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MEDICAL METHODS FOR TERMINATION OF PREGNANCY

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WHO Scientific Group



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Geneva, 25–27 April 1994

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1. Introduction

The WHO Scientific Group on Medical Methods for Termination of Pregnancy met in Geneva from 25 to 27 April 1994. The meeting was opened by Dr Hu Ching-Li, Assistant Director-General, who welcomed the participants on behalf of the Director-General.

Dr Hu noted that the first WHO Scientific Group meeting on abortion had taken place in 1969. The meeting was held in response to a resolution adopted in 1967 by the World Health Assembly, which, recognizing that abortions constituted a serious public health problem in many countries, had urged WHO to assist Member States, at their request, in the development of family planning services within the basic health services (1). In response, in 1969, a WHO Scientific Group on Spontaneous and Induced Abortion was convened to discuss definitions, terminology and sources of data, to examine the epidemiology and health effects of abortion, and to make recommendations for research (2).

In 1972, the Expanded (later called Special) Programme of Research, Development and Research Training in Human Reproduction was created. The activities of the Special Programme focus on research and training for research in reproductive health, with special emphasis on the needs of developing countries.

The Special Programme has always been concerned with the inadequacies of currently available family planning methods and services. These inadequacies are apparent from the gap between family planning intentions and contraceptive use, the high discontinuation rates of many family planning methods, and the large numbers of unplanned pregnancies, a high proportion of which end in induced abortion. Such abortions are often performed under unsafe circumstances. Unsafe abortion is a worldwide public health problem of considerable magnitude that can be solved only by better provision of contraception and safe abortion procedures.

Consequently, the Special Programme has supported research on the health consequences and the prevention of abortion as well as on the safety and effectiveness of the various methods employed for inducing abortion. The results of this research were considered by a WHO Scientific Group on Induced Abortion which met in 1977 to review the epidemiology of induced abortion, the efficacy and safety of the techniques employed, and the organization of abortion services. The

Scientific Group made a number of recommendations for research in its report, including the following:

Development of a nonsurgical method of abortion, nontoxic to the woman and nonteratogenic in an effective dosage, reliably producing complete expulsion of the products of conception, suitable for application in a nonclinical setting, and economically accessible to women in all countries (3).

Since that recommendation was made, there have been many important developments. Following clinical research on the use of prostaglandin analogues given alone, non-invasive medical termination of pregnancy with the antiprogesterone steroid mifepristone in combination with a prostaglandin analogue has become available in China, France, Great Britain and Sweden.

The specific tasks before the WHO Scientific Group on Medical Methods for Termination of Pregnancy were:

- to review new information on medical methods for the termination of first- and second-trimester pregnancy;
- to make recommendations on the service environment required to employ such medical methods; and
- to identify further research needs in the field of medical termination of pregnancy.

For the purposes of its report, the Scientific Group adopted the definition of abortion used by the medical profession and the WHO Scientific Group on Spontaneous and Induced Abortion: “the termination of a pregnancy before the fetus has attained viability, i.e. become capable of independent extra-uterine life” (2). The term miscarriage is used to describe a spontaneous abortion.

In addition, the Scientific Group defined the duration of pregnancy (or gestation) at the time of abortion as the (cardinal) number of completed days or completed weeks of amenorrhoea since the first day of the woman’s last menstrual period. This is the definition in general use by clinicians throughout the world. It has a reasonably constant relation to the biological length of pregnancy as most women have a 28-day menstrual cycle, with conception occurring on about day 14 and implantation starting 6–8 days later. Thus, when the duration of pregnancy (or gestation) is stated to be 63 days (or 9 weeks), this is the time that has elapsed since the first day of the last menstrual period and not the age of the fetus. A gestation of 64 days is described as 9 weeks and 10 weeks is not reached until 70 days.

For the purposes of this report, the first trimester of pregnancy is considered to end at 14 weeks.

During the course of its deliberations, the Scientific Group made a series of recommendations related to each of the topics under discussion, which are given at the end of the individual sections. In addition, at the conclusion of its work, the Scientific Group made the following general observations:

- Medical methods for inducing abortion increase choice and may contribute to improving reproductive health.
- Further research is required to improve current medical methods for inducing abortion through the identification of new pharmaceutical agents with superior characteristics to those currently available or with a different mode of action.

In accordance with its normative and technical roles, WHO makes available the latest scientific and technical advice on a broad range of medical and public health subjects. Experts participating in scientific groups and other meetings convened to this end serve in their personal capacities and the views expressed in their reports do not necessarily reflect those of their governments nor of WHO. In particular, with respect to the subject of induced abortion, WHO endorses the statement contained in the Programme of Action (paragraph 8.25) adopted at the International Conference on Population and Development, held in Cairo in 1994:

In no case should abortion be promoted as a method of family planning. All governments and relevant intergovernmental and non-governmental organizations are urged to strengthen their commitment to women's health, to deal with the health impact of unsafe abortion as a major public health concern and to reduce the recourse to abortion through expanded and improved family-planning services. Prevention of unwanted pregnancies must always be given the highest priority and every attempt should be made to eliminate the need for abortion. Women who have unwanted pregnancies should have ready access to reliable information and compassionate counselling. Any measures or changes related to abortion within the health system can only be determined at the national or local level according to the national legislative process. In circumstances where abortion is not against the law, such abortion should be safe. In all cases, women should have access to quality services for the management of complications arising from abortion. Post-abortion counselling, education and family-planning services should be offered promptly, which will also help to avoid repeat abortions.

2. The demography of abortion

2.1 Induced abortion as a major public health concern

A recent WHO report estimates that over 100 million acts of sexual intercourse take place each day (4). These result in some 910 000 conceptions, of which about 50% are unplanned and about 25% are unwanted. About 150 000 unwanted pregnancies are terminated by induced abortion every day — or up to 53 million each year. Demographers calculate that between one-third and one-half of all women have had at least one induced abortion before they reach the menopause (5). One-third of these abortions are performed under unsafe conditions and in an adverse social and legal climate, resulting in some 135 to 275 deaths every day (approximately 50 000–100 000 deaths each year) (6). These abortion-related deaths account for up to about 20% of the estimated 500 000–600 000 maternal deaths that occur each year throughout the world. The majority of these deaths are in developing countries, where abortion services are either not widely available or not permitted by the legal system. Many more women have immediate and long-term health problems due to unsafe abortions. According to WHO: “unsafe abortion is one of the great neglected problems of health care in developing countries and a serious concern to women during their reproductive lives” (4).

2.2 The demography of unsafe abortion

Indirect methods for estimating the incidence of unsafe abortion are based on surveys of the numbers of women admitted to hospital with conditions that can be attributed to unsafe abortion, such as pelvic infection or reproductive tract injury, information on death certificates, and surveys of samples of women (7, 8). None of these methods are likely to be accurate, since induced abortion cannot always be distinguished medically from miscarriage. Furthermore, an unknown minority of women have sufficiently severe complications from unsafe abortion to require treatment in hospital, and only a small proportion die. Also, women are reluctant to admit to having had an abortion and doctors may conceal this information, both in their case notes and on death certificates, to protect the reputation of the woman and her family and to guard them from prosecution.

Romania provides a unique example of the factors that influence the use of unsafe abortion. In 1966, legal abortion became restricted after having been available on request in the first trimester of pregnancy since 1957. In addition, the import of contraceptives was stopped and fiscal measures were introduced to encourage large families. The crude birth rate initially increased from 14.3 per 1000 population in

1966 to 27.4 in 1967 and then gradually receded to the original level of 14.3 in 1983. However, the abortion-related maternal mortality rate increased sharply from 30 per 100 000 live births in 1966 to 128 in 1984, while maternal mortality from other causes fell from 65 to 21 per 100 000 live births. In 1984, 449 cases — or 86% of all maternal deaths — were attributed to abortion. The change in the government of Romania in December 1989 resulted in abortion being made available on request again. The number of maternal deaths due to abortion fell sharply from 545 in 1989 to 181 in 1990, and subsequently decreased to 100 in 1992. At the same time, the number of legal abortions increased sharply from 82 479 in 1989 to 913 973 in 1990, and then decreased progressively to 621 166 in 1992 as contraception became more widely available (9) (M. Horga, personal communication, 1994).

