monitoring programme and the database of the WHO Collaborating Centre for International Drug Monitoring, they identified more than 470 cases of temporary visual disturbance associated with these drugs. Loss of vision is likely to be temporary, resulting from the inhibition of synthesis of prostaglandins and other compounds that control retinal blood flow.

Classification of drug reactions is inadequate

A comprehensive classification of adverse drug reaction should take into account dose response, time course of the reaction, and

susceptibility of the patient (DoTs). Aronson and Ferner (p 1222) argue that the current drug classification defined only by properties of the drug gives only a limited amount of insight into drug reactions. Their proposed classification would provide more details on adverse reactions and improve drug development and patient care.

POEM*

When DNA test for HPV is negative, patients are unlikely to have cervical cancer

Question Does HPV negative cervical cancer ever occur?

Synopsis Although human papillomavirus (HPV) is well established as a causal agent in cervical cancer, most studies have shown a subgroup of up to 10% of cervical cancers that test negative for it. In this German prospective cohort study, the investigators intended to further characterise HPV negative cases of cervical intraepithelial neoplasia (CIN) 3 and cancers in a cohort of 511 women seen at a single centre over a two year period. Testing used Cervexbrush, Digene transport medium, and Hybrid Capture 2 DNA testing. There were 419 women with a biopsy diagnosis of CIN 3, of whom seven initially tested negative. Further review of these cases showed CIN 3 was not confirmed in two women, the specimen had no chromosomal DNA in two women, and HPV was actually present in three women. Among 92 cases of cervical cancer, seven were HPV-negative. On further review, four of these were found to be other cancers (endometrial, ovarian, bladder), and the remainder had no neoplastic tissue.

Bottom line In this German cohort of more than 500 women with biopsy results showing CIN 3 and cervical cancer, DNA tests for human papillomavirus were positive in more than 99% of cases. Patients with negative results on DNA testing were unlikely to have cervical cancer.

Level of evidence 1b (see www.infoPOEMs.com/resources/levels.html); individual inception cohort study with >80% follow up.

Bohmer G, van den Brule AJC, Brummer O, Meijer CJLM, Petry KU. No confirmed case of human papillomavirus DNA-negative cervical intraepithelial neoplasia grade 3 or invasive primary cancer of the uterine cervix among 511 patients. *Am J Obstet Gynecol* 2003;189:118-20.

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* Patient-Oriented Evidence that Matters. See editorial (*BMJ* 2002;325:983)

Editor's choice Beyond doing

We all love action. We want to do. Thinking, in contrast, can be so irritating—going round in circles, confusing each other, and wasting time in mental cul de sacs. “We’re too busy around here to think” may be said with more pride than shame, but thinking hard is fundamental to medicine.

It must be hard to think in the middle of a battle, and the pressure to help those who are severely injured is extreme. Deaths in war occur in three phases, write Jon Clasper and David Rew, who served in the 2003 Gulf war (p 1178). About half of those who are going to die do so within minutes from non-survivable injuries. Medicine has nothing to offer. About a third die within hours, mostly from hypoxia and hypovolaemic shock, and a fifth die days later from sepsis, multiorgan failure, and other complications. Those who die within hours might well be saved if given everything that modern medicine can offer, which has led to the dispersion of surgical teams around war zones.

Unfortunately most of these “second phase patients” managed by the dispersed teams die—because it takes too long for them subsequently to reach a fully equipped hospital. Clasper and Frew think their way to the unpalatable conclusion that it’s best to concentrate surgical teams in well equipped hospitals. We need “realism about what is achievable.”

Monitoring drug treatment seems like a good idea in order to make sure that the drug is at a concentration where it will be effective but adverse effects are common. About half of the entries in the electronic Medicines Compendium suggest monitoring, write Munir Pirmohamed and Robin Ferner (p 1179). Yet—and have you thought of this before?—drug monitoring is rather like screening: it must meet various criteria in order to be useful and not another triumph of action over thought. Pirmohamed and Ferner have adapted criteria for monitoring from the classical criteria for screening.

The adverse effect must be potentially serious, and the test simple, safe, precise, and validated. There must be an effective, evidence based intervention, and the monitoring strategy should reduce morbidity or mortality from the adverse effect. The benefits should outweigh the physical and psychological harm, and the cost should be proportionate. Just as many screening tests advocated by zealots fail the classic criteria so may many monitoring tests.

In these two cases thought should lead to less action, but sometimes it may lead to more. Hamish Cole, a retired radiotherapist, describes a chance meeting in his village with a man undergoing radiotherapy (p 1203). One of the man’s biggest problems was erratic transport. Cole thought of organising a driver volunteer each day. An unexpected bonus was that the man and his wife felt supported by the whole community. But why, Cole wonders, hadn’t such a simple idea occurred to him in 30 years of working in radiotherapy departments?

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