

probably because its reintroduction becomes ever more unlikely. Nevertheless, the ethical issues raised by the Amnesty report concern doctors throughout the world and not merely those in the United States. Doctors have an important part to play in abolishing what is cruel, inhuman, and degrading punishment. Firstly, they must articulate and implement ethical codes that unambiguously prohibit doctors participating in executions, and, secondly, they must widen the discussion to include the broader ethical issues of the death penalty.

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1 Curran WJ, Casscells W. The ethics of medical participation in capital punishment by intravenous drug injection. *N Engl J Med* 1980;302:226-30.

2 Amnesty International. *United States of America: the death penalty*. London: Amnesty International Publications, 1987.

3 Casscells W, Curran WJ. Doctors, the death penalty and lethal injections. *N Engl J Med* 1982;307:1532-3.

4 Amnesty International. *The death penalty in the United States: an issue for health professionals*. London: Amnesty International Publications, 1987:13. (Quotation from *Jornal da Associacao Medica Brasileira* 1985 November:12.)

Penetration of antibiotics into the respiratory tract

Few antibiotics penetrate well into bronchial secretions, and yet most respiratory infections respond to treatment. The poor penetration seems to matter only in patients with chronic suppurative airways disease (bronchitis, bronchiectasis, and cystic fibrosis) and in those infected with less sensitive organisms and may then contribute to recurrent sepsis. In these patients the initial response to antibiotics may be good because the drugs penetrate the mucosa better than the secretions, but subtherapeutic concentrations in the mucus may lead to relapse. Furthermore, penetration may become worse as tissue damage progresses.¹ For these reasons doctors, and particularly those looking after patients with chronic suppurative lung diseases, need to know something about the penetration of antibiotics into the respiratory tract.

The penetration of β lactam antibiotics is modest—peak sputum concentrations of penicillins are only 5-20% of those in serum. Even 1 g of oral ampicillin will not always attain inhibitory concentrations for haemophilus, although activity against more sensitive bacteria such as *Streptococcus pneumoniae* is readily achieved.² Parenteral ampicillin gives higher concentrations in both the serum and sputum. Amoxycillin is more completely absorbed from the gastrointestinal tract and achieves higher serum and sputum concentrations than oral ampicillin,^{3,4} though even 750 mg will not always produce inhibitory sputum activity against haemophilus.⁵ Cole and colleagues have reported longer remissions in patients with chronic bronchitis after short courses of high dose oral amoxycillin (3 g 12 hourly), though peak sputum concentrations varied widely.⁶ Davies and Maesen found higher sputum ampicillin concentrations after bacampicillin (800 mg) than after ampicillin (1 g),⁵ although eight hourly 400 mg or 800 mg doses of bacampicillin controlled haemophilus infections in bronchitis.⁷ Standard oral doses of cloxacillin in patients with cystic fibrosis scarcely exceed inhibitory concentrations for *Staphylococcus*

aureus.⁸ Broad spectrum penicillins such as carbenicillin, piperacillin, ticarcillin, and mezlocillin do not always produce adequate activity against pseudomonas in respiratory secretions,^{9,11} and they are best used with an aminoglycoside with serious infection. Cephalixin is active against *Str pneumoniae* in sputum, but the concentrations are not likely to be inhibitory for *Haemophilus influenzae*.¹² Injectable cephalosporins such as cefuroxime, cefazolin, and cefotaxime achieve higher serum concentrations, and peak concentrations in sputum are at least four times higher than those resulting from oral agents.^{10,13}

Erythromycin is widely used in treating respiratory infections because of its activity against mycoplasma, legionella, and various other bacteria—pneumococci and branhamella are very susceptible, but concentrations needed to inhibit *H influenzae* are higher. Erythromycin produces good but variable sputum concentrations when given intravenously¹⁴ though much lower concentrations (which may be sub-inhibitory for haemophilus) after a 500 mg oral dose.¹⁵ Much greater activity is detected in lung tissue after oral and intravenous erythromycin. Clindamycin and rifampicin readily attain good sputum activity against *Staph aureus*,¹⁰ and rifampicin is a suitable adjunct to antibiotics such as flucloxacillin or vancomycin in staphylococcal pneumonia. Anaerobes (implicated in aspiration pneumonia) are inhibited by bronchial concentrations of metronidazole after 400 mg oral doses.¹⁶

Tetracycline concentrations in bronchial secretions are inhibitory to most strains of *Str pneumoniae*, though activity against *H influenzae* is not always adequate.¹⁷ Sputum antibiotic concentrations and clinical results may correlate poorly: Maesen and colleagues found that haemophilus strains with minimum inhibitory concentrations of doxycycline exceeding 2 mg/l were rarely eradicated by conventional doses of doxycycline in patients with chronic bronchitis, although almost two thirds of isolates with lower minimum inhibitory concentrations responded, despite a mean peak sputum concentration of only 0.3 mg/l.¹⁸ Considerably higher doxycycline concentrations are, however, reached in the bronchial wall and lung tissue.¹⁹

Treatment of respiratory infections caused by Gram negative organisms with gentamicin is most likely to succeed if peak serum concentrations exceed 8 mg/l.²⁰ Studies in dogs have shown that peak concentrations in bronchial mucus are about one quarter of those in the serum and that even high doses of gentamicin may fail to reach therapeutic concentrations against *Pseudomonas aeruginosa* in respiratory secretions.²¹ Adequate concentrations may not be readily achieved in the elderly or in patients with renal impairment, when dosage must be carefully controlled to avoid toxicity: combination with a broad spectrum penicillin may produce synergy, but newer antipseudomonal agents such as ceftazidime are safer.