2.3 Use of contraception

About 55% of all couples with the woman in the reproductive age group (15–49 years) are currently using some form of contraception (10). During the period 1965–1970 the corresponding figure was 9%. Unfortunately, many current methods of contraception are difficult for some couples to obtain and use, and all may fail to prevent pregnancy. Such failures may result in the conception of between 8 and 30 million pregnancies each year (11). It is uncertain how many of these pregnancies are terminated but they must contribute substantially to the annual total number of abortions. The other major factor leading to induced abortion is the conception of unwanted pregnancies by couples who do not use contraception for a variety of reasons.

There is an urgent need for a greater variety of more effective, culturally acceptable and affordable methods of fertility regulation. However, even if there are considerable advances in this respect, some unwanted pregnancies will still be conceived because many couples will fail to use contraception at some time in their lives. A proportion of such pregnancies will end in abortion because socioeconomic pressures not to have a baby can be so great that women are prepared to risk their health and even their life. The provision of safe abortion reduces the associated risks of mortality and morbidity to less than those associated with continuing the pregnancy to term.

2.4 Role of abortion in determining the fertility rate

The number of children a couple wishes to have is determined by social and economic factors and by their perception of the chance of their children surviving to become adults. Both contraception and abortion are important in the demographic transition from large

families and an increasing population, to smaller families and a stable population. As couples begin to feel motivated to limit the size of their families, the resulting decrease in the fertility rate tends to be a result of an increase in the use of both contraception and induced abortion. In the early stages of this process, the induced abortion rate usually increases as the availability of contraception is still low and couples are poorly informed about its use. With time, and as smaller families are achieved, the induced abortion rate declines and contraceptive use increases. It is unlikely that any population has attained a low level of fertility without the use of abortion, legal or illegal, and many developing countries are still in the course of this process (12).

2.5 **Legislation governing the provision of abortion**

The ethical status of the fetus has been debated at least since written records began (13). The Greek and Roman civilizations accepted the deliberate termination of early pregnancy. The developing Christian and Islamic cultures disapproved strongly of the destruction of the fetus but, at least until the end of the 17th century, followed the lead of the Greek philosophers in tolerating abortion during early pregnancy (usually up to the time at which the first movements of the fetus were felt by the woman, around 16–18 weeks of gestation). Religious and secular attitudes became more restrictive during the 19th century, partly as a result of the professionalization of medicine and the suppression of unqualified practitioners and partly because increasing knowledge of intrauterine development suggested that there was no precise gestation at which a fetus could be said to become a person. The new laws did not specifically allow doctors to perform an abortion to save the life of a woman, but with the exception of some religious groups, society accepted that such abortions were ethical and lawful. These laws form the basis of the restrictive legislation on abortion that still exists in many developing countries, particularly in Africa and Latin America.

During the 20th century industrialized societies became concerned about the harm caused by illegal abortion and the distress experienced by women and their families from unwanted births. The first country to make abortion available for social reasons was the former USSR in 1920 (some restrictions were introduced in 1936). Subsequently, several European countries introduced laws that gave doctors limited freedom to perform abortions in cases where the woman's health was threatened. This occurred in Iceland in 1935, Sweden in 1938 and Denmark in 1939 (14). These laws could be interpreted liberally, so that a threat to health could be judged to be present when the pregnancy would result in serious stress from adverse social

circumstances. However, except in the Soviet law of 1920, the power to make the decision to perform an abortion was left with the doctors or with a special committee rather than with the woman herself. The bureaucracy associated with many of these laws made the process of obtaining an abortion slow, so that some were delayed until the second trimester (15). Also, a few women were forced to continue their pregnancy to term because their request was refused.

The Soviet law was adopted by the countries of eastern Europe in the late 1940s. However, in western Europe, the abortion debate did not progress until the British Abortion Act of 1967, which came into force on 27 April 1968. The Act allowed abortion only if two doctors certified that the abortion was necessary to protect the woman's life or health or if there was a substantial risk that the child, if born, would be seriously handicapped. It also stated that the doctors, in considering the risk to health, should take into account the woman's "actual or reasonably foreseeable environment" and the effect of the pregnancy on the health of her children. The Act also made abortion available to women resident in other countries. In 1973, of 169000 legal abortions performed in England and Wales, 56000 were for non-residents (15). Subsequently, many developed countries passed laws allowing abortion to be performed at the request of the woman up to 10 or 12 weeks of gestation. Most laws also allow termination up to 20 or 24 weeks if the fetus is seriously abnormal or the woman has a serious condition that would be aggravated if the pregnancy were to continue.

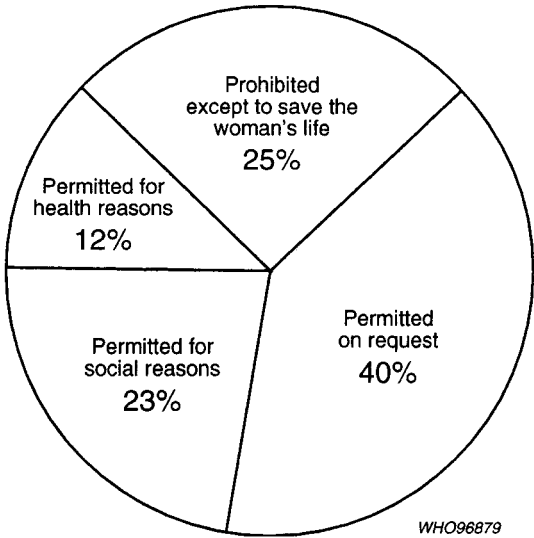
Abortion is available either on request or for social reasons to approximately 63% of women in the world (12) (Fig. 1). About 25% of women live in countries where abortion is prohibited, except when the woman's life would be endangered if the pregnancy continued. For the remaining 12%, abortion can be obtained when the woman's health is threatened, when conception resulted from rape or incest, or when fetal indications justify the termination of pregnancy.

Abortion laws may be interpreted differently by society and by medical practitioners. In Switzerland, for example, the availability of abortion varies widely between different cantons. Also a law that allows abortion for social reasons may not make abortion services widely available and accessible, so that some women may still feel compelled to resort to unsafe methods. Socioeconomic status may influence access to abortion, with the result that safe abortion may be available only to the relatively wealthy, particularly in countries with restrictive legislation. Thus, in assessing the provision of services, the number of legal abortions may not reflect the use of abortion by the population as a whole. For this reason it is important to determine the numbers

of abortions that are “safe” and “unsafe”, rather than “legal” and “illegal”.

Cost to the woman is an important factor in the provision of abortion. For example, only about 50% of the abortions obtained each year by women living in England and Wales are provided free of charge by the National Health Service (15). This is due to reluctance on the part of some gynaecologists to perform abortions and to a relative shortage of gynaecological resources. As a consequence, three large abortion-providing charities have been established. These provide abortions at charges that are appreciably lower than those prevailing in private practice, but do not usually provide abortions free of charge, even when the reason underlying the request is lack of income. In contrast, in the Netherlands, lack of provision within gynaecological units in state hospitals in the early 1970s led to the rapid growth of a network of independent clinics in which women could obtain abortions from skilled staff and could recover the fee from the state health scheme. The liberalization of abortion in the USA in the early 1970s resulted in the growth of free-standing clinics, because many established hospitals were unwilling to allow abortions to be performed. The debate continues as to whether abortions should be paid for by public funds, and because of the lack of services

Figure 1
Legal status of abortion throughout the world^a



^a Source: reference 12. Used by permission.

in some parts of the country women often have to travel considerable distances to obtain the services they need.

2.6 **Estimating the occurrence of abortion**

2.6.1 ***Annual numbers of abortions***

Abortion is common but very difficult to measure. The number of legal abortions can be determined in several ways: from notifications in countries where this is obligatory; from the records of organizations that provide abortion services; or, with medical abortion, from the number of doses of the drugs sold by the manufacturers. All these methods are unreliable as they tend to underestimate the actual numbers because of the reticence about personal involvement in abortion that is felt both by women and by health care providers. Surveys of random samples of the female population are even more unreliable. Accurate methods to determine the number of unsafe abortions have not been developed and the indirect methods available are also likely to underestimate the true situation (see section 2.2).

