

undergoes a course of rehabilitation should not be dismissed as an excessive delay before a curative procedure. Should the patient's cancer progress clinically during this period, the chances are that the patient had presented with subclinical advanced or metastatic disease.

Altering clinical perceptions and practices nationwide takes great effort, especially when there have been few breakthroughs to stimulate such change. Nevertheless, the hope is that the recommendations by the two UK-based societies, together with those being developed by other thoracic societies, will shape the management of lung cancer. The next radical step is to translate knowledge of the molecular basis of lung cancer into usable intermediate biomarkers for screening and drugs for chemoprevention to bolster secondary prevention. However, what clinicians will still need to do is to convince themselves and their national policymakers that primary prevention of 80–90% of lung cancers through reduction of tobacco addiction and dependence is desirable and achievable.

Rex C Yung, *Jonathan B Orens

Departments of Medicine and Oncology and Pulmonary and Critical Care Medicine, Johns Hopkins University, Baltimore, MD 21208, USA (e-mail: jorens@welch.jhu.edu)

- 1 American Cancer Society. Cancer facts and figures 1998. Atlanta: American Cancer Society, 1998: 1–36
- 2 Armstrong P, Congleton J, Fountain SW, et al. Guidelines for the selection of patients with lung cancer. British Thoracic Society and Society of Cardiothoracic Surgeons of Great Britain and Ireland Working Party. *Thorax* 2001; **56**: 89–108.
- 3 Jett J, Feins R, Kvale P, et al. American Thoracic Society/European Respiratory Society. Pretreatment evaluation of non-small-cell lung cancer. *Am J Respir Crit Care Med* 1997; **156**: 320–32.
- 4 National Comprehensive Cancer Network (NCCN). Complete Library of NCCN Oncology Practice Guidelines. CD-Rom Vol 1. Melville, NY: PRR Inc, Nov, 2000.
- 5 Tockman MS, Frost JK, Stitik FP, et al. Screening and detection of lung cancer. In: Aisner J, ed. Lung Cancer. New York: Churchill Livingstone, 1985.
- 6 US Preventive Services Task Force. Screening for lung cancer. In: Guide to clinical preventive services, 2nd ed. Baltimore, MD: Williams and Wilkins, 1996: 135–39.
- 7 Henschke CI, McCauley DI, Yankelevitz DF, et al. Early Lung Cancer Action Project: overall design and findings from baseline screening. *Lancet* 1999; **354**: 99–105.
- 8 Kaneko M, Eguchi K, Ohmatsu H, et al. Peripheral lung cancer: screening and detection with low-dose spiral CT versus radiography. *Radiography* 1996; **201**: 798–802.
- 9 Mountain CF. Revisions in the international system for staging lung cancer. *Chest* 1997; **111**: 1701–07.
- 10 Pisters KMW, Ginsberg RJ, Giroux DJ, et al. Induction chemotherapy before surgery for early stage lung cancer: a novel approach. *J Thoracic Cardiovasc Surg* 2000; **119**: 429–39.
- 11 McLoud TC, Bourgoin PM, Greenberg RW, et al. Bronchogenic carcinoma: analysis of staging in the mediastinum with CT by correlative lymph node mapping and sampling. *Radiology* 1992; **182**: 319–23.
- 12 Dietlein M, Weber K, Gandjour A, et al. Cost-effectiveness of FDG-PET for the management of potentially operable non-small cell lung cancer: priority for a PET-based strategy after nodal-negative CT results. *Eur J Nucl Med* 2000; **27**: 1598–609.
- 13 Ost D, Fein A. Evaluation and management of the solitary pulmonary nodule. *Am J Respir Crit Care Med* 2000; **162**: 782–87.
- 14 Lowe V, Naunheim K. Positron emission tomography in lung cancer. *Ann Thorac Surg* 1998; **65**: 1821–29.
- 15 Wang KP, Terry PB. Transbronchial needle aspiration in the diagnosis and staging of bronchogenic carcinoma. *Am Rev Respir Dis* 1983; **127**: 344–47.
- 16 Cooper JD, Trulock EP, Triantafyllou AN, et al. Bilateral pneumonectomy (volume reduction) for chronic obstructive pulmonary disease. *J Thorac Cardiovasc Surg* 1995; **109**: 106–19.

