PART III: Special cases

Antibiotics

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Summary

Reasons for prescribing antibiotics by official names are that the doctor is more likely to understand what he is prescribing, that it enables the literature to be internationally understood, and that non-branded products are less costly. The only reason to the contrary is that the original brands of some oral antibiotics are better absorbed than others.

THERE are at least four reasons why antibiotics should be prescribed by their approved names. The first is that if he uses the approved name the doctor knows, or is more likely to know, what he is prescribing. He will at least avoid such ludicrous errors as that, reported by Stille (1968), of a German doctor who prescribed Leukomycin, and when that had no effect, substituted Paraxin. Again the patient failed to respond, which is not surprising in view of the fact that these are both trade names of chloramphenicol. Widely used antibiotics on which patents have expired go by a great variety of names in different parts of the world. Even those covered by patents may do so. I was under the impression that only a single firm in the United States is licensed to produce ampicillin, but according to The Medical Letter (1973) it is available there under fourteen brand names, most of which (e.g. Alpen, Pensyn, Principen, Supen) bear little resemblance to the approved name.

The second reason is a corollary to the first, but it concerns mixtures rather than individual drugs. If a proprietary preparation is a mixture, its name always disguises the fact if one of its ingredients is hazardous. The outstanding example of this in the antibiotic field is the mixture of penicillin, streptomycin and dihydrostreptomycin which was widely used at a time when the false belief had been put forward that streptomycin and dihydrostreptomycin together are less toxic than either alone. Shambaugh *et al.* (1959) report thirty-two fully documented cases in which severe and permanent deafness had been

produced by dihydrostreptomycin, administered alone in twelve cases, together with streptomycin in four, and in various proprietary mixtures in most of the remainder. The names and compositions of twelve such mixtures are given; all contained penicillin, usually 400,000 units, and most 0.25 g each of streptomycin and dihydrostreptomycin, but Combiotic, Dihydrocillin, Durycin and Strocillin contained either 0.5 or 1.0 g of dihydrostreptomycin only. In eighteen of these patients the total dose of dihydrostreptomycin given was less than 10 g, and in ten it was less than 5 g; it may be surmised that these patients had defective renal function. The indications for the treatment included tuberculosis and urinary tract infections, which are reasonable; they also included influenza, cold, asthma, furuncles, sinusitis and dry socket, which are not. Six patients received it as cover for operations, three of which were hysterectomy, including a woman of only thirty-nine who 'was a telephone operator and became considerably disabled and depressed over her loss in hearing'.

Dihydrostreptomycin is mercifully dead, but it should be remembered that proprietary mixtures of penicillin and streptomycin are still widely used, and that only small doses of streptomycin can impair vestibular function, particularly in older people. Cawthorne and Ranger's (1957) study of this lesion bears a strong resemblance to that of Shambaugh *et al.* (1959) and betrays the same kind of indiscriminate use. Are all users of these mixtures aware (1) of what they consist, and (2) of the risks of giving streptomycin to patients whose renal function may be defective?

A third reason is purely a matter of communication. The use of trade names in medical literature may render papers unintelligible to readers in other countries where these names are unknown. The German medical press is particularly at fault in this matter. If such names must be used it should involve little trouble to translate them into approved names

if only in a footnote. International meetings of medical editors are held from time to time, and this would be an appropriate subject for their agenda.

A fourth reason for prescribing an antibiotic by its approved name is simply the cost of the prescription. Branded products are generally more expensive, but even among them the price varies considerably, and the use of the approved name enables the pharmacist to fill the prescription at the lowest price.

There is much less to be said for the opposite view. Prescription by brand name is of obvious advantage to the manufacturer. Does it ever benefit the consumer? It can only do so if thereby he secures a better product. He usually will not, but possible exceptions are some antibiotics which are administered orally, and the property in which they can differ is what has come to be known as 'bio-availability'.

This was first demonstrated in capsules of chloramphenicol. When the patent on this antibiotic expired it began to be manufactured by firms without the long experience of the original patentees. Assays showed that their capsules contained a quantity of chloramphenicol within the statutory limits, but when administered to normal subjects they produced blood levels substantially lower than those given by the original product (Glazko *et al.*, 1968). Particle size is believed to be mainly responsible for this, but the use of different fillers and perhaps other factors may also play a part. More recently the same has been shown for different brands of tetracycline (Barr *et al.*, 1972); an old-established brand was compared with two new ones, both of which gave lower blood levels, one of them so much so that the difference could well convert therapeutic success into failure. These authors studied not only blood levels but urinary excretion, and reached the valuable conclusion that the proportion of the dose excreted in a given time is a satisfactory measure of the

efficiency of absorption. It would therefore be possible to measure this by a single assay and without a series of venepunctures.

Another antibiotic of which the bio-availability is suspect is erythromycin. The estolate is reasonably well absorbed, but absorption of both base and stearate is inconstant and often inadequate. These defects are inherent in the preparation and not peculiar to different brands. Assay in the urine would not serve to control this, since only 3–5% of the dose is excreted by this route.

These peculiarities seem fully to justify the prescription of chloramphenicol or tetracycline by brand names. Ideally, of course, this could be made superfluous by statutory control of bio-availability. So far as I know there is no mechanism for this in Great Britain. Were it to be introduced, the simple determination of urinary output advocated by Barr *et al.* (1972) should serve at least for tetracycline, and much reduce the amount of work involved.

References

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Discussion

Dr T. B. Binns, Medical Director of Ciba Laboratories, pointed out, and Professor Garrod agreed, that bio-availability was not a problem exclusive to orally administered preparations. For example,

particle size and shape are known to determine the absorption characteristics of intra-muscular procaine penicillin.