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**BASIC AND CLINICAL ASPECTS
OF INTRA-UTERINE DEVICES**

Report of a WHO Scientific Group

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WORLD HEALTH ORGANIZATION

GENEVA

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WHO SCIENTIFIC GROUP ON BASIC AND CLINICAL ASPECTS
OF INTRA-UTERINE DEVICES

Geneva, 7-12 February 1966

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BASIC AND CLINICAL ASPECTS OF INTRA-UTERINE DEVICES

Report of a WHO Scientific Group

A WHO Scientific Group on the Basic and Clinical Aspects of Intra-uterine Devices met in Geneva from 7-12 February 1966. The meeting was opened by Dr J. Karefa-Smart, Assistant Director-General, who welcomed the members on behalf of the Director-General. Dr L. Snaith was elected Chairman and Professor Daphne Chun Vice-Chairman; Dr S. J. Segal, Dr C. Tietze and Dr L. L. Williams agreed to act as Rapporteurs.

The meeting was convened in part in response to a resolution adopted by the Eighteenth World Health Assembly requesting the Director-General to continue studies on the medical aspects of sterility and fertility control methods and on the health aspects of population dynamics. The increasing popularity and widespread use of intra-uterine devices provided a further reason for an evaluation by WHO of this method of conception control.

This report complements the one recently published of a WHO Scientific Group on the Clinical Aspects of Oral Gestogens.¹ It is suggested that the two reports should be studied together in order to obtain a complete and up-to-date assessment of these two methods of fertility control.

The report aims to place in proper perspective both the value and the possible hazards of intra-uterine contraception, and it should allay any undue fears about employment of the method that may have resulted from ill-informed and unscientific publicity.

Although some statements about the comparative use effectiveness of intra-uterine devices and oral contraceptives are included in the report, it was thought neither possible nor advisable to attempt a point-by-point comparison which would require a careful study of all aspects, whether medical, personal or administrative.

No attempt has been made to cite the already voluminous and rapidly growing literature relating to intra-uterine devices. Fairly comprehensive bibliographies will be found, however, in the Proceedings of the First and Second International Conferences on Intra-uterine Contraception.² Several

¹ *Wld Hlth Org. techn. Rep. Ser.*, 1966, 326.

² *Proceedings of the First International Conference on Intra-uterine Contraception, New York, 30 April-1 May, 1962*, Amsterdam, Excerpta Medica Foundation (*International Congress Series*, No. 54); *Proceedings of the Second International Conference on Intra-uterine Contraception, New York, 2-3 October, 1964*, Amsterdam, Excerpta Medica Foundation (*International Congress Series*, No. 86).

observations from unpublished studies are included in the report, and appreciation is expressed to those individuals who have made their data available to one or more members of the Scientific Group.

Four terms—intra-uterine device, intra-uterine contraceptive device, intra-uterine contraceptive, and intra-uterine foreign body—have all been used widely, and usually synonymously, by clinicians and research workers. After thorough discussion, the Scientific Group decided that only the term “intra-uterine device” would be used throughout this report and recommends its universal adoption, along with the suggested abbreviation IUD.

1. INTRODUCTION

1.1 With the development of modern intra-uterine devices a method of conception control has become available the importance and impact of which have yet to be fully recognized.

1.2 The widespread and steadily increasing acceptance of intra-uterine devices in many parts of the world and in all strata of different societies shows that they are generally considered to be effective and safe. Within the space of barely four years the number of modern devices in use has increased from a few thousand to well over one million, and the method has become the mainstay of the family planning programmes established by several Governments. The devices appeal to all types of women in all parts of the world. Once the device has been inserted no further thought or action, by either partner, is required. So long as the device remains in the uterus the woman is almost completely protected against conception. The fact that it can be left there for long periods without constant medical supervision is a further big advantage, especially in areas where there are few doctors.

1.3 Women who wish to conceive usually do so within 6 months to a year after removal of the device. In cases where an unplanned conception has occurred with a device in place, no adverse effect on pregnancy, delivery, or the health of the child has been demonstrated.