Trimethoprim passes readily into bronchial secretions, and concentrations often exceed those in serum,²² though sulphamethoxazole activity after oral co-trimoxazole may be subtherapeutic. Brumfitt and colleagues detected no sulphamethoxazole and variable trimethoprim concentrations in sputum in 24 patients given co-trimoxazole, though both drugs were equally effective clinically.²³ Quinolones have renewed interest in antibiotic pharmacokinetics in the lung because, despite effective diffusion in bronchi and good antimicrobial activity including against haemophilus and branhamella, they are only moderately active against *Str pneumoniae*. Peak sputum concentrations exceed half of those

in the serum,²⁴ but less susceptible pneumococci may not be eradicated despite lung tissue concentrations exceeding those in serum.²⁵

Even if permanently eradicating infection from patients with advanced chronic suppurative lung disease remains a forlorn hope, better recognition of the behaviour of antibiotics in the respiratory tract should help in assessing new therapeutic regimens.

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- Hallstrom O, Keyrilainen O, Markhula H. Ampicillin concentration in normal and pathological lung tissues after oral administration of bacampicillin. *Infection* 1979;7(suppl 5):469-71.
- Stewart SM, Fisher M, Young JE, Lutz W. Ampicillin levels in sputum, serum and saliva. *Thorax* 1970;25:304-11.
- Stewart SM, Anderson IME, Jones GR, Calder MA. Amoxycillin levels in sputum, serum and saliva. *Thorax* 1974;29:110-4.
- Ingold A. Sputum and serum levels of amoxycillin in chronic bronchial infections. *Br J Dis Chest* 1975;69:211-6.
- Davies B, Maesen F. Serum and sputum antibiotic levels after ampicillin, amoxycillin and bacampicillin in chronic bronchitis patients. *Infection* 1979;7(suppl 5):465-71.
- Cole PJ, Roberts DE, Davies SF, Knight RK. A simple oral antimicrobial regimen effective in severe chronic bronchial suppuration associated with culturable Haemophilus influenzae. *J Antimicrob Chemother* 1983;11:109-13.
- Maesen F, Beeuwkes H, Davies BI, et al. Bacampicillin in acute exacerbations of chronic bronchitis—a dose range study. *J Antimicrob Chemother* 1976;2:279-85.
- Saggers BA, Lawson D. In vivo penetration of antibiotics into sputum in cystic fibrosis. *Arch Dis Child* 1968;43:404-9.
- Marlin GE, Burgess KR, Burgoyne J, Funnell GR, Guinness MDG. Penetration of piperacillin to bronchial mucosa and sputum. *Thorax* 1981;36:774-80.
- Smith BR, LeFrock JL. Bronchial tree penetration of antibiotics. *Chest* 1983;6:904-8.
- Lode H, Grublike G, Hallermann W, Dzwillo G. Significance of pleural and sputum concentrations for antibiotic therapy of bronchopulmonary infections. *Infection* 1980;8(suppl 1):49-53.
- Halprin GM, McMahon SM. Cephalixin concentrations in sputum during acute respiratory infections. *Antimicrob Agents Chemother* 1973;3:703-7.
- Bergogne-Berezin E. Antibiotics in the respiratory tree. *J Antimicrob Chemother* 1981;8:171-4.
- Naeverson MA. Intravenous administration of erythromycin: serum, sputum and urine levels. *Curr Med Res Opin* 1976;4:359-64.
- Marlin GE, Davies PR, Rutland J, Berend N. Plasma and sputum erythromycin concentrations in chronic bronchitis. *Thorax* 1980;35:441-5.
- Seigler D, Kaye CM, Reilley S, Willis AT, Sankey MG. Serum, saliva and sputum levels of metronidazole in acute exacerbations of chronic bronchitis. *Thorax* 1981;36:781-3.
- MacCulloch D, Richardson RA, Allwood GK. The penetration of doxycycline, oxytetracycline and minocycline into sputum. *N Z Med J* 1974;80:300-2.
- Maesen F, Davies BI, Van Noord JA. Doxycycline in respiratory infections: a re-assessment after 17 years. *J Antimicrob Chemother* 1986;18:531-6.
- Gartmann J. Doxycycline concentrations in lung tissue, bronchial wall and bronchial secretion. *Chemotherapy* 1975;21:19-26.
- Noone P, Parsons TMC, Pattison JR, et al. Experience in monitoring gentamicin therapy during treatment of serious Gram-negative sepsis. *Br Med J* 1974;i:477-81.
- Pennington JE, Reynolds HY. Concentrations of gentamicin and carbenicillin in bronchial secretions. *J Infect Dis* 1973;128:63-8.
- Hughes DTD. The use of combinations of trimethoprim and sulphonamides in the treatment of chest infections. *J Antimicrob Chemother* 1983;12:423-34.
- Brumfit W, Hamilton-Miller JMT, Howard CW, Tansley H. Trimethoprim alone compared to co-trimoxazole in lower respiratory infections: pharmacokinetics and clinical effectiveness. *Scand J Infect Dis* 1985;17:99-105.
- Bergogne-Berezin E, Berthelot G, Even P, Stern M, Reynaud P. Penetration of ciprofloxacin into bronchial secretions. *Eur J Clin Microbiol* 1986;5:197-200.
- Schlenkoff D, Knopf J, Dalhoff A. Penetration of ciprofloxacin into human lung tissue. In: Neu HC, Weuta H, eds. *Proceedings of The 1st International ciprofloxacin workshop*. Amsterdam: Excerpta Medica, 1985:157-9. (Current Clinical Practice Series No 34).

