POLICY FORUM: MEDICINE

Toward Safe and Effective Medical Abortion

Wendy R. Ewart and Beverly Winikoff

More than 100,000 unwanted pregnancies each day, or about 36 to 53 million each year, end in induced (surgical) abortion. Estimates suggest that more than half of these abortions are performed under unsafe conditions and result in more than 70,000 deaths per year, almost all in developing countries (*1*) (see the figure). Indeed, in some developing countries the complications of unsafe abortion, including incomplete abortion, sepsis, hemorrhage, and intra-abdominal injury, cause the majority of maternal deaths, and in a few countries they are the leading cause of death for women of reproductive age (*2*). At one Brazilian hospital, for instance, abortion-related complications accounted for 47% of maternal deaths during a 9-year period (*2*). In addition, each year many women suffer the nonfatal consequences of poorly performed abortions. For example, in Vietnam, where abortion is legal, highly accessible, and widely used, the quality of surgical services remains poor (*3*). Analgesia is not routinely used and, when used, is often inadequate. Similarly, sterilization of surgical instruments is frequently inadequate or not done systematically between procedures, leading to increased rates of infection. In addition to the effects of unsafe abortion on maternal mortality and morbidity, treatment of complications from unsafe abortions has been found to strain already overburdened health-care systems. In Malawi, while the 1994 annual budgeted health expenditure per person was U.S. $2.55, the cost of treating a woman for complications from an unsafe abortion in that same year was estimated at U.S. $27.40 (*4*).

Bearing in mind the grave medical, social, and economic consequences of unsafe (surgical) abortion in developing countries (Fig. 1), there is a great need to develop safe, effective, and acceptable methods of medical abortion. Medical abortion is defined as the use of drugs to terminate pregnancy. Such methods may be particularly important in resource-poor conditions where inadequate surgical services for abortion may entail a very high risk of infection and reproductive tract injury. Despite the availability of medical abortion with mifepristone in some countries in Europe and in China for more than 10 years, this has not resulted in world-wide access to safer abortion, especially where the procedure is most risky.

The clear need to assess research and development activity in drug-induced abortion was recognized by the Population Council, a nongovernmental organization specializing in reproductive health, and the Wellcome Trust, an independent medical charity. To do so, they brought together 42 experts in obstetrics and gynecology, reproductive health, community health, health-service provision, advocacy, the law, the pharmaceutical industry, and research funding (*5*).

The experience accrued over the past 10 years with the abortifacient combination of the antiprogestin mifepristone and prostaglandins, and relevant data on methotrexate plus prostaglandin and on prostaglandins alone, provided the basis for the assessment. Four main areas that would benefit from further activity were identified: biomedical research and development, the supply and availability of mifepristone, health-service delivery of medical abortion services, and advocacy and legal issues. There was unanimous agreement that mifepristone has "come of age" for use in early medical abortion, with agreement on accepted practices for its use in this therapeutic area and a recognition that the technology was ready for use in resource-poor environments (*6, 7*). There was full consensus that medical abortion is a viable alternative to surgical abortion for early pregnancy termination. Future developments can build on the sound knowledge that the combination of mifepristone and an oral or vaginal prostaglandin is a safe and effective alternative to surgical abortion.

Biomedical Research and Development

In many countries where mifepristone is not licensed, the inexpensive oral prostaglandin misoprostol (Cytotec, already approved to treat gastric ulcers) is being used alone as an abortifacient. There are many research questions related to this activity, and further clinical trials are needed. First, however, there is an urgent need to evaluate all the available data on misoprostol-induced abortion in terms of efficacy, safety, and adverse events. The focus should be on countries where this compound is already in daily use as an abortifacient or where abortion is legally available but no medical abortifacient is used as part of the established services. These data will provide the baseline for the clinical trials needed to evaluate the use of misoprostol.

Although misoprostol treatment alone is not as effective per se as combination treatment, anecdotal experience from Brazil shows that women use it to induce bleeding and then seek help from medical services as they would for spontaneous miscarriage. This pragmatic solution, and more recent clinical experience with misoprostol alone in South Africa, Mozambique, Cuba, and the United States, raises research questions that are of special relevance in areas of the world where misoprostol remains the only available means of medical abortion; for example, what is the most appropriate dose of misoprostol, what are the advantages and disadvantages of different routes of administration, and what is the relation of gestational age to success with misoprostol alone? These questions, which are deceptively simple, are the building blocks for developing a therapeutic protocol for misoprostol that is as robust as that already available for mifepristone and have special relevance for the developing world.

Methotrexate, a potent cell toxin, is currently used in the United States, where mifepristone is not yet available, to meet the growing demand for early medical abortion. However, this drug is not as inexpensive as misoprostol or as easy to administer as mifepristone. In addition, many physicians remain uneasy about methotrexate because of its possible toxicity and teratogenic effects. Thus, for countries without access to mifepristone, misoprostol alone is potentially a more useful and acceptable alternative, assuming an effective regimen is developed.

Provision of Mifepristone

Recently, there has been considerable uncertainty about the possibility of making mifepristone available in the quantities needed for clinical use. Underlying reasons include the reluctance of some pharmaceutical manufacturers to associate themselves with any abortifacient drug.

W. R. Ewart is at The Wellcome Trust, 183 Euston Road, London NW1 2BE, UK. E-mail: population@wellcome.ac.uk. B. Winikoff is at The Population Council, One Dag Hammarskjold Plaza, New York, NY 10017, USA. E-mail: bwinikoff@popcouncil.org

Although progress toward adequate manufacturing capacity has been slow in developed countries, in China production is already well under way. This development needs to be harnessed in partnership with western manufacturers. In addition, good manufacturing practice (GMP) standards must be ensured.