1.4 Many questions, however, remain. For example, how do the various devices now available compare with one another and can their performance be further improved? Can anything be done to reduce the present high rates of spontaneous expulsion and of necessary removal of devices for medical reasons, as a result of which approximately one woman in four who wants to use the device must do without it?

1.5 Among other matters requiring attention are the problems associated with the large-scale application of the method and the assessment of results and, not least, the mode of action of the devices, which constitutes one of

the most pressing challenges now confronting research workers in the field of the physiology of reproduction.

1.6 In the sections that follow an attempt is made to examine some of these questions in the light of current information, to point out gaps in knowledge and to suggest, where possible, lines along which future research—physiological, clinical and sociological—might usefully be conducted.

2. DEVELOPMENT OF THE INTRA-UTERINE DEVICES IN CLINICAL USE TODAY

2.1 Conception control by intra-uterine or utero-cervical devices is not new. Some of the types at present employed have been in use for several decades. The "wishbone", "collar-stud" and similar stem pessaries used in the late nineteenth century were primarily intracervical and were employed not only for contraception but also for the treatment of a variety of gynaecological conditions, such as malposition of the uterus, menstrual disorders and even infertility.

2.2 In the early part of the twentieth century, German physicians began to use devices that were wholly intra-uterine for purposes of contraception. In 1928 Gräfenberg reported his results with the metal ring which has come to be associated with his name. The initial enthusiasm for the Gräfenberg ring and the quick disenchantment of many gynaecologists are common knowledge. The method soon became discredited and, with only a few exceptions, was generally abandoned throughout the following thirty years. Interest revived in 1959 with the publication of two independent reports on the long-term safe and reliable use of two types of intra-uterine ring, one fashioned of silkworm gut and the other made either of metal or moulded plastic.

2.3 Since then several additional devices, some entirely intra-uterine, others with cervical appendages, have been designed. The most extensively studied types are (1) a ring of coiled stainless steel wire very similar to Gräfenberg's original ring; (2) moulded plastics of various sizes and configurations commonly referred to as spirals, loops and bows, and (3) a flexible ring of nylon thread. New types and modifications of existing ones are under investigation and others will undoubtedly make their appearance in the future.

2.4 All currently used devices are designed to occupy the frontal plane of the uterine cavity. The plastic ones are flexible enough to be inserted through a narrow plastic tube into the uterus where their inherent resilience or "memory" permits them to regain their original shape.

2.5 Several of the modern devices have cervical extensions such as a beaded plastic stem or fine strands of nylon. These appendages permit easy removal and allow the physician and, often, the wearer herself to determine whether the device is in place or has been expelled from the uterus. Most moulded plastic devices contain barium and can therefore be visualized by X-rays, if needed.

2.6 The stainless steel ring requires some dilatation of the cervix for insertion or removal. Neither it nor the bow has a cervical appendage, and consequently uterine sounding or an X-ray is necessary to determine whether the device is still present in the uterus.

3. BIOLOGICAL EFFECTS AND MODE OF ACTION

3.1 In spite of the evident importance of knowing how intra-uterine devices exert their contraceptive action the essential mechanism remains unknown.

Effects in women and sub-human primates

3.2 One of the earliest modern theories advanced to explain the contraceptive action of IUDs in women is that the devices stimulate tubal peristalsis or tubo-uterine motility in general, as a result of which the ovum is rushed through the Fallopian tube and arrives in the uterus within a day or even less, instead of the usual 3-3½ days, after ovulation. It will therefore be unfertilized or, if fertilized, developmentally "premature", and unfit to implant on the uterine mucosa which, in turn, has not had sufficient time to undergo the full progesterational transformation essential for reception of the blastocyst.

3.3 The generally held belief that a normal period of tubal passage is required for successful implantation of the ovum is supported by the clinical observation that neither grafting of an ovary into the uterus nor surgical shortening of the tube improves the prospect of fertilization and nidation in sub-fertile women.

3.4 The additional fact that ectopic pregnancies occur considerably less frequently in women using IUDs than would be expected if the device acted purely at the uterine level is equally consistent with the theory. As will be shown, experimental evidence in its support has also been obtained in monkeys.

