

	Placebo	Active	p Value
Mean No of tender points	14.1	10.6	<0.005*
No of patients with improved pain or sleep (visual analogue scores)	27	53	0.0052†

\*Wilcoxon rank sum test. †Paired *t* test.

### Comment

Fibrositis (primary fibromyalgia) is a controversial condition but is becoming increasingly accepted.<sup>4</sup> It is difficult to treat. We showed that the homeopathic medicine *R toxicodendron* 6c was effective for a selected subgroup of patients with fibrositis. The improvement in tenderness, which is the best discriminator of

fibrositis,<sup>5</sup> was particularly distinct. The improvement experienced by our patients while receiving active treatment was at least as great as that reported for any other treatment that has been assessed double blind.

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## Incidence of transient nephrotic syndrome during pregnancy in diabetic women with and without pre-existing microalbuminuria

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Considerably different changes in renal protein excretion have been reported in diabetic women during pregnancy.<sup>1,2</sup> In pregnant diabetics with pre-existing macroproteinuria ( $\geq 0.5$  g protein in 24 hour urine samples) there is often a clear increase in the proteinuria, often resulting in development of the transient nephrotic syndrome.<sup>3,4</sup> In diabetic women with albumin excretion <30 mg/day (normoalbuminuria) or 30-250 mg/day (microalbuminuria) before pregnancy, however, the syndrome is rarely observed during pregnancy. We determined to what extent microalbuminuria (incipient diabetic nephropathy) affects the alterations of renal protein excretion and the variables of kidney function during and after pregnancy and the incidence of the syndrome during pregnancy in these women.

### Patients, methods, and results

We investigated seven pregnant women with type I diabetes and pre-existing normoalbuminuria (mean (SD) age 22 (5) years, mean (SD) duration of diabetes 10 (4) years) and seven pregnant type I diabetics with pre-existing microalbuminuria (mean (SD) age 23 (5) years, mean (SD) duration of diabetes 11 (3) years). All women delivered between 36 and 40 weeks' gestation. Before one woman became pregnant, during weeks 12, 24, 28, 32, and 36-40 of pregnancy, and in weeks 4, 12, and 24 after delivery we measured serum creatinine concentration (autoanalyser), creatinine clearance, glycated haemoglobin concentration (Biorad), blood

pressure (Riva Rocci), albumin concentration (immunodiffusion), and total protein concentration (Biuret method) in 24 hour urine samples.

In the seven diabetic women with pre-existing normoalbuminuria there was a 5.9-fold increase in albumin and a 5.7-fold increase in total protein excretion in urine during pregnancy. In the seven diabetic women with microalbuminuria we found a 5.9-fold increase in albumin excretion and a 10.0-fold increase in total protein excretion. After delivery the protein excretion fell to the values before pregnancy in all patients. The difference between the absolute increase of proteinuria in the two groups was significant ( $p < 0.005$ , unpaired *t* test). Blood pressure and metabolic control did not differ significantly during pregnancy in both groups (table), and the variables of renal function did not differ between normoalbuminuric and microalbuminuric women. The transient nephrotic syndrome with protein excretion >3 g in 24 hour samples of urine (3.178 g, 4.907 g, and 4.761 g) occurred in three of the seven women with pre-existing microalbuminuria but in none of the seven with pre-existing normoalbuminuria.

### Comment

The transient nephrotic syndrome is rare in pregnant diabetics without pre-existing heavy proteinuria and decreased glomerular filtration rate as well as in healthy pregnant women.<sup>1</sup> The extent to which albumin excretion before pregnancy influences the increase in proteinuria and the alterations of the kidney function during pregnancy has not, to our knowledge, been previously investigated in diabetic women.

In our patients with normoalbuminuria the increase in proteinuria during pregnancy remained within the physiological range seen in healthy pregnant women.<sup>4,5</sup> In the diabetic women with pre-existing microalbuminuria the increase in proteinuria during pregnancy was significantly higher. Obviously the glomerular basement membrane develops a greater permeability for protein during pregnancy in diabetic women with pre-existing microalbuminuria in com-

Urinary protein excretion and renal function before, during, and after pregnancy. Values are means (SD)

	Diabetics with normoalbuminuria			Diabetics with microalbuminuria		
	Before pregnancy	Third trimester of pregnancy	24 Weeks after delivery	Before pregnancy	Third trimester of pregnancy	24 Weeks after delivery
Albumin in urine (mg/day)	12 (3)	71 (34)	13 (4)	80 (45)	478 (247)	114 (74)
Total protein in urine (g/day)	0.073 (0.056)	0.417 (0.142)	0.096 (0.073)	0.233 (0.186)	2.353 (1.211)	0.239 (0.107)
Serum creatinine ( $\mu$ mol/l)	79 (13)	68 (10)	85 (7)	71 (15)	63 (9)	79 (13)
Creatinine clearance (ml/s)	1.72 (0.18)	2.07 (0.118)	1.72 (0.17)	1.83 (0.22)	2.12 (0.40)	1.80 (0.28)
Blood pressure (mm Hg)	120 (9)/79 (5)	121 (7)/77 (5)	118 (7)/79 (6)	118 (8)/80 (7)	118 (6)/79 (6)	117 (6)/78 (5)
Glycated haemoglobin (%)	6.2 (1.1)	4.7 (0.8)	6.2 (0.6)	6.8 (0.6)	5.4 (0.5)	6.8 (0.5)

