

agendas based on their own experience and values without adequate consultation in the countries where the actions will be based. Priority setting should include consultation with local health professionals who are aware of barriers in the health system, values of society, and deal daily with the results of these difficult priority decisions. Public-health importance, sustainability, reduction of disease burden, evidence of effectiveness in the local setting, and cost effectiveness of various HIV and AIDS interventions should all be borne in mind.

We support measures to lower drugs prices, but only in light of available resources to ensure appropriate and cost-effective use.

*Douglas Ball, Klára Tisócki, Stanley Houston

Departments of *Pharmacy and Clinical Pharmacology, University of Zimbabwe, PO Box A178 Avondale, Harare, Zimbabwe

- 1 Perez-Casas C, Chirac P, Berman D, Ford N. Access to fluconazole in developing countries. *Lancet* 2000; **356**: 2102.
- 2 Saag MS, Graybill RJ, Larson RA, et al. Practice Guidelines for the management of cryptococcal disease: Infectious Disease Society of America. *Clin Infect Dis* 2000; **30**: 710–18.
- 3 Heyderman RS, Gangaidzo IT, Hakim JG, et al. Cryptococcal meningitis in human immunodeficiency virus-infected patients in Harare, Zimbabwe. *Clin Infect Dis* 1998; **26**: 284–89

Wounding from biopsy and breast-cancer progression

Sir—Surgical wounding associated with the extirpation of experimental primary cancers can trigger angiogenesis in previously dormant micrometastatic tumour deposits, which can result in the acceleration of relapse and death.^{1,2}

The uniform incapacity of randomised controlled studies of screening mammography to show early surgical advantage of screened populations aged 40–49 years might relate to this biology.³ Data suggest such acceleration of disease occurs in 27% of premenopausal women with node-positive breast cancer—far more than in other groups. In later years, this effect is balanced by a reduction in relapses. We calculate that this effect can explain a surge of 0.11 deaths per 1000 screened women aged 40–49 at 2–3 years after the start of screening. This number is roughly equal to the significant excess 0.15 deaths per 1000 women in the intervention group that

is reported 3 years after the start of screening trials.⁴

Our calculation does not fully explain the Canadian screening trial. It began in 1980 and is the largest screening trial for young women (25 000 per group) and includes adjuvant chemotherapy for all node-positive premenopausal patients. No survival advantage in the screened group has been seen even after 10 years of follow-up.⁵ Two striking features of the trial are: the excess of deaths in the intervention group (82 vs 72) is attributed to an excess of patients diagnosed with more than three positive lymph nodes in the first year (19 vs 5 controls); and three-fold more biopsies were done in the intervention group (33/1000 in year 1) than in the control group (11/1000).

The breast is rich in lymphatics, and the wounding associated with a biopsy might upregulate the secretion of growth factors and induce lymph-angiogenesis (A Kaipainan, personal communication).

The lack of mammographic benefit in the Canadian study can be explained by the extra 550 biopsies done in year 1 in the intervention group if 14 of these biopsies showed false-negative results and caused lymphangiogenesis and stage progression. If 27% of primary tumour extirpations could produce angiogenic stimulation of dormant micro-metastatic lesions in node-positive cases, perhaps 2% of biopsies could cause lymphatic invasion and stage progression from 0–3 to more than three positive lymph nodes. This biologically and medically important effect is small enough that it would escape observation in anything other than a large screening trial.

Our hypothesis is that stage progression associated with excessive biopsies in young women with abnormal mammograms offsets any long-term benefit for the screened populations.

*Michael Retsky, Romano Demicheli, William Hrushesky

Children's Hospital and Harvard Medical School, Enders Building, 10th Floor, 300 Longwood Avenue, Boston, MA 02115, USA

- 1 Fisher B, Fisher ER. Experimental evidence in support of the dormant tumor cell. *Science* 1959; **130**: 918–19.
- 2 O'Reilly MS, Holmgren L, Shing Y, et al. Angiostatin: a novel angiogenesis inhibitor that mediates the suppression of metastases by a Lewis lung carcinoma. *Cell* 1994; **79**: 315–28.
- 3 Retsky M, Demicheli R, Hrushesky W. Premenopausal status accelerates relapse in node positive breast cancer: hypothesis links angiogenesis, screening controversy. *Breast Cancer Res Treat* (in press).

- 4 Cox B. Variation in the effectiveness of breast screening by year of follow-up. *J Natl Cancer Inst Monogr* 1997; **22**: 69–72.
- 5 Miller A, To T, Baines C, Wall C. The Canadian national breast screening study: update on breast cancer mortality. *J Natl Cancer Inst Monogr* 1997; **22**: 37–41.

Medical quotations

Sir—I read with interest David Sharp's review (Dec 2, p 1938)¹ of the 1999 book *Medically speaking: a dictionary of quotations on dentistry, medicine, and nursing* by Carl and Alma Gaither.²

Although I had not yet read Gaithers' latest book, I would like to cite a few more examples of "killing" by physicians: "What will you do, sir, with four physicians? Is not one enough to kill one body?" (Molière, 1665). "Young men kill their patients; old men let them die" (James Gregory, 1753–1821). "Why did I get into this field? I killed too many people when I was in practice" (Thomas C Chalmers, 1992).

All of the above were taken from among more than 3000 quotes from *Medicine in Quotations* by Edward J Huth and T Jock Murray.³

Tsung O Cheng

Department of Medicine, George Washington University Medical Center, Washington, DC 20037, USA

- 1 Sharp D. Give us a quote. *Lancet* 2000; **356**: 1938.
- 2 Gaitner CC, Cavazos-Gaitner AE, eds. Mechanically speaking: a dictionary of quotations on dentistry, medicine, and nursing. Bristol: Institute of Physics Publishing, 1999.
- 3 Huth EJ, Murray TJ. *Medicine in Quotations*. Philadelphia: American College of Physicians, 2000.

DEPARTMENT OF ERROR

Interferon gamma gene in rheumatoid arthritis—In this Correspondence letter by Jerry S Lanchbury and colleagues (Dec 23/30, p 2192), the footnote to the figure legend should have read "Correct size calling of polymorphic microsatellite alleles can be validated by an 'allele-specific ladder' labelled with a different fluorophore. Figure shows ladder for CRH.PCR marker and actual allele peaks for two individuals (ladder in outline, individual peaks shaded). Ladder represents most abundant alleles in population and consistent peak heights allow rapid and accurate identification of alleles across groups of unrelateds".

Burden of chronic obstructive pulmonary disease—In this Supplement article by Andrea Rossi and Marco Confalonieri (Dec 23/30 [suppl], page s56), the figure was reproduced from *Eur Respir J* 1995; **8**: 1398–420, with permission.

Defining and refining international donor support for combating the AIDS pandemic—In this Public health article by A Attaran and J Sachs (Jan 6, p 57), the Y axis on figure 2 should read, "US\$".