acquired or congenital immune defects. In addition to immunosuppression, other factors including Epstein-Barr virus infection, chronic antigen stimulation, and proto-oncogenes, have been implicated in the pathogenesis of the different clinical and histopathological manifestations of AIDS related non-Hodgkin's lymphoma, whereas human herpes virus type 8 may be an infectious cofactor which is required for all forms of Kaposi's sarcoma.[5]

Our data indicate that patients cease to be at risk of Kaposi's sarcoma once immune function has been improved by combination therapy. Conversely, patients with a history of severe immunodeficiency continue to be at risk of non-Hodgkin's lymphoma, despite antiretroviral combination therapy. Although the initiation of carcinogenesis requires an immunodeficient state, the factors promoting the development of non-Hodgkin's lymphoma further along the causal chain do not seem to be related to immune function or are related to aspects not affected by antiretroviral combination therapy. Because of the large number of susceptible patients with a history of severe immunodeficiency, the fall in the incidence of non-Hodgkin's lymphoma will probably lag behind that observed for other opportunistic diseases. Non-Hodgkin's lymphoma will thus remain a relatively common complication among patients treated with antiretroviral combination therapy.

We thank the patients for participating.

Contributors: BL initiated the study, performed statistical analyses, and participated in writing the paper. AT discussed core ideas and participated in clinical data collection and writing the paper. ME initiated the study, supervised statistical analyses, and wrote the first draft of the paper. BL and ME are the guarantors for the study.

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Competing interests: None declared.

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Randomised controlled trial of long term efficacy of captopril on preservation of kidney function in normotensive patients with insulin dependent diabetes and microalbuminuria

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In patients with insulin dependent diabetes, angiotensin converting enzyme inhibition delays the progression from microalbuminuria to diabetic nephropathy, but previous studies have been too short to show a preservation of kidney function.[1–3] We assessed the effectiveness of angiotensin converting enzyme inhibition on preservation of kidney function in an 8 year prospective, randomised controlled trial.

Patients, methods, and results

Forty four normotensive patients with insulin dependent (type I) diabetes and persistent microalbuminuria (30-300 mg/24 h) were enrolled as previously described in detail.[1] The treatment group (n = 21) was given captopril (100 mg/24 h) and bendrofluazide (2.5 mg/24 h). The 23 remaining patients were left untreated. Diabetic nephropathy was defined as albuminuria persistently > 300 mg/24 h. Glomerular filtration rate was measured annually with Crom EDTA plasma clearance over 4 hours.[1]

After 4 years two patients in each group were excluded because they did not attend follow up sessions. Four of the patients in the control group started antihypertensive treatment with diuretics, β blockers, or a calcium channel blocker. Three patients in the treatment group were changed from bendrofluazide to frusemide because of oedema or diastolic blood pressure > 95 mm Hg. After 8 years 16 of the 21 patients in the treatment group and two patients from the control group were subsequently investigated after a treatment pause of 2 months.

The proportion of patients who progressed to diabetic nephropathy was 40% (9/23) in the control group and 10% (2/21) in the captopril group (survival analysis P = 0.019). In the captopril group there was a significant increase in urinary albumin excretion (P < 0.001) during the treatment pause. In six (38%) of the 16 patients albuminuria exceeded 300 mg/24 h.

Glomerular filtration rate in the captopril group declined from 126 (24) at baseline to 114 (23) ml/min after 8 years but rose again to 126 (21) during the pause in treatment (table). Follow up values of glomerular filtration rate measured during the treatment pause were therefore used whenever available. The decline in mean glomerular filtration rate (ml/min) was 11.8 (95% confidence interval 1.2 to 22.0; *t* test P value 0.03) and 1.4 (−4.9 to 7.7; P = 0.65) in the control and captopril group, respectively (P = 0.09 between the groups). The fall in glomerular filtration rate during the 8 year study period in the

Mean glomerular filtration rates (ml/min) in normotensive patients with insulin dependent diabetes at baseline, after 8 years' follow up, and during pause in treatment in captopril and control groups

