it should be realized that even if they survive in that situation for only a short time the probability of the transmission of their resistances to human Enterobacteria is still high. To contribute to the transferable resistance factors carried by man, therefore, drug-resistant non-pathogenic *E. coli* of animal origin need not establish themselves in the human intestine in the same way as salmonellae, which are pathogens, must do in order to cause disease.

The example cited in your leading article to support the contention that transferable drug resistance in human bacteria is probably of human origin is misleading. The resistant organisms concerned in the genitourinary tract infections described by Smith and Armour,[1] *E. coli, Proteus, Pseudomonas,* and *Klebsiella,* are ordinarily found in the intestine, and in that environment they are subject to the same probability of acquiring transferable drug resistance, of animal as well as human origin, as are any other intestinal organisms. That they were ultimately isolated in connexion with urinary infection does reduce this probability. Nevertheless, I should not like it to be thought that I overestimate the animal contribution to the incidence of transferable drug resistance in human Enterobacteria. I simply insist that there is such a contribution, that denying its existence will not abolish it, that it presents an unnecessary danger to man, and that it should be eliminated as far as possible.

It is stated in your leading article that "the only permitted antibiotics [for use as feeding additives] are penicillin and tetracyclines." It would have been better to refer to these as "scheduled antibiotics," because an unscheduled antibiotic (tylosin) is now in use as a feeding additive. The justification for this is that tylosin is not used therapeutically in either animals or man. But it is a macrolide, and organisms that become resistant to it also become resistant to other macrolides such as erythromycin and oleandomycin, which are used therapeutically. It is thus no more logical to allow the use of tylosin as a feeding additive than it would be to allow that of erythromycin or oleandomycin.

Your leader-writer outlines aspects of the veterinary uses of antibiotics that would repay investigation, and I can only echo him in this. A few years ago I witnessed an explosion of infection with a drug-resistant strain of *Salmonella typhimurium* in calves, and observed the transmission of this strain to man.[2,3] The infection emerged and spread because of the unsatisfactory conditions associated with the practice of intensive farming. The resistance emerged and spread because of the indiscriminate use of antibiotics and synthetic antibacterial drugs in fruitless efforts to control the salmonellosis. Having monitored this field situation, and having studied with concern its epidemiology and ecological implications, I called almost three years ago for "a re-examination of the whole question of the use of antibiotics and other drugs in the rearing of livestock."[3] I cannot understand why this suggestion, which the passage of time has done nothing but justify, has been resisted. After all, the problem exists despite denials of its significance, and it would do no harm, and might even do good, to subject it to a critical scrutiny. Admittedly this might expose the need for more discrimination in the use of antibiotics if the useful life of the antibiotics is to be prolonged. But who would suffer from the exercise of such discrimination?—I am, etc.,

E. S. ANDERSON.

Enteric Reference Laboratory,
Public Health Laboratory Service,
London N.W.9.

REFERENCES

1 Smith, D. H., and Armour, S. E., *Lancet*, 1966, 2, 15.
2 Anderson, E. S., and Lewis, M. J., *Nature (Lond.)*, 1965, 206, 579.
3 Anderson, E. S., *Brit. med. J.*, 1965, 2, 1289.

Deaths from Asthma

SIR,—We read with interest your leading article on "Increasing Deaths from Asthma" (10 February, p. 329), but in your remarks on management we were disappointed to see no mention of the great importance of measuring the arterial blood-gas tensions in status asthmaticus. You recommend assessing ventilatory impairment by the expiratory peak-flow rate, but in our experience patients with severe asthma are too breathless to perform this or other spirometric tests properly, and we find knowledge of the blood-gas tensions combined with clinical examination the best method of assessing their progress. Spirometry is useful in the milder asthmatic to demonstrate the extent and reversibility of airway obstruction with bronchodilators or steroids.

All patients in status asthmaticus have varying degrees of hypoxaemia, but danger to life approaches only with the development of hypercapnia.[1] This finding, of which there is initially little clinical evidence, is the indication to institute assisted ventilation without delay.—We are, etc.,

K. N. V. PALMER.
M. L. DIAMENT.

Department of Medicine,
University of Aberdeen.

