experimental diabetic nephropathy: functional and structural studies. *Diabetes* 1997;46:1612-8.
- 14 Agardh CD, Garcia Puig J, Charbonnel B, Angelkort B, Barnett AH. Greater reduction of urinary albumin excretion in hypertensive type II diabetic patients with incipient nephropathy by lisinopril than by nifedipine. J Hum Hypertens 1996;10:185-92.
- 15 Goa KL, Haria M, Wilde MI. Lisinopril—a review of its pharmacology and use in the management of the complications of diabetes mellitus. *Drugs* 1997;53:1081-105.
- Sever PS. Clinical profile of the novel angiotensin II type I blocker candesartan cilexetil. *J Hypertens* 1997;15:S9-12.
 Parving HH, Jacobsen P, Tarnow L, Rossing P, Lecerf L, Poirier O, et al.
- 17 Parving HH, Jacobsen P, Tarnov L, Rossing P, Lecerf L, Poirier O, et al. Effect of deletion polymorphism of angiotensin converting enzyme gene on progression of diabetic nephropathy during inhibition of angiotensin converting enzyme—observational follow up study. *BMJ* 1996;313:591-4.
- Ritz E. Nephropathy in type 2 diabetes. J Intern Med 1999;245:111-26.
 Marre M, Jeunemaitre X, Gallois Y, Rodier M, Chatellier G, Sert C, et al. Contribution of genetic polymorphism in the renin-angiotensin system to the development of renal complications in insulin-dependent diabetes. J Clin Invest 1997;99:1585-95.
- 20 Hamroff G, Katz SD, Mancini D, Blaufarb I, Bijou R, Patel R, et al. Addition of angiotensin II receptor blockade to maximal angiotensinconverting enzyme inhibition improves exercise capacity in patients with severe congestive heart failure. *Circulation* 1999;99:990-2.

- 21 Hebert LA, Falkenhain ME, Nahman NS, Cosio FG, O'Dorisio TM. Combination ACE inhibitor and angiotensin II receptor antagonist therapy in diabetic nephropathy. *Am J Nephrol* 1999;19:1-6.
- 22 Russo D, Pisani A, Balletta MM, De Nicola L, Savino FA, Andreucci M, et al. Additive antiproteinuric effect of converting enzyme inhibitor and losartan in normotensive patients with IgA nephropathy. *Am J Kid Dis* 1999;33:851-6.
- 23 Ruilope LM, Aldigier JC, Ponticelli C, Oddou-Stock P, Botteri F, Mann JF, et al. Safety of the combination of valsartan and benazepril in patients with chronic renal disease. *J Hypertens* 2000;18:89-95.
- 24 Komers R, Cooper ME. Acute renal haemodynamic effects of angiotensin converting enyzme inhibition in diabetic hyperfiltration: the role of kinins. Am J Physiol 1995;268:F588-94.
- 25 Demeilliers B, Jover B, Mimran A. Contrasting renal effects of chronic administrations of enalapril and losartan on one-kidney, one clip hypertensive rats. *J Hypertens* 1998;16:1023-9.
- 26 Guidelines Subcommittee. 1999 World Health Organization-International Society of Hypertension guidelines for the management of hypertension. J Hypertens 1999;17:151-83.
- 27 Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. The sixth report of the joint national committee on prevention, detection, evaluation, and treatment of high blood pressure. Arch Intern Med 1997;157:2413-45.
- 28 Ramsay LE, Williams B, Johnston GD, MacGregor GA, Poston L, Potter JF, et al. British Hypertension Society guidelines for hypertension management 1999: summary. *BMJ* 1999;319:630-5.
- 29 Chaturvedi N, Sjolie A-K, Stephenson JM, Abrahamian H, Kelpes M, Castellarin A, et al. Effect of lisinopril on progression of retinopathy in people with type 1 diabetes. *Lancet* 1998;351:28-31.
- 30 Heart Outcomes Prevention Evaluation (HOPE) Study Investigators. Effects of ramipril on cardiovascular and microvascular outcomes in people with diabetes mellitus: results of the HOPE study and MICRO-HOPE substudy. *Lancet* 2000;355:253-9.

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Renal function-and how to assess it

The gold standard test for assessing renal function is the glomerular filtration rate.¹ Measuring this rate is a laborious process but is most useful for assessing renal function in patients whose serum creatinine concentration is at the upper limit of normal or in patients who develop early renal impairment secondary to treatment with non-steroidal anti-inflammatory drugs, lithium, or angiotensin converting enzyme inhibitors. The normal range is 80-120 ml/min.

A useful and practical surrogate marker for the glomerular filtration rate is creatinine clearance. Creatinine clearance measures the ability of the kidneys to clear creatinine from the circulation into the urine over a period of 24 hours. This is a much more accessible measure of renal function, but because the serum creatinine concentration is influenced by muscle mass and age (it increases with muscle bulk and decreases with age), creatinine clearance rates must be interpreted for the individual patient. Body builders have a tendency for high creatinine concentrations while frail elderly women may have misleadlingly low concentrations.

Most clinicians use serum creatinine concentrations as the most practical measure of renal function. Normal creatinine concentrations can be obtained even when the glomerular filtration rate has dropped by 50%, however, so it is fairly insensitive as an indicator of early renal insufficiency. Once serum creatinine concentrations are abnormal it can be assumed that there is measurable renal impairment (that is, more than half the filtering capacity of the kidneys has been lost).

Measuring the blood urea concentration alone also has limitations because it is influenced by protein metabolism, the state of dehydration, and the use of steroids, in addition to renal function. Thus patients with renal impairment can have relatively normal blood urea concentrations if they are grossly malnourished and not eating.

The Cockroft-Gault formula (mentioned in the paper) is a way of calculating the glomerular filtration rate without undertaking a 24 hour urine collection. The formula factors in age and body mass together with serum creatinine concentrations in an attempt to standardise the serum results and to be able to compare one person's renal function with another. It tends to be used more in research settings than in routine clinical practice as a way of improving the quality of data on renal function.

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 Cameron J, Greger R. Renal function and testing of function. In: Davison A, Cameron J, Grunfeld J-P, Kerr D, Ritz E, Winearls C, eds. Oxford textbook of clinical nephrology. 2nd ed. Oxford: Oxford Medical Publications, 1998.

Endpiece

Youth, day, old age and night

Youth, large, lusty, loving—youth full of grace, force, fascination,

- Do you know that Old Age may come after you with equal grace, force, fascination?
- Day full-blown and splendid—day of the immense sun, action, ambition, laughter,
- The Night follows close with millions of suns, and sleep and restoring darkness.
- Walt Whitman, 1881

Science commentary