Patient No	Captopril group			Control group		
	Baseline	8 Years	8 Years + pause	Baseline	8 Years	8 Years + pause
1	100	101	120	141	157*	135*
2	129	125	131	156	131	—
3	153	—	—	131	123	—
4	96	75	—	96	39*	47*
5	114	99	122*	87	84	—
6	112	98	116*	132	106*	—
7	105	105*	112*	154	68*	—
8	127	145*	140*	151	143	—
9	140	127	144	150	161	—
10	108	70	102*	117	106	—
11	169	—	—	111	—	—
12	144	120	121	148	144	—
13	117	104	—	118	119	—
14	110	100	97	108	94*	—
15	96	108	—	126	141	—
16	171	151	166	142	168	—
17	164	156	161*	145	130	—
18	128	106	103	146	140	—
19	104	116	105	122	—*	—
20	130	135	146	117	91*	—
21	132	122	128	120	112*	—
22	—	—	—	136	130*	—
23	—	—	—	120	118	—
Mean (SD)	126 (24)	114 (23)	126 (21)	129 (18)	119 (32)†	—

*Patient developed diabetic nephropathy during 8 years of follow up or during treatment pause.
†Difference from baseline significant at P=0.03.

eight control patients who developed nephropathy was 27.3 (3.7 to 51.0; P = 0.03) while glomerular filtration rate increased by 3.8 (−3.5 to 11.0) in the six patients treated with captopril with urinary albumin excretion >300 mg/24 h during the treatment pause (P = 0.02 between the groups). Haemoglobin A_{1c} and blood pressure did not differ between the two groups at any time during the study.

Comment

Our study has shown that the beneficial effect of angiotensin converting enzyme inhibition in the prevention of diabetic nephropathy is long lasting and associated with preservation of normal glomerular filtration rate. To obtain a valid determination of the rate of decline in glomerular filtration rate the applied glomerular filtration rate method should have a good accuracy and precision and the observation period should exceed 2 years.[4] These requirements have been fulfilled in our study in contrast with previous studies.[2,3] The second part of the study showed a return in glomerular filtration rate to the values before treatment after 2 months of withdrawal of antihypertensive treatment. The temporary fall in glomerular filtration rate in the intervention group was therefore regarded as a reversible haemodynamic phenomenon. Patients with persistent microalbuminuria at follow up had a stable normal glomerular filtration rate.[5] The clinically significant effect of angiotensin converting enzyme inhibition on preservation of normal glomerular filtration rate was related to prevention of progression from microalbuminuria to diabetic nephropathy in patients with insulin dependent diabetes.

Contributors: HHP had the original idea for the study. ERM and HHP were responsible for conducting the study and interpreting the results and are guarantors. ERM and EH conducted the clinical evaluation during the 8 years of study. HPH and ERM conducted the clinical evaluation during the treatment pause. UMS performed the assessments of glomerular filtration rate. All authors participated in the interpretation of the results and reporting.

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Competing interests: None declared.

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Corrections and clarifications

Ingestion of mouthwash by children
This letter by Tamsin Wade and Alison Gammon (17 April, p 1078) wrongly stated that "The mouthwash … was a supermarket 'extra strength' own brand which contains 37% alcohol." It should have stated that this type of mouthwash "may contain up to 37% alcohol." The manufacturers of the mouthwash have informed the authors that it contained about 20-25% alcohol, which is still far more than what one would expect a child to have access to.

Book reviews
In William Stoney's review of Ira M Rutkow's *American Surgery: An Illustrated History* (17 April, p 1082) William Stewart Halsted's surname was spelt incorrectly. In Alex Brooks' review of Jared Diamond's *Guns, Germs and Steel* (8 May, p 1294) the Inca emperor Atahualpa's name was spelt incorrectly and his empire was wrongly described as Aztec.

Website of the week
In his review of the NHS Direct website (24 April, p 1152) Douglas Carnall gave the wrong number for NHS Direct's telephone service: it is 0845 4647 (or 0845 4NHS on alphanumeric telephones). A copy of Tony Blair's speech about government plans to expand the service is available at the No 10 website (www.number-10.gov.uk/public/news/index.html).

Obituaries
In the obituary of Professor Henry Taylor Howat (8 May, p 1292) Professor Howat's surname was spelt incorrectly.