## Editors' view

## Rational prescribing, appropriate prescribing

## J. K. Aronson, Chairman of the Editorial Board, British Journal of Clinical Pharmacology

University Department of Clinical Pharmacology, Radcliffe Infirmary, Woodstock Road, Oxford OX2 6HE, UK

'I believe', wrote Celsus in the proem to De Medicina, 'that the art of medicine should be rational, drawing on evident causes.' But rationality may not be enough. Consider prescribing. We all aspire to rational prescribing, forgetting perhaps that that is not the same as appropriate prescribing. Rational prescribing has been described as the process whereby prescribing decisions are made; appropriate prescribing is what results, or should result [1]. And rational prescribing need not be appropriate. Consider a real example.

A woman with Liddle's syndrome presented with severe symptomatic hypokalaemia. Her doctor reasoned as follows:

- she has potassium depletion;
- spironolactone is a potassium-sparing drug;
- spironolactone will cause her to retain potassium;
- her serum potassium concentration will normalize.

But after she had taken a full dose of spironolactone for several days, based on this logical reasoning, she still had severe hypokalaemia. Her doctor should have reasoned as follows:

- she has potassium depletion due to Liddle's syndrome, a channelopathy that affects epithelial sodium channels [2];
- there is a choice of potassium-sparing drugs;
- spironolactone acts via aldosterone receptors, amiloride and triamterene via sodium channels;
- in Liddle's syndrome an action via sodium channels is required [3].

When she was given amiloride instead of spironolactone her serum potassium concentration rapidly rose to within the reference range.

Although this is an example of a rare condition, it shows that a rational argument can result in inappropri-

ate prescribing, and that appropriate prescribing depends on an understanding of the pathophysiology of the problem and the pharmacology of the drugs available to treat it. Only when the prescriber is in possession of all the necessary knowledge and understanding does rational prescribing become appropriate prescribing.

Conversely, appropriate prescribing can result even when the reasoning is faulty. In one study of antibiotic prescribing in 78 patients with bacteraemia the authors found that 'an appropriate antibiotic selection was made by some physicians despite flawed reasoning, and inappropriate antibiotic selection occurred in a few cases despite faultless reasoning' [4]. In one case Pseudomonas aeruginosa was cultured from the urine and the patient was given cefoxitin and tobramycin, which was considered inappropriate therapy; however, the patient recovered and Klebsiella was isolated from the blood. In another case, ampicillin and gentamicin were given when Proteus mirabilis was cultured from the urine, but this was considered to have been inappropriate, although logically correct, when Pseudomonas aeruginosa was cultured from the blood.

Rational argument can result in inappropriate prescribing when prescribers lack important information that affects their reasoning or if they fail to appreciate an important proviso. If, for example, one does not know that another prescriber has already prescribed paracetamol unsuccessfully for a headache, a prescription for paracetamol might be rational but would be inappropriate. Or if the patient is taking warfarin, a prescription of clarithromycin for an infection may be rational but inappropriate, unless the dosage of warfarin is changed at the same time.

Appropriateness in health care has been defined as 'the outcome of a process of decision-making that maximizes net individual health gains within society's available resources' [1]. This definition also implies that the

patient's attitude is as important in deciding appropriateness as the reasoning that underpins it. For example, a patient who suffers a severe adverse reaction to what would otherwise have been appropriate therapy may consider it to have been inappropriate, even though he makes a full recovery. Conversely, a patient who feels better after taking an ineffective remedy may consider it to have been appropriate even though it lacks an underlying rationale.

Two papers in this issue of the *Journal* and two abstracts in the Proceedings of the Dutch Society for Clinical Pharmacology and Biopharmacy deal with prescribing issues. Jackson, Mangoni, and Batty (pp. 231–6) review the optimization of drug prescribing in elderly people. They discuss in detail various definitions of appropriateness in health care and suggest that the term 'appropriate prescribing' should be used to cover overuse, underuse, and misuse of treatments. A suboptimal prescription is one that is inappropriate, and they list the several causes of such prescribing. They also refer to several methods that have been used to measure appropriateness of prescribing, one of which, the Medication Appropriateness Index [5, 6], will serve as an example. The index depends on 10 questions:

- is there an indication for the drug?
- is the medication effective for the condition?
- is the dosage correct?
- are the directions correct?
- are the directions practical?
- are there clinically significant drug-drug interactions?
- are there clinically significant drug–disease/condition interactions?
- is there unnecessary duplication with other drugs?
- is the duration of therapy acceptable?
- is the drug the least expensive alternative compared to others of equal utility?