Effective antibiotic-resistance control strategies

See page 1325

Despite improvement in the understanding of antibiotic-resistance mechanisms, measures to control such resistance have not been uniformly successful. One reason is that these measures have been based on false premises. The most pervasive antibiotic myth is the notion that antibiotic resistance is inevitable if an antibiotic is used in sufficient volume over time. Antibiotics such as doxycycline or nitrofurantoin have been used in high volume for decades without bacteria becoming resistant to them.^{1–3} The notion that volume of use is associated with resistance lay behind the study reported by Vivre Enne and colleagues in today's *Lancet*. They investigated whether a national restriction on sulphonamide prescribing reduced incidence of sulphonamide-resistant *Escherichia coli*—and found no reduction in resistance. Measures to reduce “antibiotic tonnage” by limiting, or avoiding, antimicrobial therapy for viral, non-antibiotic-responsive infections, and non-infectious diseases is good medicine, but does not reduce antibiotic resistance.¹

The other widespread myth is that antibiotic resistance is related to certain antibiotic classes—eg, third-generation cephalosporins or fluoroquinolones. Of the third-generation cephalosporins, resistance other than of the episodic clonal type is encountered only with ceftazidime.^{4–7} Similarly, with the fluoroquinolones, resistance is nearly always attributable to ciprofloxacin and the early quinolones, such as nalidixic acid and norfloxacin.⁵ Among the tetracyclines, resistance has been described only with tetracycline but not doxycycline or minocycline.⁵ With aminoglycosides, gentamicin and tobramycin are associated with resistance, but not amikacin.⁵ Among second-generation cephalosporins, there is resistance to cefamandole but not to cefuroxime, cefotetan, or cefoxitin.⁵ With carbapenems, imipenem but not meropenem has been associated with resistance.^{5,6}

Antibiotic resistance should instead be thought of in terms of the potential for resistance to develop, based on when resistance occurs in the life of the antibiotic. If resistance occurs during drug development or clinical trials, or within 2 years of general use, the antibiotic has high resistance potential. Otherwise, it is a low-resistance-potential antibiotic because resistance rarely, if ever, develops beyond this time.^{4–6} Antibiotics with high resistance potential do not lose this tendency later. Antibiotics with low resistance potential may be used freely for decades without fear of resistance developing, as has been demonstrated with all second-generation cephalosporins (except cefamandole), and all third and fourth generation cephalosporins (except ceftazidime).⁶

The concept of antibiotic cycling is being resurrected in some centres. This strategy is based on the notion that limiting general exposure to an antibiotic will reduce the likelihood of resistance. However, if antibiotics with high resistance potential are used in cycling, this strategy could introduce resistance problems that may not be easily eliminated.^{8,9} Antibiotic cycling is an especial problem in intensive-care units because of their high volume of use of high-resistance-potential antibiotics—ie, ciprofloxacin, imipenem, and ceftazidime.^{5,6}

The most effective antibiotic-resistance control measure has been the restriction of high-resistance-

potential antibiotics at formulary level. If ciprofloxacin, ceftazidime, and imipenem are restricted, most, but not all, resistance problems can be reduced or eliminated within 12 months.^{1,6} In individual hospitals, additional measures may be necessary. If there is *Pseudomonas* resistance within an institution, then amikacin substitution will eliminate the gentamicin component of the resistance, but not that due to ciprofloxacin, ceftazidime, or imipenem. Unless a particular resistance problem is shown to be due to a single agent, effective control usually requires the restriction of other high-resistance-potential antibiotics causing resistance in a given bacterial species. To control the emergence of penicillin-resistant pneumococci, macrolides, cotrimoxazole, and ciprofloxacin may have to be restricted.^{1,6,10} Vancomycin use is commonly cited as an example of a drug whose effectiveness has diminished during the past decade. However, vancomycin has not increased the degree of *Enterococcus faecalis* resistance; rather, it has increased the prevalence of vancomycin-resistant *E faecium*, so vancomycin restriction is advisable to prevent an increase in the prevalence of vancomycin-resistant enterococci.¹¹

Widespread resistance problems associated with specific antibiotics should be distinguished from clonal resistance problems that can be traced to the spread of a single strain. Clonal resistance is perpetuated or spread by ineffective infection control measures rather than by inappropriate antibiotic use.^{1,3,9}

To be effective, control of antibiotic resistance must be implemented at many levels. At the national level, governments should ban the addition of antibiotics to animal feeds or products. The volume of antibiotics used in animal feeds equals or exceeds that used to treat infections in human beings, and most antibiotics used in animal feeds are of high resistance potential. Resistant organisms in animal products eventually make their way into the human population. Antibiotics with high resistance potential should also be deleted from national formularies or their use should be restricted. The same applies to hospital formularies. Clones of highly resistant organisms at the hospital level should be countered with measures to contain the resistant organisms within the institution.^{1,3,9} At the prescribing level, physicians should preferentially select antibiotics with low resistance potential, all other factors being equal.^{1,12,13}

Pharmacokinetic optimisation of dose does not prevent resistance. Furthermore, bacterial regrowth in vitro should not be confused with resistance.^{5,6} When resistance-prone antibiotics are used, resistant strains may occur in days and persist for weeks after the antibiotic therapy. The dynamics of bacterial populations, especially the faecal flora (where most resistant strains originate), obey genetic and Darwinian principles. Antibiotic resistance is reversible over time, not by decreasing antibiotic use, but by changing to low-resistance-potential antibiotics. The more profound and pervasive is the antibiotic resistance, the longer it takes sensitive strains to re-establish themselves as the predominant flora.^{12,13}

Antibiotic resistance in a community setting is often caused by exposure to multiple antibiotics. Enne and colleagues found that *E coli* resistance was not simply due to sulphonamides but the genetic studies indicated that it was probably caused by use of other high-resistance-potential antibiotics commonly used in general practice, such as tetracycline and ampicillin. The study does not argue against national antibiotic restriction as an effective resistance-control measure.

