

Correspondence

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Self-certification?

SIR,—Your leader on self-certification (24 October, p. 192) raises wider issues than the socioeconomic framework in which the subject is discussed.

The resentment felt by many general practitioners is not merely at the waste of time or at the workload entailed—1,600 to 2,000 statutory certificates per N.H.S. general practitioner per year, with roughly an equal number of non-N.H.S. (usually "non-medical") certificates. It is the distortion of relationships with patients, with hospital colleagues, and with the public which is also important—and which, no doubt, acts as a deterrent among young doctors who might otherwise consider general practice as a career. The patient who says "I've been off three days with diarrhoea, I need a line"; the hospital doctor who says to the patient "A line? Oh, you get that from your G.P."; the chamber of commerce which finally rebels at the "vague" certification from the general practitioner in their area and makes an issue of it with the L.M.C.; these are only some of the many examples of the ways in which the general practitioner is stressed.

(1) Can we not accept short-term absence for the management problem it so often is, rather than the medical problem it has

been alleged to be?

(2) Should not personnel and works medical services assume greater responsibility in dealing with these problems?

(3) Should not the worker be entrusted with a greater degree of responsibility for his absence?

(4) Granted that the introduction of three-day self-certification has been shown to be feasible in one large works, is there not a case for a national scheme with the insured worker responsible for longer spells—more than three days, but less than, say, three weeks?

(5) Should not our highly skilled nursing sister, whether in the works or in the health centre, be granted the same authority in regard to certification as that entrusted to her counterpart in hospital?

Answers to these simple questions could go a long way towards decreasing clerical medicine, increasing clinical medicine, and raising standards of health care, without at the same time aggravating the situation regarding absence ascribed to sickness.—I am, etc.,

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Phenacetin Nephropathy

SIR,—The interesting paper by Dr. K. G. Koutsaimanis and Professor H. E. de Wardener (17 October, p. 131) and your leading article on the subject (p. 125) draw attention once more to the vexed question of phenacetin. The fact that it is never prescribed alone is of some interest, and, as the authors note, most of it is purchased across the counter in preparations based on or identical with those in the *British Pharmacopoeia* and *British Pharmaceutical Codex*.

In 1955 at Westminster Hospital we removed phenacetin from the hospital compound codeine tablet and increased the aspirin content without any apparent loss in its popularity. We did this because it saved the pharmacy £100 a year, the new compound being less expensive, and because enterogenous cyanosis occurred not infrequently in arthritics taking large doses every day rather than because of the then recent reports from Switzerland¹ of renal toxicity caused by heavy daily consumption

of compound analgesic tablets. There seemed, even in those days, no reason to retain phenacetin as an analgesic even in the absence of adequate proof that it was a nephrotoxic drug. Since then we have never regretted this move, and though the case against the drug as a nephrotoxic agent rests only on indirect evidence and could be considered non-proven we have felt for many years that its merits do not warrant its retention in analgesic tablets.

The case against paracetamol, however, we feel is different, and Dr. Koutsaimanis and Professor de Wardener have produced little evidence against the drug. It has been widely prescribed now for over ten years, its particular merit lying in its freedom from gastrointestinal irritation; in any busy rheumatism clinic this is a very considerable advantage. There is, to date, no good case against it, either in the literature or at the Ministry's Committee on Safety of Drugs. While we think there is a case for withdrawing phenacetin altogether or making it available only on prescription, we do not think, on present evidence, that paracetamol should be branded as a nephrotoxic agent or its prescribing restricted.—We are, etc.,

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REFERENCE

- ¹ Spühler, O., and Zollinger, H. U., *Zeitschrift für klinische Medizin*, 1953, 151, 1.

SIR,—In their paper on phenacetin nephropathy (17 October, p. 131) Dr. K. G. Koutsaimanis and Professor H. E. de Wardener quote a personal communication from myself about two patients who have analgesic nephropathy following consumption of paracetamol. Since this quotation has caused

some consternation to users, prescribers, and manufacturers of paracetamol, may I use your columns to set the record straight?