2.6.2 ***Abortion rates and ratios***

The occurrence of abortion is usually measured by rates, which relate the number of abortions to the population, or by ratios, which relate the number of abortions to the number of births or pregnancies. The two approaches provide different but complementary types of information.

Abortion rates can be expressed in several ways; for example, per 1000 total population, per 1000 women of reproductive age (usually defined as 15–44 years), or per 1000 women in defined (e.g. 5-year) age groups. The total abortion rate can be derived from age-specific rates and is the number of abortions that would be experienced by 1000 women during their reproductive lifetimes, assuming the present age-specific abortion rates remain unchanged.

Abortion ratios are usually expressed per 100 (or 1000) known pregnancies or live births and, like abortion rates, can be calculated for defined age groups.

Table 1 shows abortion rates and ratios for some of the countries that are thought to have reasonably reliable statistics on abortion. The values vary widely, reflecting differences in factors such as desired family size, cultural attitudes to the role of women, use of contraception, and availability of and access to contraceptive services.

The Netherlands has the lowest reported abortion rate in the world, probably because of a non-restrictive abortion law within a

Table 1

Number of abortions, abortion rate, abortion ratio and total abortion rate in selected countries, 1985–1987^a

Country	Year	Number of abortions	Abortion rate per 1000 women aged 15–44 years	Abortion ratio per 100 known pregnancies	Total abortion rate per 1000 women ^b
Australia	1988	63 200	16.6	20.4	484
Canada	1987	63 600	10.2	14.7	299
Czechoslovakia	1987	156 600	46.7	42.2	1400
Denmark	1987	20 800	18.3	27.0	548
England and Wales	1987	156 200	14.2	18.6	413
Finland	1987	13 000	11.7	18.0	356
Hungary	1987	84 500	38.2	40.2	1137
Iceland	1987	700	12.0	14.0	336
Netherlands	1986	18 300	5.3	9.0	155
New Zealand	1987	8 800	11.4	13.6	323
Norway	1987	15 400	16.8	22.2	493
Scotland	1987	10 100	9.0	13.2	255
Singapore	1987	21 200	30.1	32.7	840
Sweden	1987	34 700	19.8	24.9	600
USA	1985	1 588 600	28.0	29.7	797

^a Source: reference 12.

^b Defined as the number of abortions that would be experienced by 1000 women during their reproductive lifetimes, given current age-specific abortion rates. For example, a total abortion rate of 1000 represents one abortion per woman over her reproductive lifetime.

comprehensive framework that includes universal sex education in schools and easily accessible family planning services, with special services for adolescents, and the provision of emergency contraception (16).

The high abortion rates and ratios in central and eastern European countries can be interpreted as a consequence of a desire for smaller families in societies that, at the time abortion was legalized, had no contraceptive services or tradition of contraceptive use. In most other developed countries changes in the law made abortion more widely available at a time when family size was already partly determined by the provision of contraception. In both situations it is possible that, to a large extent, legal abortion replaced illegal abortion and that the total number of induced abortions remained relatively unchanged. A more comprehensive discussion of the factors that influence abortion statistics is provided in section 2.7.

2.6.3 *Trends in abortion rates*

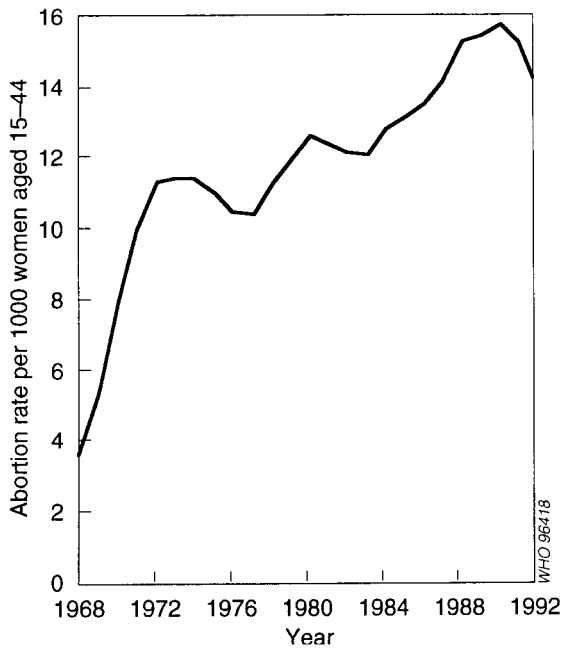
The uncertainties outlined above mean that it is not possible to be confident in the interpretation of the changes in annual abortion statistics. Moreover, the extent of under-reporting may change with time.

2.7 Demographic and social factors

A variety of factors, such as age, marital status, parity, ethnicity, the prevalence of contraceptive use and educational attainment influence the abortion rate. Data are not available that allow an analysis involving all these factors, and the reliance placed on the information that is available must take into account its limitations (e.g. the likelihood of selective under-reporting) and the possibility that access to legal abortion may vary with factors such as age and socioeconomic status.

Statistics from England and Wales provide a model for the study of factors affecting the abortion rate because there is a statutory duty to notify legal abortions, as well as all births and stillbirths. Fig. 2 shows the abortion rates for England and Wales between 1968 and 1992 (17, 18). The initial rapid rise in the late 1960s to the mid-1970s can be attributed to the increasing availability of legal abortion and the corresponding decrease in illegal abortion.

Figure 2
Abortion rate per 1000 women aged 15–44 years resident in England and Wales, 1968–1992^a



^a Source: references 17 and 18. Used by permission.

2.7.1 **Age**

Fig. 3 shows the distribution of abortions by age for selected countries that are considered to have reasonably reliable statistics. In countries in which contraception has been widely available for many years, such as England and Wales, the Netherlands and the USA, more than half of all abortions are for women under 25 years of age. In countries with no tradition of contraceptive use and with limited availability of contraceptives and sterilization, such as those in central and eastern Europe (e.g. Hungary), the majority of terminations are for women aged 35 or older. In these countries, unmarried women who become pregnant generally marry and continue the pregnancy, but abortion may be the only way in which married couples can space their children. Japan, where oral contraception is not generally available and sterilization is seldom performed, shows a similar pattern to that of eastern Europe. In several countries in western Europe such as the Netherlands and in Scandinavia, the distribution of abortion by age is intermediate between that in England and Wales and that in Hungary. This may be explained by the higher prevalence of contraceptive use among women under 25 in the Netherlands and Scandinavia but less acceptance of sterilization by older women in these countries compared to those in English-speaking developed countries.

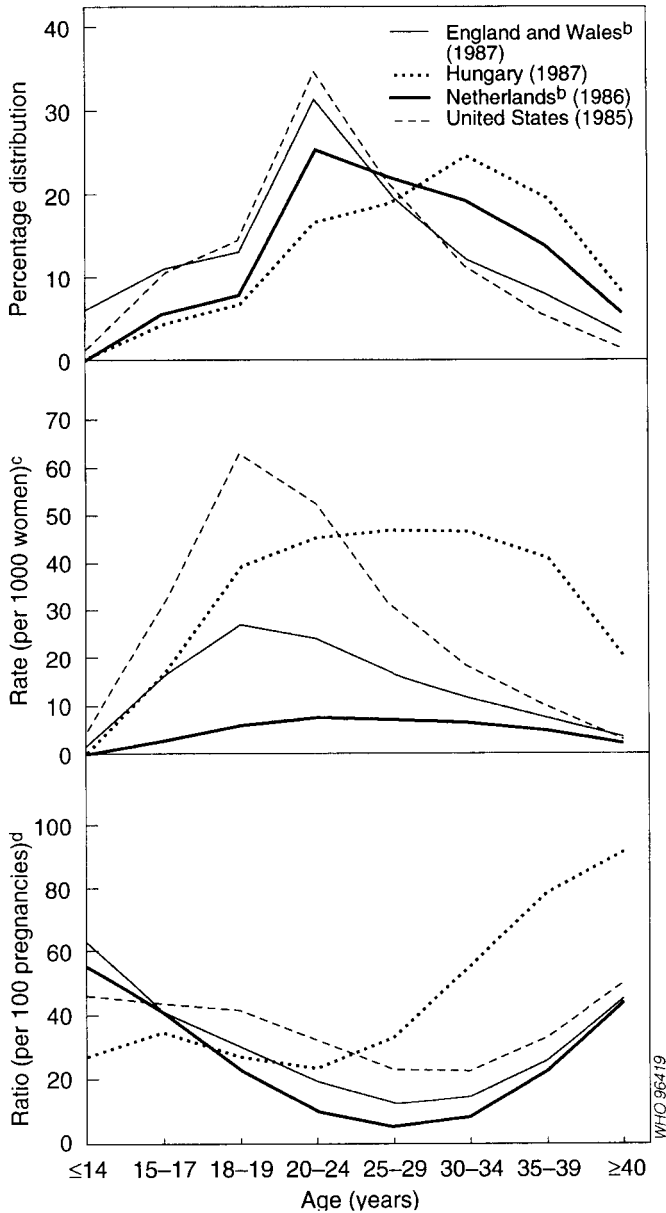
Abortion rates in teenagers vary considerably between countries (see Fig. 3). In the USA abortion rates are highest in women under 20. Rates in England and Wales are approximately half those in the USA and teenagers have slightly higher rates than those aged 20–24. Teenage pregnancy rates in Great Britain and the USA are highest in the deprived areas of large cities. In contrast, the Netherlands has the lowest abortion and birth rates in teenagers of any country with reasonably reliable statistics.