REFERENCES

1 Palmer, K. N. V., and Diament, M. L., *Lancet*, 1967, 2, 383.
2 Marchand, P., and van Hasselt, H., *Lancet*, 1966, 1, 227.

SIR,—I share the view expressed by Dr. F. E. Speizer and others (10 February, p. 339) that excessive use of corticosteroids has not been responsible for the recent increase in mortality from bronchial asthma. It would indeed not be unreasonable to conclude from the information supplied in this article that *failure* to use corticosteroids was responsible for many of the deaths, and, for all we know, inadequate dosage may have accounted for some of the others.

Bronchodilator aerosols may well be dangerous in status asthmaticus, and it would be most unwise for his patients to use these powerful drugs to excess. It must be stated, however, that much of the evidence used to incriminate bronchodilator aerosols is inferential, anecdotal, or even spurious. Your leader writer (10 February, p. 329), for example, attributes to McManis[1] the statement that isoprenaline "may induce ventricular arrhythmias, especially when stress is put on the right ventricle." This reference is to a letter, 18 lines long, which merely relates clinical impressions, and in which the words "ventricular arrhythmias" and "right ventricular stress" are not even mentioned. It is strange that no information is available on the effect of sympathomimetic drugs in the production of ventricular arrhythmias or cardiac arrest in hypoxic animals. This is the sort of evidence we need to clarify the present unsatisfactory situation in which, whenever we prescribe isoprenaline or adrenaline for potentially hypoxic asthmatics, we are uncertain whether we are more likely to kill or cure.

Most deaths from asthma occur in the patient's home or in transit to hospital. In my own series, for example, only 4 of 26 recorded deaths occurred in hospital. This implies either that there are serious problems in the recognition of dangerously severe asthma by the patients themselves, their relatives, or their general practitioners, or that grave deficiencies exist in the ambulance service or in the hospital admission system for dealing with such patients.

Even if we do not know why deaths from asthma are increasing we should at least take steps to ensure that patients do not die unnecessarily. More can be done by general practitioners and hospital physicians to identify those patients who are most likely to die from asthma, and to ensure that there is no delay in having these patients admitted to hospital when the need arises. Every patient who has had severe status asthmaticus is a potential candidate for another, perhaps fatal, episode. How these "high risk" patients are handled will of course depend on local conditions. In this unit a list of such patients is kept beside the ward telephone, and all the medical and senior nursing staff have instructions to admit any patient whose name is on the list when asked to do so, irrespective of the bed state and regardless of whether the request comes from the family doctor, a relative, or even a next-door neighbour. I have no doubt that this arrangement has already saved many lives. The "sudden and unexpected" deaths so often referred to are seldom either as sudden or as unexpected as the description implies, and so long as warning signs, such as tachycardia and the failure to obtain relief from bronchodilator aerosol, are not ignored there will usually be time to get the patient into hospital alive. Once in hospital, if up-to-date facilities are available for resuscitation, very few patients should die.

I fully endorse your leader writer's view that treatment with corticosteroids should always be started as soon as it is apparent that lesser measures are proving ineffective. I would differ from him only in respect of dosage and route of administration. In severe status asthmaticus at least 100 mg. of prednisolone should be given by mouth in the first 12 hours. Intravenous hydrocortisone is necessary only to secure a high initial blood level, or if the patient is vomiting. Retrospective studies on the drugs used immediately before death in fatal cases of asthma are unreliable, and perhaps even misleading. What is required is a prospective investigation conducted in a small number of centres where the treatment of large numbers of asthmatics is rigidly supervised, and where the benefits and dangers of the drugs employed can be critically assessed. This is surely a challenge which the Medical Research Council should be eager to accept.

Finally, I must deplore the publicity given in your leading article to disodium cromoglycate (Intal), the value of which is as yet not proved in status asthmaticus.—I am, etc.,

IAN W. B. GRANT.

Respiratory Diseases Unit,
Northern General Hospital,
Edinburgh.

REFERENCE

1 McManis, A. G., *Med. J. Aust.*, 1964, 2, 76.

SIR,—In your leading article (10 February, p. 329) you state that it comes as a shock that increasing ease of management of asthma has not resulted in a fall in mortality, but in