

digoxin the indications for the addition (or withdrawal) of other drugs need critical review, particularly those with an action on the heart and circulation. Though the mechanisms of many of the interactions with digoxin remain to be defined, appropriate dosage adjustments can be made from a knowledge of the average alterations which can be expected and measurement (when appropriate) of the plasma or serum digoxin concentration.

CHARLES F GEORGE

Professor of Clinical Pharmacology,
University of Southampton,
Southampton SO9 3TU

- 1 Ogilvie RI, Ruedy J. Adverse drug reactions during hospitalisation. *Can Med Assoc J* 1967;**97**:1450-7.
- 2 Hurwitz N, Wade OL. Intensive hospital monitoring of adverse reactions to drugs. *Br Med J* 1969;**ii**:531-6.
- 3 Beller GA, Smith TW, Abelman WH, Haber E, Hood WB. Digitalis intoxication: a prospective clinical study with serum level correlations. *N Engl J Med* 1971;**284**:989-97.
- 4 Shapiro S, Slone D, Lewis GP, Jick H. The epidemiology of digoxin. A study in three Boston hospitals. *J Chronic Dis* 1969;**22**:361-71.
- 5 Doherty JE, Perkins WH. Digoxin metabolism in hypo- and hyperthyroidism. Studies with tritiated digoxin in thyroid disease. *Ann Intern Med* 1966;**64**:489-507.
- 6 Chamberlain DA. Plasma digoxin concentrations as a guide to therapeutic requirements. In: Davies DS, Prichard BNC, eds. *Biological effects of drugs in relation to their plasma concentrations*. London: MacMillan, 1973:135-43.
- 7 Peck CP, Sheiner LB, Martin CM, Combs DT, Melmon KL. Computer-assisted digoxin therapy. *N Engl J Med* 1973;**289**:441-6.
- 8 Chamberlain DA. Digoxin. In: Breckenridge AM, ed. *Advanced medicine. Topics in therapeutics*. Tunbridge Wells: Pitman Medical, 1975:49-64.
- 9 Manninen V, Apajalahti A, Melin J, Karesoja M. Altered absorption of digoxin in patients given propantheline and metoclopramide. *Lancet* 1973;**ii**:398-400.
- 10 Gillis RA, Quest JA. The role of the nervous system in the cardiovascular effects of digitalis. *Pharmacol Rev* 1979;**31**:19-97.
- 11 Steiness E, Olesen KH. Cardiac arrhythmias induced by hypokalaemia and potassium loss during maintenance digoxin therapy. *Br Heart J* 1976;**38**:167-72.
- 12 Steiness E. Renal tubular secretion of digoxin. *Circulation* 1974;**50**:103-7.
- 13 Ejinsson G. Effect of quinidine on plasma concentrations of digoxin. *Br Med J* 1978;**ii**:279-80.
- 14 Kim D-H, Akera T, Brody TM. Interactions between quinidine and cardiac glycosides involving mutual binding sites in the guinea pig. *J Pharmacol Exp Ther* 1981;**218**:108-14.
- 15 Hager WD, Fenster P, Mayersohn M, et al. Digoxin-quinidine interaction. Pharmacokinetic evaluation. *N Engl J Med* 1979;**300**:1238-41.
- 16 Aronson JK, Carver JG. Interaction of digoxin with quinine. *Lancet* 1981;**i**:1418.
- 17 Schenck-Gustafsson K, Dahlqvist R. Pharmacokinetics of digoxin in patients subjected to the quinidine-digoxin interaction. *Br J Clin Pharmacol* 1981;**11**:181-6.
- 18 Klein HO, Lang R, Segni EDI, Kaplinsky E. Verapamil-digoxin interaction. *N Engl J Med* 1980;**303**:160.
- 19 Belz GG, Aust PE, Munkes R. Digoxin plasma concentrations and nifedipine. *Lancet* 1981;**ii**:844-5.
- 20 Moysey JO, Jaggarao NSV, Grundy EN, Chamberlain DA. Amiodarone increases plasma digoxin concentrations. *Br Med J* 1981;**282**:272.
- 21 Caldwell JH, Caldwell PB, Murphy JW, Beachler CW. Intestinal secretion of digoxin in the rat. Augmentation by feeding activated charcoal. *Naunyn Schmiedeberg Arch Pharmacol* 1980;**312**:271-5.
- 22 Renwick AG. First-pass metabolism within the lumen of the gastrointestinal tract. In: George CF, Renwick AG, Shand DG, eds. *Pre-systemic drug elimination*. London: Butterworths (in press).
- 23 Lindenbaum J, Rudd DG, Butler BP, Tse-Eng D, Saha JR. Inactivation of digoxin by the gut flora: reversal by antibiotic therapy. *N Engl J Med* 1981;**305**:789-94.
- 24 Dall JLC. Maintenance digoxin in elderly patients. *Br Med J* 1970;**ii**:705-6.

