

Walle, 1986). Differences in gut lumen or gut wall metabolism or in the extent of oral absorption between the two isomers are more likely possibilities. The AUC (0–24 h) values in Table 1 are consistent with a much poorer availability of the E isomer compared with the Z isomer. There is little known, however, about the isomer specificity of gut lumen or gut wall metabolism or of drug absorption.

In conclusion, not only is clomiphene a mixture of two isomers with different pharmacodynamics, but relative plasma concentrations of the two isomers change with time after dosage and with route of administration.

This study was supported by Merrell-Dow Pharmaceuticals, Australia, Pty Ltd.

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Received 16 August 1988,
accepted 9 December 1988

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Odorous urine in man after asparagus

It has been recognized for many years that after eating asparagus, some humans produce odorous urine. Thus, in the United Kingdom, this characteristic has been found to occur in 46 (40%) out of 115 individuals (Allison & McWhirter, 1956) and in 346 (43%) out of 800 other subjects (Mitchell & Waring, 1987). S-methyl thioacrylate and S-methyl-3 (methylthio) thiopropionate have been postulated to be the odour-causing compounds but the metabolic pathway leading to their formation was not identified (White, 1975).

Ability or not to produce odorous urine indicates a human genetic polymorphism (autosomal dominant gene) which might have potential implications for the therapeutic efficacy and/or toxicity of drugs that are metabolized similarly to asparagus. Owing to the lack of data concerning this polymorphism in France, we investigated it in the French population.

One hundred and three French citizens (100

Caucasians, 2 Asians and 1 black) from three geographically distinct areas (Paris, $n = 36$; Strasbourg, $n = 29$; Toulouse, $n = 38$) volunteered for the study. They were all members of the medical staffs of the Pharmacological Departments or students in medicine or pharmacy of the three universities. The subjects (age: 35.8 ± 1.1 years (18–61), weight: 63.8 ± 1.1 kg (42–93), 53 males, 66 non smokers) were not taking any drug, or asparagus or cabbage during the 2 days prior to the study and were not allowed to smoke or to drink coffee, tea or alcoholic beverages on the day of the experiment. After they had voided urine at 09.00 h, asparagus (five sticks, approximately 60 g) was administered to the fasting volunteers together with 250 ml of water. Urine was collected 1 and 3 h later and checked for the characteristic odour.

All volunteers (100%) were found to produce odorous urines. Thus no genetic polymorphism could be detected among the investigated French

population and especially among the 100 Caucasian subjects. Thus, in the country where Proust (1913) wrote 'mon ravissement était devant les asperges qui jouaient . . . comme une féerie de Shakespeare à changer mon pot de chambre en vase à parfum', production of odorous urine after asparagus consumption appears to be the general rule.

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Received 12 December 1988,
accepted 13 January 1989

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Asparagus and malodorous urine

I read with interest the findings of the French investigators reported in the preceding letter (Richer *et al.*, 1989). It is indeed a curiosity that the ingestion of asparagus imparts a strong characteristic odour to the urine whereas other vegetables apparently do not.

That some individuals excreted this malodorous urine was known to the late Professor W. V. Thorpe (University of Birmingham) who exploited this peculiarity during the 1930s in his practical classes to demonstrate interindividual variation to students. This common knowledge of variability remained anecdotal and was not documented in the literature until 1956 (Allison & McWhirter, 1956). The phenomenon was unfortunately regarded as an amusing though unimportant oddity; its investigation a triviality rather than serious science. Even in relatively recent times such information has been regarded as trifling. In McKusick's tome on Mendelian Inheritance a personal communication to the editor from W. K. Maas explains that a non-excretor may become an excretor during pregnancy, the unborn child presumed to be an excretor (and also, I assume, the father) (McKusick, 1983).

When a phenomenon is assessed subjectively, apprehension always exists concerning the results. Even cross-checking with independent assessors does surprisingly little to relieve this anxiety. The separation of the characteristic asparagus-related odour from the background odours of the urine, which may vary enormously with individuals, presents complications. Strict control samples from each subject are imperative. Indeed, even the odour associated with the phenomenon apparently lends itself to different subjective description. 'Rotten or boiling cabbage', due mainly to methanethiol, are the usual phrases employed within Europe but 'vegetable soup' has also been put forward in an Israeli study (Lison *et al.*, 1980). Until an objective method of assessment of the odour can be achieved, and strict criteria for sample handling and analysis laid down, the problems of individual opinion will remain.

A study involving over 300 Israeli Jews demonstrated that around 10% could not smell the odorous urine, a polymorphic smell hyposensitivity, and the authors suggested (but did not prove) that the ability to excrete pungent substances in the urine after eating asparagus