3.5 Although the mechanism of action based on studies in women cannot yet be defined with precision, several possibilities can be excluded on the basis of clinical observations or laboratory findings. These may be summarized as follows :

<i>Suggested explanation of action of device</i>	<i>Evidence of untenability</i>
(a) Blocking passage of sperm to the Fallopian tubes	Direct observations have established that motile sperm reach the Fallopian tubes in women wearing IUDs.
(b) Prevention of ovulation	The occurrence of normal, ovulatory cycles is indicated by studies of (i) endometrial biopsies, (ii) urinary pregnanediol levels, (iii) visualization of corpora lutea at laparotomy and (iv) basal body temperature records.
(c) Prevention of passage of fertilized ova from the Fallopian tube to the uterine cavity	Records indicate that the incidence of ectopic pregnancies per total months of exposure is far lower than expected.
(d) Establishment of chronic endometritis or a chronic inflammatory reaction	(i) Histological studies reveal that most endometrial biopsies show no significant changes and correspond with the phase of the menstrual cycle; and (ii) bacteriological studies of the endometrial cavity show no undue incidence of bacterial contamination.
(e) Interference with implanted blastocyst	There is no evidence of frequent prolongation of cycle length. Endometrial biopsies so far reported have failed to reveal decidual tissue or products of conception. These observations demonstrate that implantation does not occur more often in women using IUDs than would be expected on the basis of the known failure rate of the method.

3.6 Confirmatory evidence of the concept that IUDs act by speeding up tubal passage of the ovum is available in laboratory primates. It has been convincingly demonstrated that in superovulated rhesus monkeys fitted with intra-uterine plastic devices the transport of ova through the Fallopian tubes is markedly accelerated. Thus ova released in such females could no longer be found in the tubes 5 hours after the expected time of ovulation, compared with approximately 3 days in normal controls. Eggs could, however, be recovered following unilateral tubal ligation and even in the uteri of non-ligated females, provided they were examined early enough. Sperm were also present in the tubes of the experimental monkeys following artificial insemination. Fertilized ova could not be recovered after flushing the tubes and uteri of these animals, but were found in controls.

3.7 These studies therefore indicate that the devices do not interfere with ovum uptake or with sperm transport, but induce an accelerated tubal passage of the ovum. Results in naturally ovulating rhesus monkeys fitted with intra-uterine devices are not inconsistent with these conclusions. The

fertilizability of ova released in women fitted with IUDs remains to be established.

3.8 There are no observations bearing directly on the question of tubal transport in IUD-fitted women. Little concerning the speed of ovum passage can be deduced from the finding of a pronuclear egg on day 16 of the cycle in the tube of a woman with an IUD. Neither the exact time of ovulation nor the anatomical integrity of the Fallopian tube in which the egg was found could be ascertained. This egg was the only fertilized one among 11 recovered by flushing the Fallopian tubes of 92 women who had been fitted with devices and were examined at laparotomy by different groups of investigators. By comparison, 161 tubal flushings of women without devices produced 12 ova, of which 4 were fertilized. It is difficult to see how any approach, other than the one described, can ultimately resolve the question of whether fertilization occurs in women successfully using intra-uterine contraception. A far greater number of ova will have to be recovered before any definite conclusions are possible.

3.9 Up to now very little work on uterine motility has been carried out in women. The only report so far available confirms that myometrial activity is increased by the presence of a device in the uterus, at least during the cycle following insertion. Whether activation persists in subsequent cycles and is enhanced at the time of expected tubal transport of the ovum remains to be determined.

3.10 Preliminary findings in rhesus monkeys suggest that the immediate result of an intra-uterine plastic device is to convert a given motility pattern into that characteristic of menstruation and labour. This effect, however, is apparently not permanent and eventually results in a mere accentuation of the activity pattern the uterus would display without an IUD.

3.11 All studies of this type in rhesus monkeys and their interpretation are complicated by the highly contorted cervical canal in this species, as a result of which the insertion of an IUD, catheter, etc. by the vaginal route is difficult and inevitably accompanied by cervical irritation.

Effects in lower mammals

3.12 Although a great deal of recent research has been carried out in lower mammals the picture that has emerged so far is complex and confusing. Its outstanding feature is the wide range of effects and possible ways of action of intra-uterine devices in different species; consequently, the relation, as well as relevance, of many of these findings to the mechanism of action of the devices in women is not always evident.

