

A new paradox: drugs too cheap to stay available

Sir – A recent paper on the WHO Model List of Essential Drugs discussed the many factors responsible for the scarcity of reserve antimicrobial drugs, among which are cost considerations (1). Fasehun called it a paradox that people who can least afford expensive antibacterial drugs are those who are most vulnerable to infection.

We would like to point to another paradox: primary drugs may become too cheap to be available, even to people who could perhaps afford expensive ones!

Streptomycin (as its sulfate) is listed as an essential antituberculosis drug (2, 3). Isoniazid, rifampicin, ethambutol, pyrazinamide, and streptomycin are considered primary antituberculosis drugs (4). In Austria, streptomycin was withdrawn in 1998 (5). The manufacturers say that the costs of official registration and distribution do not justify continued marketing. Austrian physicians are thus no longer able to find this primary antituberculosis drug in either of the two official drug lists: *Austria Codex* and *VIDAL Arzneimittelverzeichnis*.

In Austria (population, ca. 8 million) in 1997 approximately 84 kg streptomycin (as its sulfate) were used in human medicine — the same amount was used in veterinary medicine: 50% for therapy and 50% as a preservative for semen. Though this drug could be legally imported from any European Union Member State, its absence from the Austrian drug lists has meant that its use has almost ceased. In 1998, 0.3 kg streptomycin were imported by the Federal States of Tyrol and Vorarlberg (ca. 1 million inhabitants) for human therapy, compared with 12 kg for the treatment of apple tree cultures for fire blight (*Erwinia amylovora*).

Previously we reported that niclosamide, the drug of choice for the treatment of *Taenia saginata* infestations in humans, was withdrawn from the market in Austria in 1993, while praziquantel — the only other drug effective in treating taeniasis — is registered solely for administration to animals (6). Only its veterinary use guarantees sufficient consumption of niclosamide to warrant the costs of official registration and marketing. Antibiotics now seem to be more profitable in agriculture and animal husbandry than in human therapy.

In the USA, the Orphan Drug Act was passed in 1983 to provide companies with incentives in the form of grants, tax credits and a seven-year marketing monopoly for the development of drugs for treating rare diseases. Tuberculosis, regrettably, is not a rare disease. With the recent global resurgence of tuberculosis and the concomitant rise in multidrug-resistant strains of *Mycobacterium tuberculosis* there is an increasing demand for unhampered availability of streptomycin. Perhaps time-proven drugs that are too cheap and needed in quantities too small to guarantee continued profits should be designated as orphan drugs to ensure their general availability. ■

F. Allerberger & M.P. Dierich

Professors, Institute for Hygiene and Social Medicine
University of Innsbruck
Fritz-Pregl-Strasse 3
6020 Innsbruck, Austria

1. Fasehun F. The antibacterial paradox: essential drugs, effectiveness, and cost. *Bulletin of the World Health Organization*, 1999, **77**: 211–216.
2. Williams JD. The WHO model list of essential drugs. *International Journal of Antimicrobial Agents*, 1999, **12**: 71–180.
3. *The use of essential drugs. Eighth report of the WHO Expert Committee (including the Revised Model List of Essential Drugs)*. Geneva, World Health Organization, 1998 (WHO Technical Report Series, No. 882).
4. Pfyffer GE et al. Multicenter laboratory validation of susceptibility testing of *Mycobacterium tuberculosis* against classical second-line and newer antimicrobial drugs by using the radiometric BACTEC 460 technique and the proportion method with solid media. *Journal of Clinical Microbiology*, 1999, **37**: 3179–3186.
5. Jentzsch A, Jasek W. *Austria-Codex Fachinformation 1997/1998* (51st ed.). Vienna, Österreichische Apotheker-Verlagsgesellschaft, 1997.
6. Allerberger F, Dierich MP. A new kind of orphan drug? *Nature*, 1992, **357**: 531.

Unified terminology for pathology of the cervix

Sir – In their article on risk factors for cervical dysplasia, Varghese et al. report the results of Pap smears that detected abnormalities caused by human papilloma virus, different degrees (mild, moderate and severe) of dysplasia, and cancer in situ (1). The presentation of these results is ambiguous because it does not fit in with

the evolution of nomenclature and terminology in cervicovaginal pathology.

Varghese et al. seem to be referring, on the one hand, to WHO's descriptive histological classification, under which it is impossible, in everyday practice, to distinguish morphologically between "severe dysplasia" and "cancer in situ". On the other hand, the distinction made by them between isolated lesions caused by viruses (without dysplasia) and dysplasia is at variance with the conclusions of the Consensus Conference on Cervical Neoplasia, held in Paris in 1991, which found this distinction impossible to make.

In 1973, Richart introduced the generic term cervical intraepithelial neoplasia (CIN) to cover the two entities "dysplasia" and "cancer in situ", to emphasize that CIN is a single disease that progresses (a continuum). The equivalences established between the WHO classification and Richart's classification led to the inclusion of severe dysplasia and carcinoma in situ in the same category (CIN 3). Subsequently, the Bethesda system, introduced in 1988 at the initiative of the US National Cancer Institute, made it possible to distinguish between low-grade intraepithelial lesions (CIN 1 or mild dysplasia, including viral lesions in the absence of cytological signs of dysplasia) and high-grade intraepithelial lesions (CIN 2 or moderate dysplasia; and CIN 3 or severe dysplasia, or in situ carcinoma). Since then, it has been recommended that pathologists propose precise diagnoses and refer to the Richart and Bethesda classifications.

Although not all problems of cytological interpretation have been fully resolved, the adoption by all of a common terminology is a fundamental necessity in order to facilitate understanding of the published epidemiological data and to improve the efficacy of multidisciplinary and occasionally international case management of patients with cervical neoplasia. ■

Arthur N'Golet

Professor of Histopathology and Cytopathology
University of Brazzaville, Congo
present address:
World Health Organization Office
PO Box 152, N'Djamena, Chad
fax: 235 52 31 59
e-mail: WR_tchad@intnet.td

1. Varghese C et al. Risk factors for cervical dysplasia in Kerala, India. *Bulletin of the World Health Organization*, 1999, **77**: 281–283.