2.7.2 **Marital status**

In all developed countries for which data are available the abortion ratio is higher in unmarried than in married women. Data from England and Wales provide such an example (Fig. 4). The fall that has occurred in England and Wales in the last 20 years in the proportion of young women who are married is also found in other developed countries such as France, Germany and the Netherlands and in Scandinavia. The relatively high abortion ratios among young women in developed countries reflect a change in the role of women in society and a tendency for them to delay marriage and childbearing until they have achieved their educational and occupational goals. Data for developing countries are sparse. In India and Singapore, women who

Figure 3

Percentage distribution of abortions, abortion rate (per 1000 women aged 15–44 years) and abortion ratio (per 100 known pregnancies), by age, in selected countries^a



^a Source: reference 12. Used by permission.

^b Residents only.

^c For women under 15 years of age, the rate is computed per 1000 women aged 13–14; for women under 20, the rate is computed per 1000 women aged 15–19; for women aged 40 or more, the rate is computed per 1000 women aged 40–44.

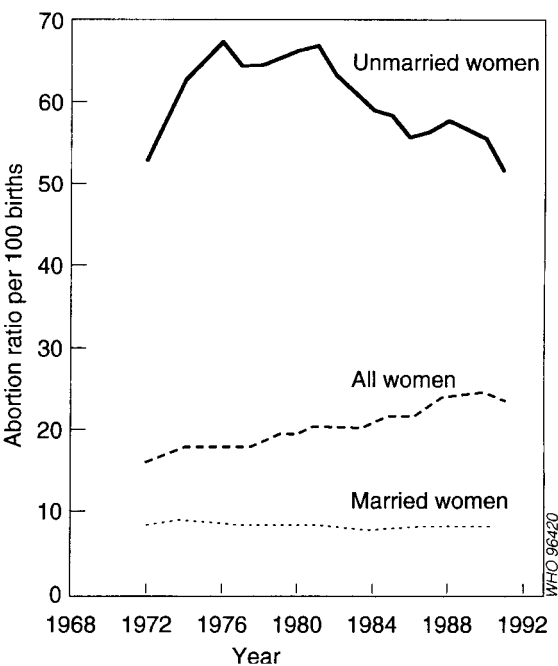
^d Ratio of abortions per 100 known pregnancies (defined as legal abortions plus live births, both adjusted to age of the woman at the time of conception). For the United States, live births 6 months later were used to match times of conception for pregnancies ending in birth and pregnancies ending in abortion; data needed for this adjustment were unavailable for other countries.

obtain abortions are usually married. The pattern is intermediate between those of Asia and Europe in both Africa and Latin America, with a higher proportion of abortions being obtained by unmarried women than by married women (21).

2.7.3 **Parity**

Parity and marital status are closely related, so that in countries in which the majority of abortions are in young unmarried rather than older married women, it follows that those having abortions tend to have few or no children. This is true for almost half of the women who obtain abortions in most English-speaking and western European countries, with the exception of Italy. In contrast, in central and eastern European countries, less than 20% of the women who obtain abortions are childless. Marked changes in this pattern have been observed in some countries in the past 10–20 years. In Singapore, for example, the proportion of childless women having abortions increased from less than 1% in 1970 to 41% in 1987, whilst the

Figure 4
Abortion ratios by marital status for women aged 15–44 years resident in England and Wales, 1972–1991^a



^a Source: references 19 and 20. Used by permission.

corresponding rate among women with at least five children decreased from 53% to 2% (12).

2.7.4 ***Socioeconomic status***

Few studies have examined the influence of socioeconomic status on abortion rates in countries with non-restrictive legislation, mainly because these data are not collected systematically. In Tayside, Scotland, the pregnancy rate during 1980–1990 among women under 20 years of age from the most deprived areas was six times that among young women from the most affluent areas. The proportion of teenage pregnancies ending in legal abortion, however, was higher in affluent areas, where two out of three such pregnancies ended in abortion as compared with one out of four in deprived areas (22). In the USA, a negative association has been reported between abortion rate and income (23).

Women living in urban areas tend to have higher abortion rates than those living in rural areas. The reasons for these differences are complex, important factors being the cost of bringing up children in a city, the motivation of women to delay childbearing in favour of career development and the greater availability of abortion services, both legal and illegal, in urban areas. Furthermore, women living in rural areas and wishing to remain anonymous may prefer to obtain an abortion from urban providers.

In countries with restrictive abortion legislation, safe abortion is generally more accessible to women from the upper socioeconomic groups than to those from lower socioeconomic groups (24). This may also be true in countries in which the law allows abortion but the level of provision is not adequate.

2.7.5 ***Ethnicity***

Within countries, abortion rates often vary markedly among different racial and ethnic groups. In 1987, the abortion rate among women from ethnic minority groups in the USA was 2.7 times that among white women (25). Few other studies have been published on abortion rates in women from ethnic minority groups, mainly because of the difficulty in controlling for factors such as educational attainment, socioeconomic status and access to contraception and abortion services. In the Netherlands, the abortion rates are far higher among immigrants than among native Dutch women (5).

2.7.6 ***Length of gestation***

Factors influencing the gestational age at abortion include the availability of adequate and accessible services and the specific abortion

legislation. In many countries, such as France and Italy, the law is non-restrictive only in the first trimester so that women can obtain abortion in the second trimester only for reasons such as fetal abnormality and when the woman has a life-threatening medical condition. In England and Wales, 13% of abortions are performed after 13 weeks. Adequate provision of abortion services is probably why only 5% and 6% of abortions, respectively, are performed in the second trimester in the Scandinavian countries and the Netherlands. Second-trimester abortions are also rare in most eastern European countries, where they are generally authorized on medical indications only (5).

The gestational age at abortion is important because the methods become more complex and more costly as pregnancy advances and because the risk of serious complications increases.

2.8 Conclusions

1. About 50% of all pregnancies are unplanned and about 25% unwanted. Some 150000 unwanted pregnancies are terminated by induced abortion each day (up to 53 million each year). Of these, about a third are performed under unsafe conditions, resulting in approximately 50000–100000 deaths each year. Many more women have complications which may have long-term consequences for their health.
2. About 55% of couples in the world use contraception but failure is common and is estimated to result in 8–30 million pregnancies each year. Many of these pregnancies end in induced abortion.
3. About 63% of women live in countries where induced abortion is permitted on request or for social reasons. Even when the law is not restrictive, the availability of abortion depends on the attitudes of medical staff and the organization of abortion services.
4. The dangers of unsafe abortion to health can be virtually eliminated by making safe abortion readily accessible.
5. Relatively few countries have reliable statistics on induced abortion, even where there is a statutory requirement to report. The occurrence of illegal abortion can be estimated, only very approximately, by indirect methods.
6. Very high rates of abortion have been reported in countries in which induced abortion was legal and contraception was difficult to obtain. The lowest rates are associated with high levels of use of effective contraception. Methods of contraception can fail and it is unrealistic to believe that unplanned pregnancy and induced abortion are totally preventable.