Each question can be answered using a three-point Likert scale, implying 'appropriate', 'marginally appropriate', and 'inappropriate'. The first two questions receive a weighting of 3, the next four a weighting of 2, and the last four a weighting of 1. The scale has been used, for example, to study polypharmacy in an elderly population [6], the management of congestive heart failure [7], and prescribing in submariners [8].

In my view the weighting that the Index gives to the second question is insufficient—if the drug is ineffective then the prescription is inappropriate and none of the other questions matters. And Jackson *et al.* conclude that the strengths of systems such as this are outweighed by their main weakness, namely that they have been based on consensus: because disagreement is rife, con-

sensus in health care is reached only on 'bland generalities that represent the lowest common denominator of debate and are embalmed as truths' [1].

How can we make sure that prescribers are equipped to prescribe appropriately? Education must be the main thrust [9]: education on the pathophysiology of clinical problems; on the pharmacology of the drugs used to treat them, including their pharmaceutical, pharmacokinetic, and pharmacodynamic properties, and how those properties are translated into a therapeutic effect via the relevant chain of biochemical and physiological events; on adverse drug reactions and interactions; on the devising of dosage regimens; on monitoring drug therapy; and on patients' attitudes to drug therapy. Other papers in this issue, by Akici *et al.* (pp. 310–21), Bartelink *et al.* (p. 354), and Franson *et al.* (p. 357), highlight different ways in which education can be valuable. And Jackson *et al.* propose a prescribing checklist as an aide-mémoire.

Logical reasoning is more likely to result in appropriate prescribing [4]. But although rationality is desirable, it is not sufficient. When we teach rational prescribing we must stress that the aim is appropriate prescribing.

## References

- 1 Buetow SA, Sibbald B, Cantrill JA, Halliwell S. Appropriateness in health care: application to prescribing. Soc Sci Med 1997; 45: 261–71.
- 2 Warnock DG. Liddle's syndrome. genetics and mechanisms of Na+channel defects. Contrib Nephrol 2001; 136: 1–10.
- **3** Jeunemaitre X, Bassilana F, Persu A, Dumont C, Champigny G, Lazdunski M, Corvol P, Barbry P. Genotype—phenotype analysis of a newly discovered family with Liddle's syndrome. J Hypertens 1997; 15: 1091–100.
- 4 Yu VL, Stoehr GP, Starling RC, Shogan JE. Empiric antibiotic selection by physicians: evaluation of reasoning strategies. Am J Med Sci 1991; 301: 165–72.
- 5 Hanlon JT, Schmader KE, Samsa GP, Weinberger M, Uttech KM, Lewis IK, Cohen HJ, Feussner JR. A method for assessing drug therapy appropriateness. J Clin Epidemiol 1992; 45: 1045–51.
- 6 Samsa GP, Hanlon JT, Schmader KE, Weinberger M, Clipp EC, Uttech KM, Lewis IK, Landsman PB, Cohen HJ. A summated score for the medication appropriateness index: development and assessment of clinimetric properties including content validity. J Clin Epidemiol 1994; 47: 891–6.
- 7 Bucci C, Jackevicius C, McFarlane K, Liu P. Pharmacist's contribution in a heart function clinic: patient perception and medication appropriateness. Can J Cardiol 2003; 19: 391–6.
- **8** Jan MH, Thomas TL, Hooper Tl. Prescription medication use aboard US submarines during periods underway. Undersea Hyperb Med 2002; 29: 294–306.
- **9** Herzig S, Jakobs KH, Michel MC. eds. Novel Teaching Techniques in Pharmacology. Naunyn Schmiedeberg's Arch Pharmacol 2002; 366 (1).