A man aged 56 was admitted to a surgical ward in 1969 with renal colic. He gave a history of consuming paracetamol in a dose of 1.5 to 3.0 g./day since 1965, and was found to have most of the accepted features of analgesic nephropathy. He was at first regarded as a case of "paracetamol nephropathy", but further probing of his history revealed that he had taken considerable quantities of phenacetin-containing analgesics—probably including several kilograms of phenacetin—in the period 1951-1965. We then reclassified him as "phenacetin nephropathy with further renal damage during paracetamol consumption" as his blood urea had risen from 47 to 75 during the last four months of paracetamol consumption. I am now doubtful whether even this slur on paracetamol is justified since he had an episode of renal colic and was dehydrated on several occasions for pyelography during this period. Dr. Koutsaimanis and Professor de Wardener suggest that acute dehydration may precipitate renal damage in these patients, and they can certainly sustain further renal injury during the passage of sloughed papillae.

Another patient, a man aged 37, consumed about 1.5 g. paracetamol a day for headache over the five years to 1969. He took small quantities of Anadin, Phensic, and other mixtures, which then contained phenacetin, but consistently maintains that his intake was very small compared with that of paracetamol. He had a duodenal ulcer in 1966, and has had mild hypertension, prominent nocturia and polyuria, sterile pyuria, hyperuricaemia, and hyperchloraemic acidosis—all features of analgesic nephropathy. Renal biopsy shows interstitial fibrosis and there is a possible ring sign on pyelography, though detail is poor. The only atypical feature is a protein excretion averaging 1.7 g./24 hours which is higher than we usually encounter in analgesic nephropathy. We have provisionally classified him as a case of "paracetamol nephropathy" though with some reservations in view of the proteinuria. Final proof of the diagnosis will have to await nephrectomy prior to transplantation and since he remains well with a stable creatinine clearance of 14 ml./minute it may be many years before this final test can be applied.

The overwhelming evidence of epidemiology is that phenacetin is the ingredient of analgesic mixtures most damaging to the kidneys of man. No amount of animal experimentation can invalidate this clinical observation. I therefore support the conclusion of Dr. Koutsaimanis and Professor de Wardener that the sale of phenacetin should be restricted, but I do not agree that paracetamol can be included in the same condemnation on present evidence. Even if we accept my second patient as a proved case of analgesic nephropathy this only makes two published cases. Dr. Koutsaimanis and Professor de Wardener exonerate aspirin by setting the five published cases of aspirin nephropathy against the vast quantities of this drug which are sold and often consumed alone (in contrast to phenacetin). The same argument can be applied to paracetamol, which is sold in quantities comparable to aspirin in the U.K., and which is also frequently consumed alone. Paracetamol has been pilloried because it is the major metabolite of phenacetin, but phenacetin has many other metabolites and may contain impurities which could be responsible for its nephrotoxicity.

It would be wise to discourage the habitual consumption of any analgesic and it is standard practice to withdraw all analgesics from patients with phenacetin nephropathy in view of the anecdotal evidence that renal

damage may progress if aspirin or paracetamol is substituted for phenacetin.³ But should we on the present flimsy evidence restrict the sale of paracetamol for self-treatment of minor ailments? Personally, I think not; a substantial minority of the population is intolerant of aspirin and I can think of no other "phenacetin substitute" which has a better safety record than paracetamol. We should certainly keep an open mind since the incubation period of this disease is long and it is unusual to find patients who have stuck to the same analgesic so consistently that one drug can be incriminated, but for the moment the verdict must surely be in favour of paracetamol.—I am, etc.,