To expedite registration of mifepristone and misoprostol, regulatory authorities, commercial entities, and nonprofit organizations should be encouraged to proceed via other obstetric uses not prohibited by current legislation; for example, fetal death in utero, induction of labor at term, and treatment of spontaneous abortion, as well as nonobstetric uses, such as the treatment of Cushing's syndrome. Another effective action would be for manufacturers, distributors, and research agencies to set up an international centralized registry of adverse events.

Distribution strategies, which will inevitably vary from country to country, need to be geared to local conditions. The pharmaceutical companies responsible for mifepristone, currently Exelgyn and Danco, and formerly Roussel Uclaf, have a strict therapeutic protocol for the introduction and licensing of mifepristone in a new country, including directives about the medical environment where the drug would be issued and control over distribution. More widely applicable principles of introduction, however, should guarantee the widest possible access and the lowest possible price to avert the development of a black market. Provision of medical abortion through primary health-care services will become increasingly important and should be accompanied by applied research to establish guidelines to allow the drug labels to anticipate this level of care.

Local Health Service Delivery

Where abortion services are available (or likely to be established) and medical abortion technologies registered, medical abortion should be integrated into standard health-care provision. To achieve this objective, applied research is needed in several areas: on user and provider perspectives, on the cost/benefit of providing medical abortion, on the effect of family planning uptake after abortion, and on failure to return for follow-up visits and its consequences. The role of the private sector as a provider of medical abortion also needs to be evaluated in some developing countries.

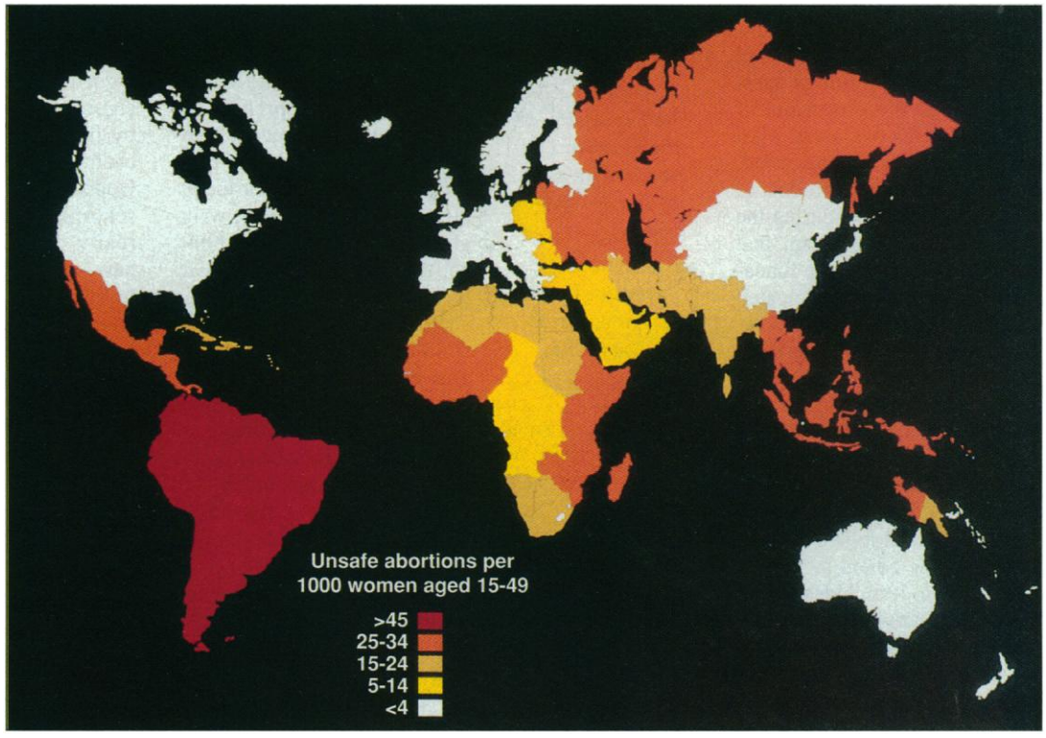
Support, beyond simple technical training, is also critical for providers of medical abortion services. Experience with "values clarification" programs in South Africa has proved beneficial in ensuring that providers are comfortable offering pregnancy termination services and are aware of their feelings toward those seeking abortion.

Advocacy and Legal Issues

Advocacy for medical abortion is essential, irrespective of the prevailing legal position regarding abortion. A crucial component of such advocacy is the documentation and dissemination of information to focus opinion on the social injustice of unsafe abortion in order to hold governments and their legislative processes accountable. To further this aim, there is a need to collect data on the health and financial costs of unsafe abortion, the existing use of medical abortion, inequalities of service provision, and the accessibility to services according to social group. To countries where abortion is illegal, evaluation of existing postabortion care is essential to estimate the likely impact of medical abortion on such services.

Conclusions

Having identified these key objectives on the path toward the introduction of safe and effective medical abortion, it is important as a next step for funders, researchers, providers, and policymakers to translate these objectives into action. Key research questions need to be addressed in such diverse areas as biomedical science and equity and social justice. Indeed, there are opportunities for many disparate groups to play a role in investigating these crucial issues. The severity of the impact of unsafe abortion on women's health, particularly in developing countries, necessitates the serious attention of researchers around the world.



World-wide rates for unsafe abortions. Data are per 1000 women aged 15 to 49. (Source: World Heath Organization)

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