the same plasma extract containing added ara-A and adenosine gave constant peak height ratios though the absolute detector response decreases following numerous sample analysis. Absolute recovery of ara-A from plasma determined by the ratio of peak height of known amounts added to plasma (concentration range 0.2–10 μg/ml) to a known amount of pure nucleoside was found to be 60–68% (range for five determinations), though the use of an internal standard (adenosine) added to plasma before extraction will overcome changes in the absolute recovery from sample to sample. The percentage recovery of adenosine from plasma was found to be the same as ara-A since the peak height ratio resulting from adding known amounts of these two substances to plasma was identical to that obtained after derivatising the same quantities of pure nucleosides.

More rigorous purification procedures (and more time consuming) for extraction of plasma by perchloric acid or trichloracetic acid protein precipitation followed by prechromatography on ion exchange column prior to derivatisation will give a cleaner extract for gas chromatographic analysis with a limit of sensitivity of less than 0.05 μg/ml. Furthermore, the hypoxanthine analogues did not give a chromatographic derivative under the conditions used and hence the presence in plasma of the deaminated metabolite of ara-A would not interfere with the assay. This method therefore will allow the analysis of ara-A in plasma, and with appropriate extraction procedures could be extended to detection of ara-A in urine and other tissues.

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J. BOUTAGY

MRC Unit and University Department of Clinical Pharmacology, Radcliffe Infirmary, Oxford

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A METHOD FOR OBTAINING SALIVA SAMPLES FROM INFANTS AND YOUNG CHILDREN

Routine measurement of plasma concentrations of drugs such as phenytoin and phenobarbitone provides a useful guide to optimal therapy (Buchtal, Svensmark & Schiller, 1960). It is possible to predict plasma concentrations of these drugs by measurement in saliva samples since there is a constant relationship between saliva and plasma concentration (Bochner, Hooper, Sutherland, Eadie & Tyrer, 1974). Saliva sampling obviates the need for venepuncture, need not be supervised and is a relatively simple procedure in adults and older children. However, infants and toddlers, in whom one particularly wishes to avoid venepuncture, will not readily provide a sample and we should like to describe a simple method of overcoming this problem.

A little citric acid in crystal form combined with Vivonex strawberry flavouring (9 : 1 mixture) is offered to the child, who will either taste the mixture himself or allow his mother to put a pinch of it on to his tongue. The unpleasant tartness of the acid is only short-lived and saliva soon flows readily. Saliva is aspirated by means of a disposable mucus extractor (Sterilin) from behind the lower lip and, if the child permits, from the buccal cavity and beneath the

tongue. The time expended depends upon the volume required: 1–2 ml can usually be obtained within 5 minutes. Occasionally a child will not co-operate and his head has to be held, but parents always agree that the procedure is much more pleasant than venepuncture.

We have used this method on more than seventy separate occasions and have never failed to obtain a sample. It has also been possible for parents to use this method at home and to post the sample to the laboratory. Citric acid and flavouring have not been found to interfere with the assay of phenytoin and phenobarbitone using either gas chromatography or enzyme immunoassay. This sampling method would seem generally applicable whenever it is appropriate to measure saliva drug concentrations in small children. However, to avoid contamination of the sample by unswallowed drug, it is advisable, unless coated tablets have been used, to delay sampling for at least 3 h after a dose.

C.J. BACON, J.C. MUCKLOW, A. SAUNDERS, M.D. RAWLINS & J.K.G. WEBB

Departments of Child Health and Pharmacological Sciences, The University of Newcastle upon Tyne, Newcastle upon Tyne

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EVALUATION OF ONCE A DAY ALLOPURINOL ADMINISTRATION IN MAN

The allopurinol 100 mg tablet has been in clinical use now for about 12 years. The most commonly used dosage is 300 mg, given as divided doses through the day. Although the serum half life of allopurinol itself is short, about 1.25 h, the half life of its active metabolite, oxipurinol, is much longer, of the order of 28–30 h (Elion, Kovensky, Hitchings, Metz & Rundles, 1966). As a consequence of this, it has been suggested that allopurinol may be administered as a single daily dose. When 300 mg of allopurinol given in a single dose was compared with 100 mg given three times a day, it was found to be equally effective in reducing and controlling uric acid levels and also equally well tolerated (Brewis, Ellis & Scott, 1975; Rodnan, Robin, Tolchin & Elion, 1975; Zollner & Griebsch, 1974). A single daily dose regime may be expected to enhance treatment adherence, a factor which is especially important for drugs like allopurinol, which require long-term continuous usage for maximum patient benefit. Although it has been established that a 300 mg dose of allopurinol may be taken as a single tablet, no reports are available showing the effect of giving up to 600 mg allopurinol as a single dose. The aim of this study was to assess patient acceptability of allopurinol when given in single daily doses of 400–600 mg.

Thirty-three patients, with no known renal impairment, who were currently taking allopurinol in doses of 400–600 mg daily and who had been on that dose for at least 3 weeks, entered the study. The mean duration of treatment with allopurinol was 2.9 years (range, 1 month – 10 years) and mean duration of treatment on present dosage 1.9 years (range, 1 month – 10 years).

An initial blood sample was taken for uric acid, creatinine and urea estimations and the patients were asked to comment on their usual dosage regime. They were then asked to take their tablets in a single daily dose, preferably immediately after breakfast. After 2 weeks of the single daily dosage regime, a second blood sample was taken and the patient questioned again. Of the 33 patients, 32 were diagnosed as having gout and one had renal lithiasis with a raised serum urate level. The distribution of dosages was as follows: 26 patients were taking 400 mg daily, 1 was taking 500 mg daily and 6 were taking 600 mg daily. The only side effect volunteered at the first visit was occasional giddiness by one patient. No further side