7. Induced abortion contributes to the demographic transition from high to low fertility. In the initial phase the use of both contraception and reported abortion increases; thereafter, as contraceptive use increases further, recourse to abortion declines.
8. The factors influencing abortion rates are complex. Changes in the proportion of younger women in the population and in the proportion married should always be investigated before attributing a rise or fall in the abortion rate to changes in contraceptive use or socioeconomic influences.
9. The degree of under-reporting of abortion varies among countries and is unknown. This must be considered where comparisons between countries are made.

2.9 Recommendations

1. Where abortion is not prohibited by law, safe abortion should be readily accessible.
2. Effective sex education and easy availability of contraception should be promoted to lower recourse to induced abortion.
3. Estimates of the accuracy of the number of reported abortions should be available in those countries where national statistics are collected.
4. The safest and most effective methods for inducing abortion should be available and should be recommended, where abortion is not prohibited by law.

3. Mechanisms for medical abortion

3.1 Reproductive physiology

Knowledge of the physiology and biochemistry of the female reproductive system and of early pregnancy has enabled the identification of critical points at which pharmaceutical agents might be used to interrupt the pregnancy process and thus cause the pregnancy to end in abortion. Theoretically, agents could be developed to specifically inhibit certain aspects of implantation and placentation, but those currently available interfere with the mechanisms that prevent the uterus from contracting and keep the cervix closed until the fetus is mature enough to be born. From the physiological point of view, pregnancy is an extension of the luteal phase of the menstrual cycle so that an understanding of the menstrual cycle is the foundation for understanding pregnancy.

3.1.1 **Menstrual cycle**

The female reproductive tract is prepared for pregnancy during each menstrual cycle by the production of estrogen by ripening ovarian follicles. Estrogen stimulates growth and increases vascularity in the endometrium, and the rapidly rising estrogen concentration in the blood triggers ovulation in the dominant follicle by a complex interaction involving the hypothalamus and the release of luteinizing hormone by the pituitary gland. After ovulation, the ruptured follicle is transformed into the corpus luteum and produces progesterone in increasing quantities. Progesterone makes the glands of the endometrium wider and more coiled, and stimulates secretion by the glandular epithelium (26). During the luteal phase there is a decrease in the number of estrogen and progesterone receptors in the epithelial cells of the endometrium, but an increase in the number of progesterone receptors in the endometrial stromal cells (27). The stromal cells enlarge and the stroma becomes oedematous so that the endometrium is transformed into the decidua. This occurs to some extent in every cycle but, in the absence of conception, progesterone production by the corpus luteum begins to decline 11–12 days after ovulation and, after a further 2–3 days, this leads to the disruption of the endometrium and thus to menstruation. Prostaglandins are important in this process. Both estrogen and progesterone increase the capacity of the endometrium to produce prostaglandins but synthesis is suppressed and tissue concentrations remain low until late in the luteal phase, when the sudden fall in progesterone levels inhibits prostaglandin dehydrogenase (28, 29).

The luteal phase of the menstrual cycle shows little variation in fertile women and averages 14 days, but the proliferative phase is more variable. Consequently, conception (which usually occurs within 24 hours of ovulation) has a closer relation to the date of a woman's first missed menstrual period than to the date on which her last menstrual period actually began. In women with a 28-day cycle, both the proliferative and the luteal phases last about 14 days, but in a 35-day cycle the proliferative phase is extended to 21 days. This has importance in relation to the clinical diagnosis of pregnancy, particularly if early medical abortion is being considered.

3.1.2 **Implantation**

If the ovum is fertilized, progesterone production by the corpus luteum is maintained and increases so that the decidual changes become more pronounced. Progesterone causes the decidua to produce a variety of specialized proteins such as pregnancy proteins (PP14, PP12), relaxin and prolactin (30). Their roles are uncertain but PP14

and PP12 are likely to play a part in the implantation process (31). The developing ovum remains in the fallopian tube during the early stages of development, entering the uterus after about 3 days. Implantation occurs after a further 3–5 days, i.e. 6–8 days after ovulation.

The biological events of implantation in humans have not been fully investigated. In nearly all mammalian species, trophoblast cells penetrate the uterine epithelium and its associated basal lamina (26). Some trophoblast cells form chorionic villi while others invade the walls of the maternal arterioles in the decidua, replacing both the endothelial and muscular layers. This means that the trophoblast becomes the tissue controlling the calibre of the maternal vessels that will supply the placenta and control the blood supply to the growing fetus. The regulation of this process involves cytokines and growth factors of both trophoblast and maternal origins (32, 33).

All the cells of the blastocyst contain paternal genes but immunological rejection is prevented by mechanisms that are still largely unknown (34). The trophoblast expresses a Class 1 human lymphocyte antigen (HLA) not found in other tissues, but which is the same in all pregnancies. This antigen may prevent rejection by interacting with the large granular lymphocytes of the decidua which, otherwise, would be expected to kill the trophoblast cells (35).

3.1.3 *Maintenance of pregnancy*

Human chorionic gonadotropin (hCG) is essential for the continued production of progesterone after conception. It is secreted by the trophoblast into the blood as soon as the blastocyst becomes attached to the decidua and, by binding to the receptors for luteinizing hormone in the corpus luteum, sustains the secretion of progesterone. hCG can be detected in maternal blood from about 8 to 9 days after conception (36), and its presence in blood or urine forms the basis of tests for the diagnosis of pregnancy.

In the luteal phase, and then in pregnancy, the uterus becomes enlarged but does not contract and the cervix remains closed with the canal blocked by viscid mucus, thus providing a protected environment for the growing fetus and placenta. Estrogen is responsible for uterine enlargement but progesterone is essential for preventing uterine contractions and for keeping the cervix firm and closed. Both these steroid hormones are produced initially in the corpus luteum, but secretion by the trophoblast increases progressively and is sufficient to maintain pregnancy from about 35 days after conception (37). Progesterone changes the electrical charge on the outer surface of the myometrial cells so that a greater stimulus is necessary to

induce uterine contractions. Progesterone also impedes the transmission of electrical impulses across the gap junctions, the links between the cells of the myometrium that are involved in the coordination of contractility in the uterus as a whole (38). If the progesterone levels fall, prostaglandin and cytokine production is activated in the decidua, fetal membranes and cervix. The effect of these substances on the tissues is similar to that occurring during an inflammatory reaction associated with trauma or infection (39, 40). These substances end the pregnancy by softening the cervix and inducing uterine contractions.

3.2 **Agents used for medical abortion and their mode of action**¹

3.2.1 **Prostaglandins**

Dinoprost and dinoprostone

The natural prostaglandins $\text{PGF}_{2\alpha}$ and PGE_2 play an important role in the regulation of uterine activity, particularly with regard to labour, whether this is at term or associated with a miscarriage. PGE_2 has a softening effect on the cervix and so facilitates dilatation. Both prostaglandins have effects on the smooth muscle of the alimentary tract, the peripheral vascular system and the bronchi, and can cause diarrhoea and vomiting, as well as vasodilatation and hypotension. $\text{PGF}_{2\alpha}$ can also induce bronchospasm. They are active in $\mu\text{g/l}$ concentrations and are rapidly degraded by tissue enzymes.

These natural prostaglandins became available in the late 1960s (41), as dinoprost ($\text{PGF}_{2\alpha}$) and dinoprostone (PGE_2). Dinoprostone is about five times as potent as dinoprost in inducing uterine activity. Both drugs are available for intravenous, intra-amniotic and extra-amniotic use; dinoprostone is also available as a vaginal pessary. Although effective in inducing abortion, they are not entirely satisfactory clinically because of their short half-life and the risk of causing potentially dangerous side-effects if given accidentally by intravenous or intramuscular injection in doses that would have been safe by the intra- or extra-amniotic routes. The clinical use of dinoprost and dinoprostone is declining in those countries in which the pharmaceutical licensing authorities have approved the sale of one or more of the synthetic prostaglandin analogues.

¹ In some cases, the devices described in this section (and elsewhere in the report) have been identified by the manufacturer's name or trademark. However, this does not imply that such products are endorsed or recommended by WHO or the Scientific Group in preference to others of a similar nature that are not mentioned. Rather, the specific products mentioned represent those that are known to the Scientific Group to be in common use. In the event that there are others in common use, WHO would be pleased to be so informed for the purpose of including a description of their use in future reports on induced abortion.

