Letter from . . . Chicago

Generic acrimony

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In America, as in most other parts of the world, preclinical medical students are taught by their professors to refer to drugs by their generic names. Yet even the most junior clinical clerk soon finds out that in the real world doctors prescribe brand names, and use fixed-dose combinations. On the wards, the student sees that most of his attending physicians rarely use generic names; and at the clinic the nurse practitioner, tired of writing hydrochlorothiazide 30 times a day, has taken to ordering Esidrix. By the time he is ready to graduate, the student has concluded that it is foolish and pedantic to prescribe metaproterenol because the pharmacist writes Alupent on the bottle anyway, the patient knows he is taking Alupent and the nurse knows it too, and, though the fledgling doctor may compromise for a while and ask the patient if he is taking his metaproterenol-Alupent, he eventually gives up and joins the crowd in ordering Alupent.

A deluge of colourful advertising mail and regular visits from the friendly detail man help perpetuate this state of affairs; and it may be no coincidence that, while brand names are short and catchy, generic names induce dysarthria, echolalia, and perseveration, being mostly made up of unpronounceable syllables derived from modern Esperanto and ancient Aramaic. In addition, there is no handy formulary available in the US other than the ubiquitous and free *Prescribers' Desk Reference*, in which pharmaceutical firms advertise whatever they want to sell, so that one can find dozens of proprietary antispasmodic agents but no atropine tablets or tincture of belladonna. To most practising doctors, moreover, generic names reek of sophistry, socialism, bureaucracy, and government control, representing a violation of the physician's sacred right to decide what is best for his patients. To require use of generic names is a disservice to the patient, writes a doctor from the real world, proud of his armament of psychotropic agents and fixed-dose combinations, convinced that, as the man says on TV, "all aspirins are not alike," and worried that his patient will get short shrift if his favourite tranquilliser is replaced by a biologically inequivalent and inferior generic preparation. Nevertheless, brand names may cost ten times more than the corresponding generics, as professional consumer activists never tire of pointing out, and, with politicians and Government regulators constantly trying to cut the cost of drugs (which amounts to 10% of the national health bill), the large pharmaceutical companies increasingly feel compelled to protect their investments and profits, arguing that the vast sums spent on development and research must be recouped.

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Russian roulette with patients

The issue is becoming increasingly important because drugs are held under 17-year patents, and because by 1983 the patents for some 70% of the top 200 drugs in use will have expired. Not surprisingly, then, the doctors and the public are constantly being warned about the horrors of generic deceit; about how the advocates of generic drugs are perpetuating a cruel hoax and playing Russian roulette with their patients; and how it is a great disservice to substitute inadequate cheap generic drugs for the brand names that doctors have come to know and trust. And in their opposition to generic drugs the drug manufacturers are joined by some very determined medical practitioners. "No matter what laws are passed," writes one doctor, "we will never abandon our patients and the brand-name drugs that we know will help them . . . and if pushed to the wall we will dispense drugs from our own offices . . ." Another doctor writes that unfamiliar generic names are like Latin proverbs, never used in daily speech, and that blocking the doctor's pathway to rapid communication will do more harm than could be recouped by saving a few pennies in prescription writing.

The main argument against generic prescribing, however, has been the longstanding contention that the same chemical drug may have different biological effects because of particle dispersion and size, pH, stability, compression of the tablet, thickness of the coat, and characteristics of the binder. It has been argued that the purity of generic drugs varies considerably and that taste, colour, and odour are important with children and for ensuring long-term compliance. In the 1960s there were problems with the efficacy of certain prednisone, enteric-coated aspirin, and antibiotic formulations; more recently with thyroid, tetracycline, and notably with digoxin and phenytoin; and the arguments continue, even though at present all marketed drugs must be produced in accordance with US pharmacopia and Food and Drug Administration (FDA) specification.

The controversy about bioequivalence goes back at least to 1967, when, as a result of a directive from President Johnson, John Gardner—then Secretary of the Department of Health, Education, and Welfare (HEW)—set up a task force to study prescription drugs. The conclusion, after 20 months of investigation, was that on the basis of available evidence the lack of clinical equivalence among drug formulations meeting official standards had been grossly exaggerated. Thousands of tests were subsequently conducted under the auspices of the FDA; and in the summer of 1973 Dr Henry Simmons of that agency concluded that he also could find no important differences between generic and brand-name products; but he declared that he was discouraged by the quality of the dialogue on this subject, and that the statements made were often biased and at times misleading.

Equivocally equivalent

Since that time other officials have also concluded that the bioequivalence issue has been greatly blown out of proportion. Last year, at a Senate hearing, FDA commissioner Donald

Kennedy testified that in most cases generic and brand-name products were medically equivalent; and that based on the evidence of 250 000 annual inspections it was found that only a few firms were not in compliance with compendial specifications and that no widespread differences between large and small firms had been uncovered. It was also noted that some large pharmaceutical firms were buying generic products from smaller drug houses and reselling them under their own trademarks; and also that anyway the large companies were manufacturing more than 90% of the generic products in America. In fact, the large pharmaceutical firms are increasingly entering the generic market, in some cases producing so-called branded generics, and even cutting prices to drive the small generic drug houses off the market. Meanwhile, at state level, the industry has fought a long and hard campaign to stave off the repeal of the so-called antisubstitution laws.