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- 2 *British Medical Journal*, 1965, 1, 673.
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SIR,—I read with some dismay the article by Dr. K. G. Koutsaimanis and Professor H. E. de Wardener (17 October, p.131). The authors suggest that both phenacetin and paracetamol should be described as Schedule 4 drugs. Although I in no way advocate the further use of phenacetin in large quantities, I am prompted to ask what analgesics will be left on the market for the general public to purchase? At the present time the following are the main analgesics available over the chemists counter: aspirin, paracetamol, codeine, and phenacetin. Phenacetin is being withdrawn slowly and it may be that paracetamol will follow shortly. It is my experience in retail pharmacy that aspirin, although still by far the major analgesic ingested per capita, is by virtue of its gastrointestinal side effects falling into disrepute, and compound codeine tablets, because of their content of aspirin and phenacetin, are following likewise.

Sales rates of analgesics in Britain, whether rightly or wrongly, are very large, and if paracetamol is withdrawn the only drug left which is available without prescription will be aspirin. Surely there must follow from any change in the pattern of analgesic availability a veritable flood of patients seeking mild analgesics from their doctors, not because they want their professional advice but simply because they can no longer obtain suitable analgesics from their chemists.—I am, etc.,

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SIR,—Dr. K. G. Koutsaimanis and Professor H. E. de Wardener (17 October, p. 131) have underlined aspects of analgesic nephropathy and rightly emphasized that patients who take large amounts of drugs over many years may be at risk of developing renal failure and that surgical procedures in such patients may cause rapid deterioration.

It is now nearly 20 years since the original work on phenacetin nephropathy was published,¹ and the fact that the original paper could well have been written on isopropylantipyrine and the paper by Dr. Koutsaimanis and Professor de Wardener

could have been written about aspirin implies that we are still in doubt about the absolute pathogenesis of the end lesion and even uncertain as to the importance of papillary tip necrosis. While it is true that animal studies may not be relevant to human disease when doubt exists we cannot ignore them.

It is probable that this nephropathy represents a general response to many factors including dehydration, nutrition, individual susceptibility, and the isolated or combined effects of numerous compounds—for example, acetylsalicylic acid,² vinylamine,³ phenazone, amidopyrine,⁴ phenylanthranilic acid,⁵ and flufenamic acid.⁶ Whether the banning of phenacetin and similar products is the answer is perhaps questionable. It is not justifiable to compare phenacetin with cyclamates—even penicillin is not welcome as a food additive. If an argument is put forward for banning phenacetin the same reasons are applicable to most of the minor analgesics all with their own, potentially lethal side effects. There is probably greater risk of gastric bleeding from 24 aspirin tablets a year than of nephropathy from the same amount of phenacetin.

On the evidence supplied so far it may be suggested that all common analgesics be supplied on a doctor's prescription only, but this is hardly practical, and hardly necessary, as analgesic nephropathy does not occur in the vast majority of people who take a few analgesic tablets in the course of a year but in patients who should be under attention for chronic conditions.

Zollinger,⁷ commenting on the fact that 90% of women carried analgesics in their handbags, said that the efforts to warn people of the possible dangers of this abuse should be intensified.

Rather than banning one substance only for people to turn to others, we should be more concerned in emphasizing to our patients that any drug has possible harmful effects, and it is up to the profession to keep a careful watch on those patients most likely to abuse the use of analgesics and to carefully re-examine cases of "chronic pyelonephritis" for a history of excessive drug-taking.—I am, etc.,

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- 3 Ham, K. N., and Tange, J. D., *Australasian Annals of Medicine*, 1969, 18, 199.
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- 6 Kaump, D. H., *Annals of Physical Medicine*, 1966, Suppl., p. 16.
- 7 Zollinger, H. U., *Schweizerische Medizinische Wochenschrift*, 1955, 85, 746.

Race and Commonwealth

SIR,—As I have had several inquiries on the point, I hope you will allow me to explain why in my letter (19 September, p. 705) I asserted that the existence in South Africa of a medical school reserved for non-Whites, cited in the C.M.A. discussion at Singapore as conclusive evidence thereof (29 August, p. 517), does not in fact involve