Carboprost

Carboprost (15(*S*)-15-methyl PGF_{2α}) is the only PGF_{2α} analogue that has become available for clinical use. It is about 20 times as potent, weight for weight, as its parent compound and its biological effects persist for 3–6 hours rather than for a few minutes. Carboprost can be given by intramuscular or intra-amniotic injection and its methyl ester can be given by vaginal suppository. Carboprost and its methyl ester are both effective in inducing uterine contractions and abortion, but cause more gastrointestinal side-effects than the PGE analogues described below.

Sulprostone

Sulprostone (16-phenoxy-ω-17,18,19,20-tetranor PGE₂ methyl sulfonylamide) is a PGE₂ analogue. It has some selective action on the uterine muscle and, in equivalent doses, is significantly less likely to cause gastrointestinal side-effects than carboprost. It is used clinically as a controlled intravenous infusion.

The intramuscular preparation of sulprostone has recently been withdrawn because it has, in very rare cases, induced coronary spasm, hypotension and cardiac infarction (42).

Gemeprost

Gemeprost (16,16-dimethyl-trans-Δ²-PGE₁ methyl ester) is a PGE₁ analogue. It is used only as a vaginal pessary. A 1-mg pessary has an effect that persists for 3–6 hours. As with all prostaglandins administered vaginally, the rate of release is critically dependent on the vehicle used to form the pessary. Gastrointestinal side-effects are less frequent and less severe than with carboprost but diarrhoea and nausea affect a significant minority of users. No fatal cardiovascular side-effects have been reported. Gemeprost is available in several countries and has become the most widely used of the prostaglandin analogues.

Meteneprost

Meteneprost (9-deoxo-16,16-dimethyl-9-methylene PGE₂) is a PGE₂ analogue that has not been marketed yet but has shown considerable promise in clinical trials (43, 44). Use has been almost exclusively by the vaginal route, although oral administration has been tried on an experimental basis in conjunction with the antiprogesterone, mifepristone (see section 3.2.2). Weight for weight it has about one-third the potency of gemeprost, but otherwise its effects are similar.

Misoprostol

In contrast to all the prostaglandins discussed above, the PGE₁ analogue misoprostol ((±)-15-deoxy-(16*RS*)-16-hydroxy-16-methyl-PGE₁

methyl ester) is stable at temperate room temperatures and is active when given by mouth, with a half-life of about 1.5 hours. Gastrointestinal side-effects are relatively mild. Misoprostol induces regular uterine contractions when given orally (300–600µg), but it is relatively less active than a 1-mg pessary of gemeprost. No dangerous side-effects have been reported. Misoprostol inhibits the gastric secretion of acid and thus protects the gastric mucosa from ulceration, particularly in patients taking non-steroidal anti-inflammatory agents. It is approved and marketed in more than 60 countries for this indication. Unlike the other prostaglandin analogues it is inexpensive. Tablets of misoprostol, for oral use, have also been shown to be effective in inducing uterine contractility when given by the vaginal route.

3.2.2 **Antiprogestogens**

Mifepristone

Mifepristone is a 19-norsteroid that specifically blocks the receptors for progesterone and glucocorticosteroids. It is active when given by mouth and peak plasma levels are reached within 2 hours. Its half-life in plasma is 26–48 hours but nanomolar concentrations persist for several days (45). Uterine contractility increases within 12 hours of administration and reaches a maximum after about 36 hours (46).

The blockade of the glucocorticosteroid receptors is rapidly compensated for by an increase in the pituitary production of adrenocorticotrophic hormone (ACTH) and an increase in the adrenal secretion of glucocorticosteroids.

The blockade of the progesterone receptors results in the breakdown of maternal capillaries in the decidua (47), the synthesis of prostaglandins by the epithelium of the decidual glands (48), and inhibition of prostaglandin dehydrogenase (49). The resulting increase in prostaglandin levels induces uterine contractions. Changes occur in the decidua that resemble those of inflammation and are associated with the release of additional prostaglandins (50). Similar changes also occur in the cervix (51), but prostaglandin E levels are not increased in the cervical tissues and cervical ripening is not blocked by non-steroidal anti-inflammatory drugs. This may be explained by a mifepristone-induced increase in the number of prostaglandin receptors in the cervical tissues. Softening and dilatation of the cervix precede the onset of uterine contractions (52). The above changes are complex and not fully understood. One problem is that there is some variation in response, so when mifepristone is administered alone at

up to 56 days of amenorrhoea, only about 60–65% of pregnancies abort even when the dose given is considerably in excess of that which induces bleeding in most women.

Mifepristone makes the uterus about five times as sensitive as usual to the prostaglandin analogues (53). This effect develops over 24–48 hours and is the basis of the regimen for early medical abortion in which orally administered mifepristone is followed 36–48 hours later by a prostaglandin analogue (see section 4.3.3).

Lilopristone and onapristone

Lilopristone is structurally very similar and has comparable abortifacient activity to mifepristone (54).

Onapristone is a somewhat unusual steroid owing to its configurational inversion at positions C-13 and C-17 resulting in a change from *trans*-fusion to *cis*-fusion between the C and D rings of the steroid skeleton. The abortifacient potency of this antiprogestogen in humans has not been determined.

3.2.3 **Epostane**

This compound inhibits the action of the enzyme, 3 β -hydroxysteroid dehydrogenase, which has a critical role in the synthesis of progesterone. Unlike the chemically related compound trilostane, epostane has little or no effect on the production of adrenal corticosteroids. Epostane in an oral regimen of 200mg given four times daily for 7 days induced abortion in 84% of women with pregnancies of less than 56 days gestation (55). These results are similar to when mifepristone is given alone, and epostane is also similar to mifepristone in that the abortion rate increased significantly when a prostaglandin analogue was added sequentially (56). Epostane is not currently available for the induction of abortion.

3.2.4 **Oxytocin**

Synthetic oxytocin, when given by intravenous infusion, induces regular uterine contractions. The half-life of synthetic oxytocin in plasma is 5–10 minutes. At term, or in spontaneous labour, the uterus responds to 1–10 milli-international units (mIU) per minute but, earlier in pregnancy, infusions of 50 or more mIU per minute may be necessary and the resulting contractions may not be effective in dilating the cervix. With high rates of administration, uterine tone increases and the uterus may rupture. Oxytocin is also active when given by intramuscular injection, but uterine hypertonus is common and this route of administration has been abandoned.

Oxytocin is a relatively inefficient method of inducing abortion when used alone but the uterine muscle is more responsive if a prostaglandin has been administered some hours previously. An important and potentially dangerous side-effect of oxytocin is anti-diuresis. A reduction in the ability to excrete a water load is detectable at infusion rates of 8mIU per minute, clinically significant at 10–20mIU per minute, and maximal at 50mIU per minute (57). Prolonged infusions in which 3 or more litres of fluid have been given over 24 hours have resulted in water intoxication. Recovery is possible with prompt recognition of the early signs of water overload and withdrawal of the oxytocin, but permanent brain injury and death have been reported (58). Plasma sodium concentrations of 125 milli-equivalents (mEq) per litre or less provide clear evidence of water overload. To avoid this effect, oxytocin should be administered in a very small volume of fluid with an infusion pump. Close attention must always be given to fluid balance, particularly when the drug flow is controlled by the drip rate of a gravity-fed infusion.

3.2.5 ***Hypertonic agents***

Hypertonic saline

The intra-amniotic injection of hypertonic saline solution causes osmotic damage that leads to necrosis of the amnion, chorion and fetal surface of the placenta. Fetal death is usual, unless the injection-to-abortion interval is unusually brief. Most clinical studies have used 40g of sodium chloride dissolved in 200ml of water. Larger amounts are no more effective and are more likely to result in dangerous side-effects (59). Uterine contractions develop 5–10 hours after the injection and, if no other agents are used, the mean injection-to-abortion interval is about 35 hours. Prostaglandin concentrations increase in the amniotic fluid and maternal plasma following the saline injection (60). All women show an increase in plasma sodium and chloride concentrations after the injection but thirst, leading to the intake of water, results in the efficient excretion of the sodium load, providing there is no pre-existing cardiac or renal disease. Hypertonic saline should not be used in women with renal or cardiac disease. Impaired renal function can prevent the rapid excretion of the sodium chloride so that the plasma volume increases and congestive heart failure may occur. Accidental intravenous injection of hypertonic saline can result in coma and brain damage.