Postoperative pneumonias

The changes in pulmonary function after surgery and anaesthesia range from a fall in arterial oxygen tension to bronchial and pulmonary infection and collapse of the lung. Of these, postoperative pneumonia most concerns the average

surgeon and anaesthetist. The incidence of chest complications has not changed appreciably over the past 30 years,¹ suggesting that the main determinants have been largely unaffected by changes in medical and surgical practice. The problem is substantial: depending on the rigour of the diagnostic criteria, the incidence of pulmonary infections after upper abdominal surgery ranges from 5%² to about 70% of patients,³ with most surveys agreeing on an incidence close to 20%.¹

Suggestions about the aetiology of these infections have included abdominal distension due to ileus, pneumoperitoneum, inhibition of cough by postoperative pain, reflex spasm, cough reflexes depressed by opiates, lowered end-tidal point, collapse of the lung from absorption of soluble gases, use of monotonous low tidal volumes leading to loss of surfactant, increased viscosity of secretions due to atropine and dry inhaled gases, effects of anaesthetic (and atropine) and intubation with cuffed tubes on ciliary action, depression of cellular defence mechanisms, immunosuppression by anaesthesia, and contaminated anaesthetic equipment. Of these, the only factor that has been put to the test of prospective controlled trials with unequivocal results is the last. Two studies comparing the outcome in terms of postoperative chest infections when the anaesthetic was given with or without bacterial filters failed to show any difference.^{4 5}

Surveys of postoperative infections highlight quite different factors as the major determinants, the most important being the site of operation: the incidence of pneumonia after operations outside the chest or upper abdomen in fit patients is negligible.¹ Next, chronic respiratory disease trebles the complication rate.⁶ Obesity (above 120 kg), old age (above 70 years), and history of smoking¹ are also associated with a greater probability of postoperative pneumonia. Men have an incidence two to three times that in women,⁶ though in one study no difference was found when correction was made for operative site.¹ Duration of operation is also a factor if it extends beyond two hours, as is evidence of a general lower level of fitness and a longer preoperative stay in hospital.¹

What can be done? Three possibilities suggest themselves: improving the preoperative and postoperative management of chronic chest disease, the prophylactic use of antibiotics, and more effective control of postoperative pain.

Breathing exercises and postural drainage were shown to be effective in reducing exacerbations of chronic infection almost 30 years ago.⁷ Breathing exercises have also been shown to be effective in patients having open-heart surgery if they are over 60, heavy smokers, or have a forced vital capacity less than 80% of the predicted value or a forced expiratory volume less than 75% of the forced vital capacity.⁸

Preoperative lung function tests do not seem to discriminate reliably between those patients likely to develop pneumonia and those not despite some reports to the contrary. Patients with limitation of flow below 1 litre/second at functional residual capacity accounted for over half of the pneumonias in one series of thoracic operations.⁹ In another study the extent of the fall in the peak flow on the first postoperative day proved a good discriminator in a group of patients undergoing repair of hernia.¹⁰ Unfortunately, the same was not true in patients with abdominal incisions, where the effect on peak flow of pain or reflex muscle rigidity or both presumably swamped any effect.

