RU 486

The development of the antiprogestin mifepristone, popularly known as RU 486, was a major advance in the field of reproductive health. The search for antiprogestins had been a long-term goal of researchers in this field. The Roussel Uclaf Company announced the discovery of RU 486 in the 1980s, and, in conjunction with a prostaglandin, RU 486 was approved for use by the French government in 1988.[1] For the first time, a safe medical approach for the termination of pregnancy was available, although there remains the serious limitation that the two drugs must be taken within 2 or 3 weeks of a missed menstrual period.

Of great importance is the fact that antiprogestins have other potential medical uses in the treatment of conditions such as certain types of breast cancer, meningiomas, Cushing's Syndrome, and glaucoma.[2] Further, studies are under way to assess the drug's potential as a contraceptive method and also as a postcoital drug. If effectiveness can be demonstrated as a postcoital preparation, this will be a further significant development.

Because of political and ideological concerns on the part of Roussel Uclaf and its parent company, Hoechst, this new drug is currently far less available than could have been expected. As of June 1992, RU 486 is available chiefly in France. Even there, a woman cannot simply go to her personal family doctor or obstetrician and expect to receive a prescription for the drug. Women wishing to use it must go to one of a relatively small number of clinics approved specifically by Roussel and must be willing to follow a very tight, company-mandated protocol. Recently, with company approval, RU 486 was introduced in England, where a somewhat similar protocol will be used. Introduction of the drug into Sweden is also being considered. Overall, the company is proceeding internationally with extreme caution and at a very slow pace.

The chances appear slim that American women will have access to RU 486 in the foreseeable future, despite much pressure from many advocacy groups in the United States. A change of administrations in Washington might alter this prediction. One apparent absolute condition of Roussel Uclaf (and probably of Hoechst) for the marketing of RU 486 is governmental support. Since a Clinton administration will be pro-choice, a formal administration request might induce the company to alter its policy.

RU 486 has generated intense media attention as well as advocacy since it was first approved in France by the Ministry of Health, then removed from the market by the company in the face of anti-abortion protests and threats, and subsequently restored on the order of the Minister of Health.[3] Banwell and Paxman, in this month's issue of the Journal, review the legal issues that are so much involved in questions of RU 486 availability around the world.[4] They make an interesting assessment of the potential spread of RU 486 to other countries in the light of each country's laws and/or regulations concerning abortion. They stress that, where abortion is not available essentially on demand, it is important to conduct a careful review of the definitions of both abortion and pregnancy, with particular attention to whether pregnancy is considered to begin at fertilization or implantation.

First-trimester suction curettage is probably the safest of all surgical procedures performed in this country. The procedure is simple, relatively inexpensive, and safe, and it completes the termination at the time of the procedure. Why, then, has the development of this medical means of termination generated so much attention and concern on the part of both anti-abortion and pro-choice groups? The answer is that many women prefer the privacy of a medical termination.

In France, more than 100 000 women have chosen this method since it was first introduced. This despite the fact that under present conditions women have to make four visits to the clinic (the first for diagnosis; the second a week later to receive the drug, following a legal requirement in France that a woman must wait 1 week after pregnancy diagnosis before receiving an abortion; the third 2 days later for prostaglandin; and the fourth for a post-abortion check to ensure completion). One can assume that, in the United States, even more women would choose this method. Pregnancy diagnosis has become progressively early, rapid, and reliable, and if women could receive medical treatment from their private physicians, they could bypass the anti-abortion protestors that obstruct so many clinics and be spared the ensuing emotional trauma.

Banwell and Paxman question whether RU 486 is safe when it is not used in strict adherence to the Roussel Uclaf protocol. I attach little weight to this concern. Much of the company's protocol has nothing to do with medical safety but rather with political concerns. This drug could be provided safely by trained obstetrician-gynecologists using normal prescription drug protocols, and its use need not be limited to a few selected clinics as it is in France. Further, I believe that the drug could with equal safety be prescribed by properly trained nurse-practitioners and nurse midwives who already have been trained successfully to insert IUDs safely and to prescribe oral contraceptives.

For developing countries, the implications of antiprogestin therapy are immense. The World Health Organization estimates that 500 000 women die annually from pregnancy-related causes; between 100 000 to 200 000 of these deaths are estimated to be due to improperly performed—and usually illegal—abortions.[5] These unnecessary deaths represent one of the world's great tragedies. Moreover, it has been shown that the death of a mother increases significantly both the morbidity and mortality rates of her surviving children, particularly those under age 5.

Even in those developing countries where abortion is legal, such as India, funding is inadequate to make safe services available to all who need them. Thus, in India, legal abortions by unskilled practitioners contribute considerably to the death toll. Inequitable access compounds the tragic situation: whether a country has legalized abortion or not, women who can pay are more likely to receive better services.