parison with normoalbuminuric women. The variables in renal function did not differ during and after pregnancy in both groups of patients. Serum creatinine concentration and creatinine clearance showed the same kind of alterations that are generally observed in healthy pregnant women.<sup>5</sup>

The nephrotic syndrome occurred temporarily during the third trimester of pregnancy in three of the seven diabetic women with pre-existing microalbuminuria but in none of the patients with normoalbuminuria. The occurrence of the transient nephrotic syndrome in these pregnant women must be related to the pre-existing incipient diabetic nephropathy. All three patients with the nephrotic syndrome had peripheral oedema. In all cases a healthy baby was delivered by caesarean section.

In conclusion, during pregnancy a greater increase in renal protein excretion, associated with a higher risk of the transient nephrotic syndrome can be seen in diabetic women with pre-existing microalbuminuria compared with those with normoalbuminuria.

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## Uptake of influenza vaccination by patients with serious cardiac disease

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Although influenza vaccines are poor at preventing infection, they reduce the incidence of bronchopneumonia, hospital admissions, and mortality in those most at risk.<sup>1</sup> The Department of Health recommends annual vaccination for patients, especially elderly patients, with chronic pulmonary, cardiac, or renal disease; those with endocrine diseases such as diabetes; and those who are immunosuppressed.<sup>2</sup> Little is known, however, about the extent of vaccination among these target groups. We report results of a survey of influenza vaccination in patients who required cardiac operations.

### Patients, methods, and results

We sent a postal questionnaire to the 251 patients aged 45 and over who were waiting for a cardiac operation and 349 randomly selected patients of similar age who had had a cardiac operation within the previous two years. Completed questionnaires were received from 565 (94%) people; 14 people had died, and only 21 questionnaires were not returned. A concurrent review of medical notes provided additional medical details about 437 patients.

Altogether 145 of the respondents had been offered vaccination in the past, and 122 had accepted it. Thirty three had requested a vaccination. Only 85, however, had been vaccinated within the past five years; of these, 28 had been vaccinated only once, 19 twice, 17 three times, eight four times, and 13 annually. Fifty (12%) of the 425 patients aged 45-64 and 35 (25%) of those aged  $\geq 65$  had been vaccinated during the past five years. There was no significant difference in the vaccination rate between men and women. Influenza vaccine had been given to only three of 57 people who had diabetes or chronic chest, endocrine, renal, or multisystem disease in addition to their cardiac problem. Eleven (8%) of the 138 patients who had had cardiac disease for less than two years and 50 (17%) of the 299 who had had it for more than two years had been vaccinated.

The patients fell into six diagnostic categories: the proportions who had been vaccinated within the past five years were 50 (15%) of the 335 with coronary artery disease; six (10%) of the 63 with aortic valve disease; 15 (19%) of the 80 with mitral valve disease; two (12%) of the 17 with mixed valvular disease; eight (19%) of the

41 with both coronary artery disease and valvular disease; and four (14%) of the 29 with rarer lesions. Vaccinations had been offered by the general practitioner (69/145), an employer (67), nurse (4), others (3), or a hospital doctor (2). The offer had been made during a consultation in 65 cases, a general notice in 42, word of mouth in 34, and a postcard in four.

### Comment

Influenza epidemics result in increased death rates, particularly in older patients and those with chronic disease or cancer.<sup>3</sup> During such outbreaks the mortality is 0-1% for all patients aged  $\geq 45$  with cardiovascular disease and 0-9% for those with additional respiratory disease. Admissions to hospital and deaths associated with pneumonia and influenza can be significantly reduced by vaccination,<sup>4</sup> and it is unfortunate that only 17% of patients who had had serious cardiac disease for over two years, for whom considerable resources are required, had been vaccinated within the previous five years. In the United States the National Institute of Allergy and Infectious Diseases reviewed more than 40 medically important diseases and ranked influenza among the top five in terms of the cost efficacy of an accelerated programme to develop vaccine.<sup>5</sup>

It is encouraging that 84% of the group who had been offered vaccination had accepted it and that several patients had requested it. Remarks made by many other respondents indicated the need to educate patients and professionals about the indications for and efficacy and safety of influenza vaccination. Target groups could be identified in general practice by using the age-sex and chronic disease registers,<sup>5</sup> and offers of vaccination could be attached to repeat prescriptions for the groups most at risk. Specialist outpatient clinics also provide opportunities to educate patients.

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