Nor have special postoperative routines much contribution to make. Postoperative physiotherapy, often accompanied by intermittent positive-pressure breathing, is popular in the United States. Treatment with an incentive spirometer is probably better as well as vastly cheaper.¹¹ Neither, however,

seems to make much difference to the overall incidence of chest complications.

Prophylactic antibiotics, too, have been generally viewed with reserve. Several reports have shown no overall benefit,¹²⁻¹⁴ but another study, in which the appropriate antibiotics were given in therapeutically effective regimens, showed a reduction in the frequency of infections.¹⁵ No benefit was found from routine bronchodilator treatment.

Improving the relief of pain has proved equally disappointing as an approach to preventing chest infections. Additional morphine¹⁵ was of no benefit, and systemic analgesia with procaine, while effective in helping patients to clear sputum, had only a marginal influence on vital capacity.¹⁶ Mid-axillary nerve blocks of the 6th to 11th intercostal nerves were no more effective.¹⁷ One early report suggested that epidural opiates do not restore pulmonary mechanics to anything like normal either,¹⁸ suggesting that reflex muscle spasm is as important as the pain itself. Even so, effective relief of pain has yet to be shown to be worthless in terms of actual complications rather than changes in pulmonary function.

There remains the observation in 1976 that the respiratory stimulant doxapram reduced the incidence of cough and expectoration of purulent sputum without any major effect on analgesia.¹⁹ More recently doxapram was, however, found not to have any effect in patients with preoperative symptoms having thoracotomies who were given prophylactic antibiotics,²⁰ a finding in keeping with another study which found a beneficial effect from doxapram only in patients not given antibiotics.²¹

What conclusions can be reached? Prophylactic treatment of any kind seems scarcely justifiable for all patients, since some 80% will suffer no complications; but either doxapram or prophylactic antibiotics may reasonably be prescribed for patients at high risk.

M D VICKERS

Professor of Anaesthetics,
Welsh National School of Medicine,
Cardiff CF4 4XN

- ¹ Garibaldi RA, Britt MR, Coleman ML, Reading JC, Pace NL. Risk factors for postoperative pneumonia. *Am J Med* 1981;**70**:677-80.
- ² Davidson J. Prevention of postoperative chest complications. *Lancet* 1953;ii:1225-6.
- ³ Gawley TH, Dundee JW, Gupta PK, Jones CJ. Role of doxapram in reducing pulmonary complications after major surgery. *Br Med J* 1976;ii:122-4.
- ⁴ Feeley TW, Hamilton WK, Xavier B, Moyers J, Eger EI. Sterile anesthesia breathing circuits do not prevent postoperative pulmonary infection. *Anesthesiology* 1981;**54**:369-72.
- ⁵ Garibaldi RA, Britt MR, Webster RN, Pace NL. Failure of bacterial filters to reduce the incidence of pneumonia after inhalation anesthesia. *Anesthesiology* 1981;**54**:364-8.
- ⁶ Wightman JAK. A prospective survey of the incidence of postoperative pulmonary complications. *Br J Surg* 1968;**55**:85-91.
- ⁷ Palmer KNV, Sellick BA. The prevention of postoperative pulmonary atelectasis. *Lancet* 1953;ii:164-8.
- ⁸ Vrii JK, Vrii RA. Effectiveness of breathing exercises in preventing pulmonary complications following open heart surgery. *Phys Ther* 1977;**57**:1367-71.
- ⁹ Yoshida T, Ushijima Y, Inokuchi K, Hirose T, Shirakusa T, Katayama N. Evaluation of the risk of postoperative pulmonary complications. *Jpn J Surg* 1977;**7**:131-8.
- ¹⁰ Clague MB, Collin J, Fleming LB. Prediction of postoperative respiratory complications by simple spirometry. *Ann R Coll Surg Engl* 1979;**61**:59-62.
- ¹¹ Van De Water JM, Watring WG, Linton LA, Murphy M, Byron RL. Prevention of postoperative pulmonary complications. *Surg Gynecol Obstet* 1971;**135**:229-33.
- ¹² Barnes J, Pace WG, Trump DS, Ellison EH. Prophylactic postoperative antibiotics. *Arch Surg* 1959;**79**:190-6.
- ¹³ Thulbourne T, Young MH. Prophylactic penicillin and postoperative chest infections. *Lancet* 1962;ii:907-9.
- ¹⁴ Palmer KNV, Sellick BA. Effect of procaine penicillin and breathing exercises in postoperative pulmonary complications. *Lancet* 1952;ii:315-6.
- ¹⁵ Collins CD, Darke CS, Knowelden J. Chest complications after upper abdominal surgery: their anticipation and prevention. *Br Med J* 1968;ii:401-6.