Evaluating mass training in cardiopulmonary resuscitation

The Save a Life campaign, which was started in October 1986 to stimulate mass training in emergency first aid, rightly emphasised cardiopulmonary resuscitation—the most complex first aid skill. Such campaigns are not new, and the teaching of rescue breathing has been compulsory in Norwegian schools since the early 1960s.¹ Recommendations have been made for including training on resuscitation in schools,² and there is advice on organising community or mass training.³⁻⁷ But do the benefits of these schemes justify the costs or could the resources be better used?

Many researchers have explored the benefits for real

casualties of bystanders being trained in cardiopulmonary resuscitation,⁸⁻¹⁴ and empirical calculations suggest that a trained bystander can improve the survival chance of somebody with ventricular fibrillation from 21% to 43%.¹⁵ Up to two lives for every 10 000 people could thus be saved annually.¹⁶⁻¹⁸ Such calculations also suggest that a trained lay person will meet a casualty between once in 25 years to once in over 112 years.¹⁶⁻²⁰

Some of these uncertainties have been incorporated into a model of the cost effectiveness of training programmes in cardiopulmonary resuscitation.²¹ Important questions are how often people should be retrained, whether resources should be concentrated on training key groups, and what sort of people should be trained. Over 40 studies have shown that the skills of cardiopulmonary resuscitation decay rapidly.^{19 22 23} Research is equivocal whether training should be concentrated in medical and paramedical groups.²⁴⁻²⁷

A survey of over 3000 people showed individual differences in willingness to attempt cardiopulmonary resuscitation, but over 40% reported that they would do something.²⁸ Reported willingness and actually carrying out cardiopulmonary resuscitation are, however, different things: when medical or paramedical people witnessed a collapse then cardiopulmonary resuscitation was performed in one third of cases, but when only non-medical people were present then resuscitation was performed in about one in every 25 cases.¹⁷ Whether people help depends on how clearly they understand what is happening and on whether other people are present.²⁹ This study also found that women helped less often than men and that, though training did not raise the intervention rate, it did increase dramatically the effectiveness of help given.

Some have argued, however, that even when a rescuer does little or performs cardiopulmonary resuscitation inadequately the survival chances still improve.³⁰ Others have questioned whether "retention of classroom skills is related to performance during actual resuscitation attempts or to eventual clinical outcomes."²² The dearth of empirical studies comparing "classroom skills" with actual performance means that this assertion remains untested. In studies of medical students and hospital staff it has been suggested that some may have performed better in real emergencies and some worse.^{31 32}

Many cases are required to determine the effectiveness of interventions. Assessment is complicated by the nature of the incident that causes breathing to fail and the heart to stop. In some cases cardiopulmonary resuscitation would be unsuccessful however well performed, but developing and maintaining the blood pressure and circulation of oxygen for adequate tissue perfusion and continuing brain function demand a high level of skill. Therefore, there is no basis for assigning low importance to initial and refresher training in cardiopulmonary resuscitation. As rescuers will not require the full repertoire of skills in every incident excellent training is required for trainees to have adequate knowledge and skills from which to draw should the need arise.

Criticisms of mass training in cardiopulmonary resuscitation are that trainees develop a false sense of competence²⁰ and that resuscitation might be performed unnecessarily or hazardously.³³⁻³⁵ High drop out rates among volunteer instructors have also been encountered.³⁶ Some of these problems would be overcome by thorough training and regular refresher training, with particular emphasis on diagnosis. Evaluation of mass training should also take account of possible hidden benefits. For example, we have shown that