used in patients with leprosy. When thalidomide has been used to treat non-leprosy disorders the frequency of neuropathy is at least 21%.¹ Waters accepts this figure but claims that "the nerves [of patients with lepromatous leprosy] are relatively insusceptible to thalidomide-induced peripheral neuropathy."² Without application of the already mentioned safeguards, plus details of the clinical neurological findings, this assertion cannot be sustained. Because of the failure of leprologists to take thalidomide neuropathy seriously the drug has been distributed widely in developing countries, culminating in the disaster in Brazil, where to date 47 children have been born deformed after their mothers took thalidomide during pregnancy.³

C L CRAWFORD
Lecturer

Department of Anatomy,
Charing Cross and Westminster Medical School,
London W6 8RF

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Supervised administration of methadone by pharmacists

EDITOR,—The Advisory Council on the Misuse of Drugs recently concluded that structured methadone maintenance programmes should be developed throughout Britain.¹ Putting this recommendation into practice is not free from controversy. In the debate on the place of prescribing for drug misusers a criticism commonly made concerns "street leakage," whereby some or all of the prescribed drug is diverted by various means from the patient for whom it is intended towards illicit users.²

In an attempt to minimise the possibility of such street leakage several doctors in Glasgow have arranged with several pharmacists for methadone to be administered under the pharmacists' supervision in community pharmacies (P Wilson, personal communication). This frequent, often daily contact with patients by the pharmacist thus offers the opportunity for an increased contribution towards the patients' care. This is in keeping with a report on the future role of community pharmacies in Britain, which notes that pharmacists should aim to provide a full service to drug misusers, particularly those receiving a maintenance prescription.³

In order to assess the pharmacists' current role in dispensing methadone a questionnaire was distributed to all community pharmacies in the area covered by Greater Glasgow Health Board (n=214). This questionnaire formed part of a letter introducing the newly established Glasgow drug problem service. The letter was sent out after discussion with the board's area pharmaceutical committee, which had given its support to the supervised administration of methadone. The response rate to the questionnaire was 63% (n=135).

Of the 97 pharmacies currently dispensing methadone, 43 supervised its administration. An additional 38 would be willing to do so if given guidance from the drug problem service. Of the 38 not dispensing methadone during the survey, 15 expressed a similar view. Thus 96 of those that returned the questionnaire were either already supervising the administration of methadone or prepared to do so. This represents a quite remarkable total of 45% of all community pharmacies in Glasgow.

Some respondents expressed concerns about the security of their stock, staff, and other customers. There were also anxieties about the possibility of being overwhelmed by requests for this service should substitute prescribing of methadone substantially increase in the city. Additional collaboration among general practitioners, the Glasgow drug problem service, the area pharmaceutical committee, and individual pharmacists will seek to resolve these problems, while further studies will examine in greater detail the relation between the patients' health and behaviour and supervised administration of methadone.

ROBERT T A SCOTT
Medical director

SCOTT J BURNETT
Research officer

Glasgow Drug Problem Service,
Ruchill Hospital,
Glasgow G20 9NB

H McNULTY
Chief area pharmaceutical officer

Greater Glasgow Health Board,
Glasgow G1 1ET

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Safety of tamoxifen

EDITOR,—Rivalry among pharmaceutical companies and their products is a fact of modern life. But Gary M Williams overstates concerns about tamoxifen, and, in suggesting that toremifene, an antiestrogen that is not yet approved for treating advanced breast cancer in Britain or the United States, should be substituted for tamoxifen in prevention studies, he is suggesting the use of a drug whose long term toxicological effects in women are unknown.¹ The rationale for his recommendation is that large doses of tamoxifen cause liver tumours in rats but toremifene does not.² Had I found that tamoxifen was producing liver tumours in rats two decades ago I would not have advocated long term adjuvant tamoxifen treatment for node positive or node negative breast cancer. The risks of introducing a dangerous drug would have been too great. Thousands of women would have lost their lives prematurely if tamoxifen had not been developed.³

It is of concern that excessive doses of tamoxifen produce liver tumours in rats, but it is lifetime high dose, not short term low dose, tamoxifen treatment that does so. Rats require 40 times the daily human dose of tamoxifen to produce the tumours.² No liver tumours have been reported in women taking 20 mg of tamoxifen daily for five years. The fact that blood concentrations of the drug in rats and humans are similar^{1,2} is irrelevant because 40 times the drug is being processed by the rat liver, inducing unknown metabolic pathways peculiar to the overdosing schedule. An effective daily dose for tamoxifen to produce antimammary cancer effects in rats is 250 µg/kg⁴—almost identical with the human experience. This dose does not produce liver tumours in rats.

In prevention trials tamoxifen is given for only five years—that is, less than 6% of a life span. No one has reported the effects of tamoxifen for an equivalent duration of treatment in rats. Similarly, Williams refers to the formation of adducts in mice and hamsters,¹ but no evidence is presented that tamoxifen causes liver tumours in these species when given for short periods at appropriate, or even excessive, doses. Large doses of tamoxifen may invoke carcinogenic pathways unique to the rat liver, but whether the results of extensive laboratory studies counterbalance the more than

five million woman years of experience recorded in the clinic is questionable.

In contrast, there is up to a 10-fold increase in the risk of hepatocellular carcinoma in women who use oral contraceptives for more than five years.⁵ The mechanism of action of oral contraceptives as liver carcinogens is not relevant.¹ The only relevant fact is that society (that is, drug regulatory authorities) accepts the increased risk of a xenobiotic that does not treat or prevent a fatal disease. To be relevant, the particular risk of hepatocellular carcinoma with tamoxifen must exceed the 10-fold increase established for oral contraceptives.

I believe that recruitment to prevention trials must continue. No alternative strategies wait in the wings to replace tamoxifen tomorrow. The view that middle aged women can prevent breast cancer by reducing their fat intake for several years¹ is not supported by the disappointing results of the nurses health study.⁶ The calculations of benefits, safety, and toxicity used for the tamoxifen prevention study, however, are essentially unchanged from the original projection. Tamoxifen is not for everyone. The risk and benefits are being assessed in a well monitored group of volunteers who have chosen to contribute to clinical research. Without the clinical trials mechanism there will be no answers to any questions.

V CRAIG JORDAN
Professor of cancer pharmacology

Robert H Lurie Cancer Center,
Northwestern University Medical School,
Chicago, Illinois, USA

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The scandal of poor medical research

EDITOR,—Douglas G Altman and most of the correspondents writing in response to his editorial equate better research—a fine aspiration—with less research.^{1,2} We also aspire to better football, cricket, tennis, athletics, industry, writing, and drama (to mention a few activities). To achieve these goals seems to require more and earlier participation and constant practice. Competition is deemed essential to raise performance. Is research different? I believe not.

To get more good research we need to tolerate, indeed encourage, the work of the novice and the enthusiast so that talent can be spotted and developed. The price to pay is more supervision, close peer review, and, when peer review fails, publication of unsatisfactory work. The (elitist) alternative is to foster the view that doing and publishing research are the responsibility only of the talented. Their approach may lead to the extinction of research.

Altman's goals are correct, but his remedy is too stringent. In my view neither the quantity of research done nor the motivation behind it is relevant. (Like Altman I deplore the fact that some doctors are forced into research to achieve clinical career goals.) Two things matter: identifying,