3.13 In view of the many and profound differences in the anatomical and functional patterns of the reproductive systems between different mammals

this is not surprising. Of those so far studied no two species appear to react to intra-uterine devices in identical fashion, and consequently extrapolation of results from one species to another is rarely justified.

3.14 The value of the comparative studies carried out to date is further restricted for the following reason. A distinction must be made between the actions of intra-uterine materials as such and those of devices which, in addition to occupying the lumen of the uterus, also distend and presumably stimulate it. Most studies in lower mammals have been carried out with short pieces of thread or silk sutures, but, in ruminants, monkeys and women, plastic coils and other solid materials have invariably been used.

3.15 The following sections give an outline of the information available about sub-primate mammals. So as to avoid a mere tabulation of findings, the material has been grouped according to physiological effects and "points of impact" on the reproductive cycle, irrespective of the species concerned.

Effect on ovulation and corpus luteum formation

3.16 The only evidence that intra-uterine devices may exert their contraceptive action through an effect on ovarian function has been obtained in ruminants. In the Indian water buffalo and, to a lesser extent, in cows suppression of ovulation and failure of corpus luteum development were observed following insertion of plastic coils in the uterus.

3.17 By contrast, in the closely related sheep, ovulation appears to be unaffected, and the same is probably true of all other lower mammals that have so far been studied (rat, mouse, hamster, rabbit, ferret).

Fertilization

3.18 Observations on rats, rabbits and ferrets suggest that in none of these species is fertilization adversely affected by intra-uterine devices.

3.19 In sheep and probably cows there appears to be interference with fertilization, but this may also be due to defective sperm transport. In the ewe fitted with unilateral or bilateral plastic coils, no cleaved ova and no sperm (or only greatly reduced numbers) have been found in tubal washings, although both ova and sperm were present in controls.

3.20 In the sheep, eggs recovered from coil-fitted females can be transferred into the uteri of host ewes and, following mating of the host, they will become fertilized and undergo implantation. This demonstrates that in this species IUDs do not affect fertilizability of the ovum.

Intraluminal secretions

3.21 Little is known about the functions of these secretions in the reproductive tract of female mammals, nor is it known whether IUDs produce any alterations in their quantity and composition that might be responsible for the contraceptive action of the devices. The possible effects of intraluminal fluids in this connexion, for instance on the capacity of spermatozoa to fertilize (and *vice versa* of ova to be fertilized) should, however, not be overlooked.

Blastocyst development, implantation and post-implantation

3.22 The effects of IUDs on these stages have been intensively studied in the rat and rabbit and less closely in the mouse and ferret. Two slightly different patterns of reaction to IUDs (almost invariably intra-uterine sutures) can be recognized among these four species.

3.23 In the rat and the mouse blastocyst development appears entirely normal until about the day before implantation. The contraceptive effect becomes manifest, and most effective, just before expected nidation, that is, on arrival of the blastocysts or morulae in the uterus. After this stage blastocysts can no longer be recovered and either disintegrate or are quickly expelled from the uterus unless the uterine horn is ligated near the cervix.

3.24 In the rabbit and the ferret, too, implantation is the critical stage at which the majority of blastocysts die. Of the rest, some become attached and may survive for variable periods, a few even until term. Thus, in both species there is a progressive loss of embryos, indicating that the effect of an IUD in these animals is not confined to the stage of implantation but continues throughout pregnancy.

Reversibility of contraceptive action

3.25 The relatively high degree of reversibility of the contraceptive effect of IUDs has been repeatedly demonstrated.

(a) Following removal of intra-uterine sutures from either one or both horns rats will readily conceive in those horns and carry normal litters to term. Rats fitted with an intra-uterine suture before puberty will not become pregnant in that horn after reaching maturity, but will do so after removal of the device.

(b) Removal of an intra-uterine suture (inserted during a preceding cycle) on day 2 of pregnancy in the rat leads to a substantial reversal of the contraceptive effect, but removal on day 4 no longer has this effect in the horn with an IUD.