Hypertonic urea

The use of hypertonic urea solution for inducing abortion was introduced into clinical practice in 1971 (61). The solution, which consists

of 80 g of urea dissolved in 100 ml of 0.9% saline, is administered by intra-amniotic injection. Its mode of action has not been investigated, but it is assumed that osmotic damage to the amnion and chorion leads to the release of prostaglandins, which induce uterine contractions and abortion. Fetal death is usual, unless expulsion of the fetus is unusually prompt. The injection-to-abortion interval is usually about 50 hours, but can be 100 hours or more if no other uterine stimulating agents are used.

Urea is distributed in the body fluids more rapidly and more widely than sodium chloride and, providing there is no pre-existing renal disease, the plasma osmolality is adjusted to accommodate the transient increase in urea concentration. Hypertonic urea should not be used in women with renal disease. Accidental intravenous injection is better tolerated than when hypertonic saline is used and no dangerous side-effects on the brain or cardiovascular system have been reported.

3.2.6 *Ethacridine lactate*

This compound is an acridine dye with weak antiseptic properties. A 0.1% solution is injected extra-amniotically via a catheter passed through the cervical canal; the usual dose is 10 ml per week of gestation up to a maximum of 150 ml. Ethacridine has been shown to stimulate endogenous prostaglandin production, probably as a result of chemical trauma to the fetal membranes and the decidua.

Published clinical data suggest a lack of toxicity in humans (62), but there is evidence of some acute toxicity in laboratory animals (63–65).

3.2.7 *Hydrophilic cervical dilators (tents)*

Laminaria

Laminaria tents are 5-cm lengths of the dried stems of the seaweeds *Laminaria japonica* or *L. digitata* and are available in a range of diameters. The tents are sterilized by irradiation and are discarded after use. One or more tents are placed in the cervical canal so that the leading ends pass beyond the internal os whilst leaving the other ends in the upper vagina. Anaesthesia is not necessary. The tents absorb water from the cervical secretions and increase in diameter by a factor of 3–5 within 4–12 hours. The physical dilatation of the canal is accompanied by softening of the cervical tissues. Wide dilatation can be obtained by a second insertion, 12 hours after the first, of as many tents as the cervix can accommodate. Problems such as uterine

perforation, migration into the uterine cavity, or impaction and breakage in the cervix are uncommon (66).

Lamigel

Lamigel is made of a polyvinyl alcohol polymer sponge impregnated with about 450mg of magnesium sulfate to form a cylindrical tent with a diameter of 3–5 mm and a length of 75 mm. The diameter of this tent increases with the absorption of moisture from the cervix but it exerts relatively little force on the cervix as it becomes relatively soft. The device stimulates collagenolytic activity in the cervix and increases the sensitivity of the cervical tissues to PGE₂ (67).

Dilapan

Dilapan is a thin plastic rod coated with a hydrophilic polymer of polyacrylonitrile (Hypan). It swells more rapidly and dilates more effectively than other hydrophilic dilators, opening the cervix from 5 mm to 12 mm within 2–4 hours (66). It acts mainly via mechanical forces. Insertion and removal are usually easy but minor problems can be experienced if the device is left in the cervix for more than 4 hours, when a waist-like constriction can hinder removal. Occasionally, as with laminaria, the device may migrate into the uterine cavity or break during extraction through the cervix (68).

3.2.8 **Cervical ripening devices**

Balloon catheters introduced through the cervix probably cause cervical softening and dilatation through a combination of mechanical action and the induction of biochemical changes in the lower uterine and cervical tissues. They do not change in size, in contrast to hydrophilic cervical dilators, which swell as they absorb water.

Foley catheter

The insertion of a Foley urinary catheter, so that the balloon is above the internal os, induces softening and dilatation of the cervix if left in situ for 12–18 hours. A controlled trial among women at between 12 and 16 weeks of gestation showed that insertion of a 14-gauge catheter with a 25-ml balloon caused significantly more cervical dilatation than treatment with a 3-mg dinoprostone pessary (69).

Atad double-balloon catheter

A double-balloon catheter was used to dilate the cervix in 32 women at 12–15 weeks of gestation (70). One uterine balloon was placed just above the internal os while the other was located at the external os by

pulling the catheter after inflating the inner balloon. Each balloon was filled with 60–80 ml of saline. The device induced cervical dilatation of 10–18 mm within 9 hours in most of the women. The results of this study must be interpreted with caution as the study included both nulliparous and multiparous women, some women received extra-amniotic PGE₂ and the intervals between insertion and evacuation were variable.

4. Methods of abortion up to 63 days of amenorrhoea

4.1 Methods available

Dilatation and vacuum aspiration became established as the standard method for abortions performed at up to 63 days of amenorrhoea in the early 1960s. The procedure can be carried out under either local or general anaesthesia and does not usually require an overnight stay in hospital. The rate of serious complications is low.

The clinical availability of prostaglandins in the 1970s, and of the progesterone receptor-blocking agent mifepristone in the late 1980s, has made medical abortion an alternative method at this stage of gestation. Medical abortion with mifepristone and a prostaglandin has been shown to be safe and effective with no more complications than dilatation and vacuum aspiration. Medical abortion is more acceptable to certain women and can facilitate the provision of abortion services.

4.2 Surgical methods

4.2.1 *Menstrual extraction*

Menstrual extraction involves aspirating the uterine cavity and inducing uterine bleeding in women whose menstrual period is no more than 14 days overdue. After the cervix has been exposed with a speculum, a 4–6-mm flexible cannula attached to a 50-ml syringe is passed into the uterine cavity. Cervical dilatation is not usually necessary (71). Anaesthesia is not customary, but as a substantial proportion of women experience pain, some operators routinely use a paracervical block and/or analgesia.

Because the procedure was originally intended to be offered to women who were concerned that they might be pregnant but who had not had a pregnancy test, it has been used in some countries with restrictive abortion legislation but in which menstrual extraction

is not regarded legally as an abortion. When the procedure is offered on this basis, some of the women prove not to be pregnant, the proportion falling from about 40% when the period is 7 days overdue to about 20% at 14 days (72). Complications, such as uterine haemorrhage and infection, are as frequent in non-pregnant women as in those who are pregnant. Thus, unnecessary morbidity is avoided if menstrual extraction is offered only to women who have had a positive pregnancy test. This brings the procedure under the control of the abortion law, whereas this may not have been the case previously.

4.2.2 *Dilatation and vacuum aspiration*

This procedure involves removing the products of conception via a cannula inserted through the cervical canal into the uterine cavity. A large manually operated syringe can be used to evacuate the uterus but it is more convenient and quicker if the cannula is attached by flexible tubing to a glass or plastic container that is evacuated either by an electric or a manual pump. An 8-mm cannula is the largest that is necessary for abortions up to 63 days of amenorrhoea. In a minority of parous women the cannula can be inserted without discomfort, but most require cervical dilatation. This is usually easy and non-traumatic and, up to 63 days of gestation, there is no evidence that preparation of the cervix with either a prostaglandin analogue or a hydrophilic dilator reduces the incidence or severity of immediate or long-term complications.

The procedure can be performed under either local or general anaesthesia and does not usually require an overnight stay in hospital. When local anaesthesia is used, the pain of dilating the cervix is blocked, but the woman remains conscious of the speculum in her vagina and can still feel uterine pain or cramping during the evacuation of the products of conception. Women having abortion by vacuum aspiration under local anaesthesia need emotional support from both the operator and the operating room staff. Some women benefit from additional analgesia; pethidine (meperidine), fentanyl, diazepam and midazolam have all been used and shown to be effective (73). Care must be taken when such drugs are given to ensure that the woman remains conscious enough to maintain an adequate airway. In addition, she must have enough supervised recovery time to ensure that she can return home safely. The complete evacuation of the products of conception must always be immediately confirmed by examination of the material aspirated as it is possible that the pregnancy may be ectopic, in which case the uterus will be empty. The woman should not leave the operating room until this has been done.

The complications associated with abortion are discussed in more detail in section 7.