In a country such as India, RU 486 could make safe, early abortion available to many more women than can now be treated. Nonphysician personnel can be more easily trained to use this drug than to perform a surgical procedure. Facilities to treat the small percentage of women who would require curettage would still be needed and could be provided much more easily than the currently needed facilities either to perform surgical abortions for all who want them or, alternatively, to treat the complications of illegally induced abortions.

Given the tremendous toll in human life that is now taken by illegal abortion, the potential impact of a safe, early med-

Editor's Note. See related editorial by Sussor (p 1323) and article by Banwell and Paxman (p 1399) in this issue.

ical abortifacient is considerable. The serious levels of morbidity and mortality from illegal abortion must be faced by medical professionals, government officials, and the general public. Of course, RU 486 therapy should always be provided under medical supervision. In the developed world, where abortion is legal the use of the drug is a lesser physical and emotional undertaking for a woman than the surgical procedure even in less than ideal circumstances, and where abortion is not legal, the drug poses considerably less risk than illegal surgical abortion. In the less developed world, the advantages for women and their societies of so safe, efficacious, and economical a treatment are immense. □

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Global Microbial Traffic and the Interchange of Disease

On the 500th anniversary of Columbus' voyages to the New World, it is fitting to note how the global communication begun 5 centuries ago has powerfully altered the world. We now live in a world of increasing mobility on all levels. As Giovanni Berlinguer demonstrates in his paper, "The Interchange of Disease and Health Between the Old and the New Worlds" in this issue of the Journal, since the beginning of recorded history the trend has been towards increased communication and movement between different parts of the world.[1] Berlinguer speaks of going from the age of geographic separation to one of intercontinental communication to the present era of global interdependence. Although physical isolation still exists, it is and will continue to be increasingly rare, occasional political disruptions notwithstanding.

Berlinguer points out that the "discovery" of the New World was really a mutual process, an interchange between Europeans and people already long settled in the New World. The many New World agricultural products that became European staples—from potatoes to tobacco—bear ample witness to the mutual nature of this discovery. But the voyages of discovery also meant the discovery of new territories by previously localized microbial pathogens: as Berlinguer reminds us, infectious diseases were among the most important items exchanged. Increasing mobility also meant increasingly mobile disease, sometimes with dire consequences when a new disease was introduced into a previously isolated area whose inhabitants lacked acquired immunity. The historian William McNeill suggested that the Spanish conquest of the Aztec empire was made possible by a devastating outbreak of smallpox, a new disease inadvertently introduced to the Aztecs by the Europeans.[2] Alfred Crosby has pointed to a number of similar examples.[3] While some of the specifics are still controversial, the archaeological evidence also favors the hypothesis that, in at least some regions of North America, European contact and introduced disease initiated a rapid decline in indigenous populations.[4]

This spread of infectious diseases to new areas is thus a strong historical lesson. But even today history has a tendency to repeat. This should be no surprise, because the factors involved in the historical introduction and dissemination of disease—including travel and exploration—still exist. As Berlinguer notes, with increasing global interdependence, these factors are probably even more prevalent today than they were 5 centuries ago. For example, cholera probably originated in Asia and, in ancient times, was well established in India. In the 19th century, railroads and steamships allowed faster travel, and cholera spread rapidly into many regions, including Europe and the New World.[1] History repeats: In the past year, cholera entered South America for the first time this century. Although it is still uncertain how this happened, some reports implicate contaminated bilge water released from a freighter arriving from China.[5] Many similar instances of imported exotic diseases are known, although fortunately most of these diseases never become established.[6]

In general, the causes of most emerging infectious diseases are the same as they have been throughout recorded history: the transfer and dissemination of existing agents to new host populations (a process we may call "microbial traffic"). At least over the span of human history, most emerging pathogens have probably already existed in nature and have simply gained access to new host populations. Many of the conditions that promote microbial traffic are anthropogenic, reflecting changes in the relationship between humans and their environments. Therefore, in explaining the causes of emerging diseases and disease outbreaks, we need to carefully consider environmental changes and especially anthropogenic factors.[6,7]

Because human activities are often involved in emergence, anticipating and limiting microbial emergence is in principle more feasible than previously believed. Basically, people are creating much (although by no means all) of the traffic, even if we are doing it inadvertently. We need to recognize this and learn how to be better "traffic engineers." At a practical level, we must put into place mechanisms for recognizing disease emergence and for initiating appropriate action.

Global infectious-disease surveillance is the most urgently needed first step to protect ourselves against the inroads of microbial traffic and possible new epidemics. A promising start is the plan described by the prominent US epidemiologist D. A. Henderson that would establish an international network of centers for disease surveillance and human health, with stations located in tropical areas and especially near cities.[8] Surveillance would be linked to a worldwide rapid response system.

Our awareness of microbial traffic factors should make it easier to focus sur-

Editor's Note. See related article by Berlinguer (p 1407) in this issue.