(c) In rabbits (in which suppression of implantation is incomplete) removal of an IUD between 84 and 160 hours after coitus permits a virtually normal implantation rate and survival of normal embryos.

Correlation between inhibition of implantation and decidual response

3.26 It has been amply demonstrated in rats that there is a close association between the inhibition of implantation induced by an IUD and failure of the endometrium to undergo decidual transformation. There is reason to believe that in rodents decidualization of the uterus precedes implantation, and it has been suggested that IUDs prevent the normal course of pregnancy by interfering with this specific uterine response.

3.27 The fact that both implantation and decidualoma formation can occur in the control horn appears to exclude an interference at the systemic level. On the other hand, the action of the IUD, though confined to one horn, is not purely local, but affects the horn throughout its entire length.

3.28 It may be that some local trigger compound or mechanism, whether biochemical, pharmacological or neuro-endocrine in origin, which is necessary for the initiation of both the decidual cell reaction and implantation, is exhausted or competed for by the presence of the foreign body.

3.29 The possibility that an IUD sets up a uterine environment hostile to the blastocyst can by no means be excluded, either in lower mammals or in women.

Other endocrine studies

3.30 There is no evidence that intra-uterine sutures in rats affect the gonadotrophin content of the anterior pituitary, lactation and milk ejection or the release of oxytocin; nor is there any indication that they alter the biochemistry of the uterus and its sensitivity to oxytocin, gonadotrophin and oestrogens.

3.31 Such studies as are available on urinary gonadotrophins, oestrogens and pregnanediol levels in women using IUDs fail to reveal any unusual pattern. Milk ejection, too, does not appear to be affected in women by the presence of a device.

Change in vascularization of the uterus

3.32 There is some evidence that in rats an intra-uterine suture reduces capillary permeability in the horn containing the thread. This may provide

an important lead for the investigation of the contraceptive effect, both in rodents and other mammals.

Role of inflammation and leucocytes

3.33 Inflammatory changes in the uteri of experimental animals fitted with IUDs are generally slight or absent, and are not believed to be responsible for or contribute materially to the contraceptive effect.

Neurogenic factors

3.34 The convincing demonstration of an accelerated tubal transport of ova in superovulated and device-fitted rhesus monkeys strongly implies the involvement of a neurogenic mechanism triggered by stretching or direct stimulation of the uterus (cf. 3.6, above).

Provisional conclusions on mode of action

3.35 In surveying the assembled facts, derived from studies in several species, the following tentative conclusions may be drawn.

3.36 No single cause or mechanism of action of an IUD has so far come to light. The multiplicity of observed effects, in fact, suggests that these devices may act at several levels and in several ways, not only in different species, but possibly also in the same species. This would not be wholly surprising; the position with regard to the oral gestogens is comparable.

3.37 There appear to be three distinct patterns in the overall effects of IUDs.

(a) In *sub-human primates*, accelerated passage of ova through the tube and the rest of the reproductive tract appears to be the major, but not necessarily the only, mechanism of action. This may also prove to be true in women.

(b) In *ruminants*, such as sheep and cattle, the contraceptive action is exerted, at least in part, at the ovarian level, leading to deficient ovulation and luteal function, and probably also to impaired sperm transport.

(c) In *rats, mice, rabbits, and ferrets*, the main effect is suppression of implantation. In the rabbit and the ferret, the action is not confined to the stage of implantation but continues throughout pregnancy. Whatever may be the ultimate mode, or modes, of action of IUDs in the human species, it appears justifiable to conclude that their contraceptive effect is exerted before the stage of implantation.

4. TISSUE REACTIONS

The uterus

4.1 Early workers believed that intra-uterine devices induced "hyperplasia" of the endometrium and ascribed their contraceptive action to the prevention of nidation by this reaction. This has not been confirmed by more recent studies. It is generally believed that the devices cause few, if any, significant tissue reactions. Atrophy and denudation of the epithelium at the point of contact have been described; oedema of the endometrium and increased vascularity of the stroma also occur and may represent the reaction of the endometrium to the presence of a foreign body. The latter changes may account for the frequency of menorrhagia and metrorrhagia after insertion of an IUD.

