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- No letter should be more than 400 words.
- For letters on scientific subjects we normally reserve our correspondence columns for those relating to issues discussed recently (within six weeks) in the *BMJ*.
- We do not routinely acknowledge letters. Please send a stamped addressed envelope if you would like an acknowledgment.
- Because we receive many more letters than we can publish we may shorten those we do print, particularly when we receive several on the same subject.

## Overprescribing

SIR, — Yesterday I met four of my grandchildren at the airport on their return from a holiday on the continent. I had been warned that two of them, twin boys aged 11, had been taken ill two days previously with what appeared to be feverish upper respiratory infections and were under treatment prescribed by a local practitioner. They emerged looking well and cheerful, carrying a plastic bag containing erythromycin 250 mg, twice daily for eight days for one boy, together with a drug described as “anti-inflammatory,” which I was not able to identify, 30 doses of which were dispensed, though only four were to be taken; amoxicillin 500 mg twice daily for six days for the other boy, plus an antiemetic because he had complained of feeling sick; for both, a powder aerosol to relieve the pain of a sore throat, to be used four or five times daily; and finally, for both, paracetamol to be taken three or four times daily while fever persists. Interestingly, these had been prescribed initially by a locum, and confirmed by the principal on a second visit.

Their NHS general practitioner agreed with me that they should discontinue all drugs. The only one that either of us would be likely to have prescribed was paracetamol. Evidently the marketplace economics of the medical care system in the country where they had spent their holiday does less to encourage cost effectiveness and discrimination in prescribing than does the social conscience of our NHS.

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## Transient nephrotic syndrome during pregnancy in diabetic women

SIR, — We think that two points should be made concerning the paper by Drs G Biesenbach and J Zazgornik on the transient nephrotic syndrome during pregnancy in diabetic women.<sup>1</sup>

The term “the nephrotic syndrome,” although vague, should be used to describe patients in whom proteinuria lowers the serum albumin concentration below a value at which normal renal perfusion and salt excretion can be maintained. The resultant expansion of body sodium and water is usually visible as oedema. From this arises a common definition of the nephrotic syndrome as the presence of detectable oedema (usually dependent), proteinuria of >3.0 g protein in 24 hour urine samples, and a serum albumin concentration of <30 g/l.<sup>2</sup> This allows distinction between a patient with persistent and profuse but symptomless proteinuria and one who requires specific management.

Drs Biesenbach and Zazgornik found that three

of seven pregnant diabetic women with microalbuminuria before pregnancy developed proteinuria of >3 g protein in 24 hour urine samples. They state that these patients also had peripheral oedema. No mention is made, however, of the serum albumin concentrations, nor is the presence or absence of oedema in the other 11 patients detailed. Oedema is extremely common in normal pregnancy, with one study finding dependent oedema in 50% of pregnant women.<sup>3</sup> Diabetics have an increased incidence of polyhydramnios and “large for dates” infants and so may therefore have a greater risk of developing dependent oedema. Unfortunately, no details of the pregnancies or whether the increase in proteinuria led to an alteration in management are given. The use of the term the nephrotic syndrome and the implication of a distinct entity (from increased urinary protein loss) is therefore questionable.

We also doubt the authors’ statement that “the glomerular basement membrane develops a greater permeability for protein excretion during pregnancy in diabetic women with pre-existing microalbuminuria.” In non-diabetic women pregnancy causes an increased urinary protein excretion.<sup>4</sup> Likewise, diabetics with or without microalbuminuria show an increase in glomerular protein loss during exercise.<sup>5</sup> Although still to be explained, these findings are usually attributed to changes in intrarenal haemodynamics, leading to raised intraglomerular filtration pressure. As the study of Drs Biesenbach and Zazgornik gives the expected changes in creatinine clearance one would assume that the usual pregnancy related increase in glomerular filtration rate occurred. The development of increased proteinuria may simply be a reflection of hyperfiltration in patients who already have a leaky glomerular membrane. This is also consistent with the observed return to the levels of proteinuria before pregnancy.

The authors have shown that diabetic women with microalbuminuria leak more protein when they are pregnant and that some develop oedema. The same can be said of non-diabetic women and diabetic women with overt diabetic nephropathy.<sup>6</sup> To introduce the label of the transient nephrotic syndrome of pregnancy and imply a specific pregnancy related increase in permeability of the glomerular basement membrane in diabetic women with microalbuminuria is not justified by the evidence presented.

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- 1 Biesenbach G, Zazgornik J. Incidence of transient nephrotic syndrome during pregnancy in diabetic women with and without pre-existing microalbuminuria. *Br Med J* 1989;299:366-7. (5 August.)
- 2 Cameron JS. Proteinuria and the nephrotic syndrome. In: Weatherall D, Ledingham JGG, Warrell DA, eds. *Oxford textbook of medicine*. Vol 2. Oxford: Oxford University Press, 1987:18-58.

- 3 Hytton FE, Thompson AM, Taggart N. Total body water in normal pregnancy. *Obstetrics and Gynaecology of the British Commonwealth* 1966;76:553-61.
- 4 Elrad H, Gleicher N. Physiologic changes in normal pregnancy. In: Gleicher N, ed. *Principles of medical therapy in pregnancy*. New York: Plenum Press, 1985:43.
- 5 Mogenson CE, Vittinghus E. Urinary albumin excretion during exercise in juvenile diabetes. A provocation test for early abnormalities. *Scand J Clin Lab Invest* 1975;35:295-300.
- 6 Kitzmiller JL, Brown ER, Phillippe M, et al. Diabetic nephropathy and perinatal outcome. *Am J Obstet Gynecol* 1981;141:741-51.

AUTHORS’ REPLY, — We agree with Dr S C Bain and Sister B R Rowe that the use of the term “the nephrotic syndrome” in our pregnant diabetic women with microalbuminuria before pregnancy who developed proteinuria of >3 g protein in a 24 hour urine sample is a matter for discussion. The three pregnant women showed a borderline serum albumin concentration of 29 g/l, 29 g/l, and 30 g/l and concomitant peripheral oedema. Therefore, in our opinion, the term the transient nephrotic syndrome could be used. The increase in urinary protein excretion to >3 g in a 24 hour urine sample occurred at 32-34 weeks’ gestation, and in all three cases premature delivery was performed at 36-38 weeks’ gestation. As the duration of pronounced proteinuria was limited to a few weeks in the third trimester the dynamic in the development of the nephrotic syndrome could be variable in the different cases. Only one pregnant woman without the nephrotic syndrome also showed important peripheral oedema; in this patient a “large for dates” infant was shown on ultrasonography. In all other cases there were no signs of fetal macrosomia.

We believe that our statement that “the glomerular basement membrane develops a greater permeability for protein excretion during pregnancy in diabetic women with pre-existing microalbuminuria” is well documented in our earlier study.<sup>1</sup> In pregnant diabetic women with pre-existing normoalbuminuria the increase in proteinuria is comparable with the increase in proteinuria during pregnancy in non-diabetic women. In pregnant diabetic women with pre-existing microalbuminuria the protein excretion in urine increases significantly, though the pregnancy related increase in glomerular filtration rate is the same in the two patient groups. In pregnant diabetic women with pre-existing impaired renal function and hypertension a transient increase in proteinuria with the highest values in the third trimester can be seen in some cases despite a further decrease of the glomerular filtration rate during pregnancy.

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- 1 Biesenbach G, Stoger H, Zazgornik J. Changes in proteinuria and renal function in female type I diabetics during and after pregnancy dependent on the stage of pre-existing diabetic nephropathy. *Klin Wochenschr* 1987;65:1048-53.