Only one of many high-resistance-potential antibiotics were restricted. The results might have been different if amoxicillin had been substituted for ampicillin, doxycycline for tetracycline, and another quinolone for ciprofloxacin.^{5,6,14,15}

Burke A Cunha

Infectious Disease Division, Winthrop-University Hospital, Mineola, NY 11501, New York, and State University of New York School of Medicine, Stony Brook, New York, USA
(e-mail: llusardi@winthrop.org)

- 1 Levy SB. Antibiotic resistance: origins, evolution, selection, and spread. New York, John Wiley & Sons, 1997: 1–239.
- 2 Shlaes DM, Gerding DN, John JF Jr, et al. Society for Healthcare Epidemiology of American and Infectious Diseases Society of America Joint Committee on the Prevention of Antimicrobial Resistance: guidelines for the prevention of antimicrobial resistance in hospitals. *Clin Infect Dis* 1997; **25**: 584–99.
- 3 Gross PA. The potential for clinical guidelines to impact appropriate antimicrobial use. *Infect Dis Clin North Am* 1997; **11**: 803–12.
- 4 Cunha BA. Antibiotic resistance. *Drugs for Today* 1998; **31**: 691–98.
- 5 Cunha BA. Antibiotic resistance. Control strategies. *Crit Care Clin* 1998; **14**: 309–27.
- 6 Cunha BA. Antibiotic resistance. *Med Clin North Am* 2000; **84**: 1407–29.
- 7 Monnet D, Gaynes R, Tenover F, McGowan J. Ceftazidime-resistant *Pseudomonas aeruginosa* and ceftazidime usage in NNIS hospitals: preliminary results of Project ICARE. Phase one. *Infect Control Hosp Epidemiol* 1995; **4** (suppl): 19.
- 8 McGowan JE, Jr. Strategies for studying the role of cycling on antimicrobial use and resistance. *Infect Control Hosp Epidemiol* 2000; **21** (suppl 1): S36–43.
- 9 Mainardi JL, Carlet J, Acar J. Antibiotic resistance problems in the critical care unit. *Crit Care Clin* 1998; **14**: 199–219.
- 10 Rice LB. Successful interventions for gram-negative resistance to extended-spectrum beta-lactam antibiotics. *Pharmacotherapy* 1999; **19**: 120S–28.
- 11 Smith DW. Decreased antimicrobial resistance after changes in antibiotic use. *Pharmacotherapy* 1999; **19**: 129S–32S.
- 12 Levy SB, Marshall B, Schluederberg S, Rowse D, Davis J. High frequency of antimicrobial in human fecal flora. *Antimicrob Agents Chemother* 1988; **32**: 1801–06.
- 13 Levy SB. Antibiotic resistant bacteria in food of man and animals. In: Woodbine M (ed). *Antimicrobials and Agriculture*. London, Butterworths, 1984: 525–31.
- 14 Krcmery V, Jeljaszewicz J, Grzesiowski P, et al. National and local antibiotic policies in central and eastern Europe. *J Chemother* 2000; **12**: 471–74.
- 15 Reinert RR, Smiljna S, Al-Lahham A, Reinert S, Lemperle M, Lutticken R. Antimicrobial resistance of *Streptococcus pneumoniae* recovered from outpatients with respiratory tract infections in Germany from 1998 to 1999: results of a national surveillance study. *J Clin Microbiol* 2001; **39**: 1187–89.

Bedside treatment of chronic subdural haematoma?

Chronic subdural haematoma (CSDH) is one of the commonest disorders requiring neurosurgery. It is largely a disorder of old age, with two-thirds of cases occurring in patients over the age of 65 and 40% in those aged over 75.¹ In younger patients it generally occurs in patients with premature cerebral atrophy and/or a propensity to minor head injuries—characteristically either in patients with epilepsy or in alcoholics. Unusually for a mass lesion within the skull vault, the intracranial pressure may be normal or raised only slightly, which reflects the fact that CSDH generally develops as an ex vacuo lesion (one that fills the gap) following a minor head injury, the lack of any tamponading effect permitting the expansion of the surface collection of fluid and blood.² Symptoms may not start until weeks or even months after a minor head injury (which is often forgotten), and once symptoms appear they commonly fluctuate in severity from day to day.² The