4.3 **Medical methods**

4.3.1 ***Prostaglandin***

Gemeprost and meteneprost given vaginally have been shown to induce abortion effectively at up to 49 days of amenorrhoea but neither has been adopted for routine use in this gestation range (43, 74). This is because several doses at intervals of 3–6 hours are necessary, the process is slow and side-effects are troublesome.

Bleeding starts about 3–6 hours after the first dose and resembles a heavy period, with a mean blood loss of 62ml. The bleeding persists for 1–2 weeks and occasional spotting may occur until the first menstrual period (43).

All women have uterine pain, which may be severe enough to require narcotic analgesics in 12–56%, and 30–40% have occasional episodes of vomiting or diarrhoea. Abortion is incomplete in 3–7% of women and the pregnancy continues in spite of treatment in up to 3%. In a WHO randomized study of abortions performed at up to 21 days delay of menses, vacuum aspiration resulted in fewer incomplete abortions than intramuscular injections of sulprostone (2.8% vs 7.4%) (74).

4.3.2 ***Mifepristone***

Mifepristone alone is relatively unsatisfactory as an agent for terminating pregnancies of up to 56 days of amenorrhoea as complete abortion occurs in only 60–70% of women. This was observed after using a variety of regimens in which divided doses of up to a total of 1600mg were given over a period of 4–7 days (75). Efficacy was highest very early in pregnancy; abortion occurred in 85% of women who were within 10 days of their missed period and received a total of 400–800mg over 2–4 days (76).

4.3.3 ***Mifepristone in combination with prostaglandin***

Complete abortion occurs in about 95% of women with up to 63 days of amenorrhoea when mifepristone is given, in either a single dose of 600mg or five divided doses of 25mg (at 12-hour intervals), and followed 36–48 hours later, by a single dose of a suitable prostaglandin. This was first demonstrated in 1985 in Sweden using 0.25mg of sulprostone administered by intramuscular injection (53), and then confirmed in Scotland, using 0.5 or 1.0mg of gemeprost given as a

vaginal pessary (77), and in France, using 1 mg of gemeprost (78). These small-scale clinical trials were followed by two large multicentre studies in France and the United Kingdom (79, 80). The studies confirmed that administration of a single oral dose of 600mg of mifepristone followed, 48 hours later, by either 0.25–0.50mg of sulprostone by intramuscular injection or 1mg of gemeprost as a vaginal pessary, results in complete abortion in about 95% of pregnancies. Only 0.4–0.8% of the pregnancies were unaffected by treatment.

Dosage

The optimum dose of mifepristone remains to be established. Several studies have suggested that, when followed by the prostaglandin analogue, gemeprost, similar efficacy can be obtained with single doses of mifepristone that are less than 600mg. A recent WHO multicentre trial reported that single doses of mifepristone of either 200, 400 or 600mg, followed 48 hours later by 1mg of gemeprost as a vaginal pessary, resulted in complete abortion in 95% of women with up to 28 days delay of menses (81). There were no significant differences between the three regimens in relation to outcome of treatment, the numbers of reported complaints, bleeding patterns, and changes in blood pressure and haemoglobin concentration.

Alternative prostaglandins

Many women do not like having drugs administered by the vaginal route. Sulprostone for intramuscular injection is no longer available, but misoprostol administered orally has been found to be as effective as gemeprost given by the vaginal route, at least up to 49 days of amenorrhoea (82). A multicentre study was conducted in France which involved 895 women with up to 49 days of amenorrhoea (83). A total of 505 women received 600mg of mifepristone, followed 48 hours later, by 0.4mg of misoprostol; complete abortion occurred in 97%. The remaining 390 women received the same regimen with an optional additional dose of 0.2mg of misoprostol 4 hours after the first dose if abortion had not occurred. This regimen increased the proportion of women having a complete abortion to 99%. These results strongly suggest that, at least up to 49 days of amenorrhoea, misoprostol is as effective as gemeprost when given in combination with mifepristone. The low cost, stability at room temperature of misoprostol compared to other prostaglandin analogues and the greater acceptability of this orally administered prostaglandin, are important advantages for those providing clinical services, particularly in developing countries.

Effects

Abortion. Recognizable products of conception are passed within 4 hours of receiving the prostaglandin in 60–70% of women, and within 24 hours in 85%. About 95% of women have a complete abortion within 7 days of prostaglandin treatment. Incomplete abortion is managed by vacuum aspiration. In about 0.5–1% of women the procedure needs to be carried out for haemostatic purposes, to control significant bleeding. In the remaining 2–3% of women the evacuation procedure is carried out electively, usually because of persistent vaginal blood loss or spotting, or other signs suggestive of incomplete abortion.

Continuing pregnancy. All large clinical studies report that mifepristone administered in combination with prostaglandin fails to interrupt pregnancy in about 0.5–1% of women. There is a need for further research into the reasons underlying these failures, including the relationship between the proportion of pregnancies that continue, the dose of mifepristone, and the type and dose of prostaglandin.

Bleeding. Nearly all women have bleeding from the uterus after receiving mifepristone and this begins before the administration of the prostaglandin in about 50–60%. In the remainder, bleeding usually starts within the first few hours after receiving the prostaglandin. In a multicentre study in France, blood loss persisted for a mean of 8 days, and for 12 days or less in 90% of the women (84). Although most women perceive the bleeding as somewhat heavier than a menstrual period, treatment is rarely required. In multicentre studies in France and Great Britain evacuation of the uterus to control haemorrhage was considered necessary in 0.4% and 1% of women, and blood was transfused in 0.1% and 1%, respectively (84, 80). The lower proportion needing treatment for haemorrhage in the French study was probably a consequence of the upper gestation limit being 49 days rather than the 63 days specified in the British study.

Blood loss increases with gestation and appears to be independent of the amounts of mifepristone and gemeprost used to induce the abortion. In one study the median blood loss was 74 ml; however, the range was 14–512 ml (85). The average fall in haemoglobin concentration was only 0.3 g/dl in the WHO multicentre study (87), but was 2–4 g/dl in 1% of women in the British multicentre study in which the gestation limit was higher (80).

Pain. Some pain is experienced by almost all women, particularly during the first few hours following the administration of the prostaglandin. In the British multicentre study, 21% of women required an opioid analgesic, but there was considerable variation between study

centres (80). In the WHO multicentre study, 13% of women were given opioid analgesics, with a further 11% receiving non-opioid analgesics, mostly oral paracetamol (81). As in the British study, the centres participating in the WHO study differed significantly in their use of analgesic drugs. In contrast, opioid analgesics were not used in the multicentre study in France in which misoprostol was given in combination with mifepristone and only 20% of women required any analgesia (83).

Ectopic pregnancies. Some early medical abortions are inadvertently attempted in women with ectopic pregnancies because the latter may not have caused any signs or symptoms by the gestation at which the mifepristone and prostaglandin are administered. The combined treatment regimen does not terminate pregnancies that are not in the uterine cavity.

Women who change their mind after taking mifepristone. Occasionally a woman decides to continue her pregnancy after taking mifepristone. To date the manufacturers of mifepristone have been informed of 27 such pregnancies carried to term, all of which have resulted in the birth of apparently healthy babies. One baby had minor nail abnormalities (A. Ulmann, personal communication, 1994). In a further pregnancy a scan early in the second trimester showed that the fetus had syrenomelia and the pregnancy was then terminated (86). However, a review of the timing of the mifepristone treatment suggested that the fetal abnormality was likely to be coincidental. Very much larger numbers of pregnancies exposed to mifepristone must be observed to define any possible teratogenic effect. Similarly, the effect of prostaglandin on the fetus is not known and, for the present, any agent that produces a marked increase in uterine tone and contractility and, presumably, a decrease in blood flow to the placenta and fetus must be regarded as potentially harmful.

4.3.4 **Provision of medical abortion**

Women generally attend the abortion clinic on three or four occasions. The first involves the standard pre-abortion assessment at which the stage of gestation is determined, the woman's general health is checked, information is provided about the abortion methods that are available and help is offered with contraception. Counseling is offered to those who are ambivalent about their decision or who are having difficulties with anxiety or guilt. Women who decide to have an early medical abortion can take the mifepristone then or at the second visit a few days later. Anti-D immunoglobulin is given to women who are Rhesus negative either at the time of mifepristone intake or when the prostaglandin is given.