These laws, passed in the 1950s, ostensibly to protect the public against unscrupulous pharmacists, stipulated that drugs must be dispensed exactly as written on the prescription. But in the early 1970s, largely in response to consumer activism, many states began to repeal these statutes, so that at the present time at least 40 states have enacted some kind of substitution law. Most of these laws are of the "dual-line" type, giving the doctor the prerogative to indicate whether the pharmacist may or may not substitute with another item, chosen from a list of bioequivalent drugs, usually drawn up by the state health department and validated by the FDA. It was hoped that this approach, combined with consumer education, would reduce the drug bill by millions of dollars a year. In addition, the Carter administration acting on the recommendations of the Federal Trade Commission, has recently developed a model substitution Bill to be recommended to the states. This Bill, if adopted, would still allow the doctor to prescribe a brand name, if "medically necessary." It would apply to some 2000 generic drugs designated medically equivalent by the FDA, and resembles the more liberal statutes adopted by Illinois in 1978 rather than the more radical approach used by a few states that have mandated generic substitution.

According to Mr Califano, secretary of HEW, adoption of the proposed model legislation by most states could save the consumer $400m a year. The president of the Pharmaceutical Manufacturers' Association, however, thought that the law "would do nothing for consumer savings." Others, too, have pointed out that, so far, substitution laws have produced far less saving than expected—at least partly because of lack of co-operation from doctors and pharmacists, as well as a result of an effective campaign to alert the public to the dangers of substitution. Nor are the savings from generic drugs necessarily passed on to the patient, so that in some cases this merely leads to increasing the pharmacist's profit. But the Federal Government, now one of the largest purchasers of drugs by virtue of its Medicaid and Medicare programmes, has long tried to contain overall expenditure; and there have even been, at various times, Bills in Congress prohibiting the use of any drug names other than the officially designated one. None of these Bills has ever been passed.

In 1973, however, President Nixon's secretary of HEW, Casper Weinberger, announced plans to save the Government and the consumer millions of dollars with its MAC (Maximal Allowable Cost) programme. Under MAC, the Government would concentrate at first on the most widely used drugs; the FDA would have to certify the bioequivalence of different proprietary brands; and the Government would then limit the pharmacist's reimbursement to a dispensing fee plus the acquisition cost determined by a pharmaceutical reimbursement board. Because of widespread opposition from the pharmaceutical industry and medical societies, including several unsuccessful law suits, implementation was delayed until 1977. At present, the programme is being limited to about 100 drugs but is expected to expand fourfold by the end of 1979.

Meanwhile, the controversy about generic drugs goes on, with opposing sides confronting each other with great bitterness, for of the various sensitive issues in American medicine generic prescribing takes second place only to abortion. The causes of this generic acrimony are clearly economic. Yet the professor who taught his students to use generic names did so not to save money but because using multiple trade names for one agent promotes ignorance and causes confusion—such as can be readily seen on the ward, where the house officer thinks Tedral (a combination of ephedrine and aminophylline) is a glucocorticosteroid and prescribes it in conjunction with more ephedrine; at the clinic, where the patient is found to be taking Apresoline as well as hydrallazine; in the doctor's lounge, where someone wonders why Largactil, so popular in England, was never released in the US; and in a general practitioner's office where one patient has been taking three times the recommended dose for the same drug under the guise of Hydropress, Aldoril, and Diazide.

What is the best management of proctalgia fugax which sometimes occurs after intercourse?

Thaysen[1] first used proctalgia fugax to describe an obscure type of rectal pain in adults. It commonly occurs at night and often wakes the patient. It may occur by day, however, sometimes after a bowel movement and may follow intercourse. It occurs at irregular intervals, is described by the patient as being above the anal canal, and is a severe cramp-like pain that lasts for some minutes. Examination between the attacks of pain shows absolutely no abnormality. The cause of the pain is obscure. It has been ascribed to sexual activity, faecal or gaseous distension, or even as a sign of epilepsy. Most authorities regard it as being due to spasm of levator ani. Certainly it appears to occur in tense, anxious individuals and indeed is supposed to be particularly common among members of the medical profession.

Treatment is difficult. Some patients respond to inhalation of amyl nitrite, and others find relief from a soluble tablet of glyceryl trinitrate (0·3 mg) placed beneath the tongue. Others get relief from the passage of flatus or of a stool, a hot bath, the application of a hot water bottle to the perineum, or simply by firm pressure with a fist against the anal verge. Perhaps the most important part of treatment is for the patient to undergo a careful examination, including proctoscopy and sigmoidoscopy. The next most important part of treatment is the strong reassurance of this usually anxious individual that there is no underlying disease, particularly of a malignant nature. The surgeon should avoid operating on incidental minor anal conditions, such as skin tags, since the patient will naturally be disappointed when the discomfort of having such procedures dealt with does not eliminate his attacks of proctalgia.

[1] Thaysen, T E H, *Lancet*, 1935, **2**, 243.

A patient reports that she and her husband intermittently pass urine that smells like metal polish. Might there be a connection with the use of a dishwasher?

Presumably the questioner is worried about the possibility of detergents used in the dishwasher appearing in the urine. The rinsing programme should preclude this. Many detergents contain non-ionic surfactants of the alkyl phenyl polyethoxy-ethanol or polyalkylene glycol types, although some ("hard" cleaners) contain trisodium phosphate. Urine containing traces of the latter may occasionally have a metallic odour. I wonder if there could be other explanations—for example, the somewhat characteristic odour of the urine (especially when alkaline) that some people pass after eating corned beef. This is probably related to the presence of antioxidants used as preservatives. A patient once commented that his urine "smelled of boot polish." Most metal polishes are formulated around petroleum solvents ("naphtha") or oxalic acid. I cannot believe that the former would be associated with detergents, and oxaluria has no characteristic smell.