- ¹⁶ Pooler HE. Relief of post-operative pain and its influence on vital capacity. *Br Med J* 1949;iii:1200-3.
- ¹⁷ McCleery RS, Zollinger R, Lenahan NE. A clinical study of the effect of intercostal nerve block with nupercaine in oil following upper abdominal surgery. *Surg Gynecol Obstet* 1948;**86**:680-6.
- ¹⁸ Bromage PR, Camporesi E, Chestnut D. Epidural narcotics for post-operative analgesia. *Anesth Analg (Cleve)* 1980;**59**:473-80.
- ¹⁹ Gawley TH, Dundee JW, Gupta PK, Jones CJ. Role of doxapram in reducing postoperative pulmonary complications after major surgery. *Br Med J* 1976;ii:122-4.
- ²⁰ Sebel PS, Kershaw EJ, Rao WS. Effects of doxapram on postoperative pulmonary complications following thoracotomy. *Br J Anaesth* 1980;**52**:81-4.
- ²¹ Downing JW, Jeal DE, Allen PJ, Buley R. Doxapram hydrochloride and pulmonary complications after lower abdominal surgery. *Br J Anaesth* 1977;**49**:473-7.

Dog bites man

Writing about dogs is apt to stir passions, but statistics at least give a dispassionate starting point. Every year in the United States a million dogs bite the hands that feed them and doubtless shatter the illusion of trust and friendship. But is it the dog's fault? The highly strung, untrained, bored dog may turn on the taunting child; the one goes to the condemned cell and the other to the accident and emergency department. How should the wound be treated?

Animal teeth are far from clean and sharp and so create a contused and contaminated wound, in which bacteria may multiply and scar tissue may form. The prevention of wound sepsis has both surgical and medical aspects. Careful cleaning, irrigation, trimming of wound margins, elimination of dead space during closure, and avoiding overtension of sutures are all important factors. Two cardinal sins to be avoided are shaving eyebrows and failing to match the vermilion of the lips. Use of fine suture materials, removed early and replaced by surface closures, will reduce the chance of skin marking or sepsis. Only in extensive wounds or difficult cases is delayed primary suture usually required.

The medical aspect of management includes prophylaxis against tetanus and, where appropriate, rabies. The controversial issue, however, is the prevention or management of wound sepsis. The dog's mouth acts as host to a wide range of pathogens, including *Pseudomonas* spp, *Staphylococcus aureus*, *Streptococcus viridans*, and *Pasteurella multocida*. A greater risk of sepsis is to be found in patients aged over 50, wounds over 24 hours old, puncture wounds, injuries of the hand, and the presence of pre-existing illness. Among the reported complications of wound sepsis are abscess formation, osteomyelitis,¹ and disseminated intravascular coagulation.

Prevention of infection is obviously the ideal. Callaham² favours the use of prophylactic antibiotics, especially in the case of bites on the hands. The choice of antibiotic lies between the penicillinase-resistant broad-spectrum penicillins and the equivalent cephalosporins with an early parenteral first dose as the ideal.³ Callaham recommends erythromycin or tetracycline as an alternative for those significantly allergic to the penicillin group, but co-trimoxazole might be considered as a better alternative with the added advantage of being active against other Gram-negative organisms. Elenbaas *et al*,⁴ in contrast, recently completed a prospective, double-blind, placebo-controlled study on the use of prophylactic oxacillin in dog-bite wounds and concluded that prophylactic antibiotics were of no value in the care of dog-bite injuries treated within 24 hours of accident. (Oxacillin is not much used in Britain.) If nothing