4.2 It is also not unusual to find signs of true inflammatory changes, with small round or plasma cell infiltration, both local and generalized. Whether such changes represent low-grade infections, exacerbations of pre-existing infection or merely a foreign body response of the endometrium is not clear. They tend to occur mainly in the initial stages after insertion and to regress later.

4.3 Some 20% of endometrial samples taken after insertion of the device show positive histological and bacteriological signs of infection. The proportion is, however, not much higher than in pre-insertion specimens, and the changes are sub-clinical, usually slight and reversible.

4.4 Several studies have yielded little or no evidence of changes in endometrial histochemistry and enzyme activity in women fitted with IUDs or of loss of sensitivity to ovarian hormones. There is no evidence that a decidual cell reaction occurs in response to an IUD. Whether the large amount of clear mucus that has been repeatedly found to surround devices within the uterus has any significance remains to be established.

The vagina

4.5 Normal vaginal cytology cycles occur both in women and in rhesus monkeys with intra-uterine devices. The occurrence of increased numbers of inflammatory cells in vaginal smears has been reported in women using devices. Cells thought to be of endometrial origin have also been described. Neither is considered to be of pathological significance.

Possible carcinogenesis

4.6 The presence of an IUD is not known to produce a generalized systemic effect. Considerations of possible carcinogenesis can, therefore,

be confined to local action on the endometrium and/or cervical epithelium.

Endometrial cancer

4.7 Cancer of the endometrium usually occurs after the menopause. When it occurs before the menopause it is generally preceded by episodes of irregular cycles, strongly suggestive of an ovarian dysfunction as one of the predisposing causes. There are no adequate studies to suggest whether or not the presence of a foreign body plays a part in the etiology or genesis of cancer of the endometrium. Studies of endometrial biopsies and of uteri removed at hysterectomy have been carried out by investigators in many countries in an effort to evaluate the safety of intra-uterine contraception. Results are available on histological examinations involving several hundred women who have been evaluated at various times after IUD insertion. Most of these women were subjected to biopsy within three years after insertion, but some had used the method for over a decade before being studied. There has not yet been a single case reported of endometrial carcinoma in a woman using an intra-uterine device, nor have the histological studies so far done in women shown any evidence of progression towards cancer.

4.8 Several prospective studies of endometrial cytology and histology in users of IUDs are now in progress. In one such study, one hundred women were randomly selected for brush smears of the endometrial cavity prior to insertion of an IUD, and have had repeat smears taken periodically, thereafter. At the end of one year in this continuing study, no significant changes in the endometrial smears have been noted. Another study of one hundred women, now extending over two years, in which biopsies have been taken before and after insertion, has failed to reveal any evidence of premalignant change.

4.9 Although the available information is insufficient to permit a final conclusion to be drawn on a possible relationship between intra-uterine contraception and endometrial cancer, it is evident that the use of an IUD is not associated with rapidly developing neoplastic changes in the endometrium.

Cervical cancer

4.10 The possibility that intra-uterine contraception may promote cancer of the uterine cervix needs to be evaluated, not only because several devices have a trans-cervical appendage, but also because abnormal secretions of the uterine cavity due to the presence of an IUD could be a cause of cervical irritation. It is generally believed that cancer of the cervix is often associated with chronic irritation. Evaluation is complicated by several uncertainties

concerning cervical cancer in the general population. It is usually considered that abnormal Papanicolaou smears of the cervix may indicate a pre-cancerous condition. In most laboratories, however, repeat smears show regression to normal in a considerable proportion of such cases.

4.11 Limitations of the method notwithstanding, the prospective study by cervical smear cytology is an indispensable tool for evaluating the possibility of pre-malignant or malignant changes in the cervix associated with the use of intra-uterine devices. In many countries, studies of this kind are in progress, and several reports involving many thousands of women are already available. So far, all valid studies suggest that the incidence of cervical cancer is not increased in women using intra-uterine contraception. A similar statement regarding dysplasia cannot be made because of the difficulty in ascertaining the expected incidence of this condition in the population concerned. However, all IUD studies demonstrate frequencies of newly found abnormal smears that do not appear to be in excess of those spontaneously occurring in the population studied. Most of these prospective studies have not progressed beyond three years of follow-up, so that consideration must be given to the relative shortness of the period of observation. Nevertheless, there is no acceptable evidence that normal or early abnormal cervical smears in women with IUD's progress toward carcinoma *in situ* more rapidly than usual. A recent study of over one thousand women followed without treatment for as long as two and a half years has failed to reveal any significant influence of the presence of the device on the rate of progression from dysplasia to carcinoma *in situ*.

