As is so often the case in medicine, the more cumbersome the diagnostic label the more likely that it is being used to hide our ignorance of its pathogenesis.

References

- Meadow, S. R., Glasgow, E. F., White, R. H. R., Moncrieff, M. W., Cameron, J. F., and Ogg, C. S. (1972). Schönlein-Henoch nephritis. *Quarterly Journal of Medicine*, **41**, 241-258.
- Pedersen, F. K., and Petersen, E. A. (1975). Varicella followed by glomerulonephritis. Treatment with corticosteroids and azathioprine resulting in recurrence of varicella. *Acta paediatrica Scandinavica*, **64**, 886-890.

S. R. MEADOW
University of Leeds,
Department of Paediatrics and Child Health,
27 Blundell Street,
Leeds LS1 3ET

Slow-release theophylline preparations

Sir,
The study by McKenzie and Baillie (*Archives*, 1978, **53**, 943) indicates the growing appreciation that theophylline has the potential to control the symptoms of chronic asthma when serum levels are maintained at between 10 and 20 µg/ml. As they suggest, sustained-release theophylline formulations offer therapeutic advantage by allowing more stable serum theophylline concentrations; this results in longer intervals between doses than are possible with either cromoglycate or β-agonist bronchodilators. Not all sustained-release theophylline preparations are completely and reliably absorbed, however, and each product differs in its absorption characteristics even when absorption is complete (Weinberger *et al.*, 1978).

The degree to which a theophylline formulation maintains acceptably stable levels relates to both the rate of absorption of the product and the rate of elimination of the individual. As children have average half-lives of elimination of 3-7 hours, slowly absorbed products are particularly important if excessive fluctuations in serum theophylline concentration are to be avoided. The clinical importance of lessening these fluctuations has been shown by the decrease in bronchodilatation (Levy and Koysooko, 1975), and blocking of exercise-induced bronchospasm that is parallel to decreasing serum concentration (Pollock *et al.*, 1977). While McKenzie and Baillie argue for the convenience of 12-hour dosing with the sustained-release preparations, their data (McKenzie and Baillie, 1978) and ours (Weinberger *et al.*, 1978) suggest that 8-hour dosing may often be more appropriate except for the slowest of the reliably and completely absorbed sustained-release preparations or for patients with slow rates of elimination.

The rate of elimination of theophylline also determines dosage (Jenne *et al.*, 1976; Ginchansky and Weinberger, 1977). The problems that can result from the variable dosage requirements for theophylline were illustrated in a study that compared theophylline with cromoglycate

(Cromolyn, Intal) performed at the Hammersmith Hospital and at two residential treatment centres for asthma in Denver (Hambleton *et al.*, 1977). Whereas all of the patients in Denver tolerated theophylline, 6 patients at the Hammersmith Hospital did not, and therefore could not enter the study. The difference can be attributed to the manner in which theophylline dosage was determined. Each patient in Denver was given an individual theophylline dose while an 'average' dose, similar to that recommended by McKenzie and Baillie, was initiated in all the Hammersmith Hospital patients. The resulting intolerance in some patients was predictable (Wyatt *et al.*, 1978).

We have found that clinical titration using serum theophylline measurement as a guide gives a high degree of safety and provides the greatest likelihood of efficacy in the management of chronic asthma (Ekwo and Weinberger, 1978; Hendeles *et al.*, 1978).

References

- Ekwo, E., and Weinberger, M. (1978). Evaluation of a program for the pharmacologic management of children with asthma. *Journal of Allergy and Clinical Immunology*, **61**, 240-247.
- Ginchansky, E., and Weinberger, M. (1977). Relationship of theophylline clearance to oral dosage in children with chronic asthma. *Journal of Pediatrics*, **91**, 655-660.
- Hambleton, G., Weinberger, M., Taylor, J., Cavanaugh, M., Ginchansky, E., Godfrey, S., Tooley, M., Bell, T., and Greenberg, S. (1977). Comparison of cromoglycate (Cromolyn) and theophylline in controlling symptoms of chronic asthma. *Lancet*, **1**, 381-385.
- Hendeles, L., Weinberger, M., and Wyatt, R. (1978). Guide to oral theophylline therapy for the treatment of chronic asthma. *American Journal of Diseases of Children*, **132**, 876-880.
- Jenne, J. W., Nagasawa, H. T., and Thompson, R. D. (1976). Relationship of urinary metabolites of theophylline to serum theophylline levels. *Clinical Pharmacology and Therapeutics*, **19**, 375-381.
- Levy, G., and Koysooko, R. (1975). Pharmacokinetic analysis of the effect of theophylline on pulmonary function in asthmatic children. *Journal of Pediatrics*, **86**, 789-793.
- McKenzie, S., and Baillie, E. (1978). Serum theophylline levels in asthmatic children after oral administration of two slow-release theophylline preparations. *Archives of Disease in Childhood*, **53**, 943-946.
- Pollock, J., Kiechel, F., Cooper, D., and Weinberger, M. (1977). Relationship of serum theophylline concentration to inhibition of exercise-induced bronchospasm and comparison with Cromolyn. *Pediatrics*, **60**, 840-844.
- Weinberger, M., Hendeles, L., and Bighley, L. (1978). The relationship of product formulation to absorption of oral theophylline. *New England Journal of Medicine*, **299**, 852-857.
- Wyatt, R., Weinberger, M., and Hendeles, L. (1978). Oral theophylline dosage for the management of chronic asthma. *Journal of Pediatrics*, **92**, 125-130.

MILES WEINBERGER
University of Iowa,
Department of Pediatrics,
Pediatric Allergy and Pulmonary Division,
Iowa City,
Iowa 52242, USA