5. EFFECTIVENESS, EXPULSIONS AND REMOVALS

5.1 Many reports on the effectiveness, acceptability and safety of IUD's are now available from various countries. A recent comprehensive evaluation is based on more than 22 400 first insertions and a total of over 260 000 woman-months of uninterrupted use. Data obtained with the large sizes of plastic devices (spiral, loop and bow), and with the stainless steel ring, are included in this survey. The overall results are presented in the table on page 17. The figures shown are cumulative rates for the first year of use, computed by means of a life table procedure that permits the comparison of data obtained during various periods of observation.

Use effectiveness

5.2 The failure rates shown in the table include pregnancies occurring with the device *in situ* as well as those after unnoticed expulsion. Concep-

tions thought to have occurred prior to insertion are excluded. The failure rate varies with the type of device, but the more effective devices are associated with an incidence of 1.8 to 2.9 pregnancies per 100 insertions during the first year of use. This is slightly higher than comparable rates reported for oral contraceptives, but much lower than those for the traditional methods, such as the diaphragm or the condom, as used by most population groups that have been studied. The incidence of unintended pregnancy appears to drop after the first year. This may be due to the fact that expulsions of the device are less frequent at that time.

Theoretical effectiveness

5.3 This term refers to the degree of protection against unwanted pregnancy that can be achieved by a contraceptive method if it is used in complete conformity with instructions. The theoretical effectiveness of IUDs is thought to be similar to that of the diaphragm or condom methods when these are used consistently, i.e., at every coitus. Intra-uterine devices do not offer the virtually complete protection that can be obtained with oral contraceptives if the latter are taken without any omission of tablets.

Expulsions

5.4 Spontaneous expulsion of an IUD from the uterus into the cervix or vagina may occur. The frequency ranges from about 5% to over 20%, depending on the type of device (see table, p. 17). For all types of device the expulsion rate is highest immediately after insertion. About one half of all expulsions occur in the first three months and comparatively few after the first year. Expulsion is particularly likely to occur during menstruation. Some expulsions occur unnoticed by the women, usually with the result that they become pregnant. About half the spontaneously expelled devices that are reinserted are expelled again. The prospect of ultimate retention decreases with each reinsertion.

Removals

5.5 Removal of the device because of side effects remains the biggest problem associated with the use of IUDs. The incidence of removal for medical reasons ranges from approximately 10% to 25% of first insertions during the first year (see table, p. 17). It is probably true to say that the removal rate has not been materially reduced in the course of the three or four years since the method was introduced on a wide scale, and this constitutes one of its least satisfactory features. As women and medical practitioners gain greater confidence in the method some improvement can be expected.

**CUMULATIVE RATES OF EVENTS TO END OF FIRST YEAR PER 100
FIRST INSERTIONS, BY TYPE OF DEVICE, WITH STANDARD ERRORS ***

Events	Type of device ^a			
	Loop (7399)	Spiral (2535)	Bow (2557)	Ring (1851)
Pregnancies	2.9 ± 0.3	1.8 ± 0.4	5.9 ± 0.5	6.9 ± 0.7
Expulsions	11.3 ± 0.4	22.3 ± 0.9	4.5 ± 0.5	18.7 ± 1.0
Removals for medical reasons	14.1 ± 0.5	23.8 ± 1.0	13.5 ± 0.8	8.7 ± 0.8
Pelvic inflammatory disease	2.2 ± 0.2	3.5 ± 0.5	3.2 ± 0.4	2.6 ± 0.4
Cases lost to follow-up	8.3 ± 0.4	10.0 ± 0.7	8.0 ± 0.6	13.6 ± 0.9

* Compiled from data supplied by the Cooperative Statistical Program for the Evaluation of Intra-uterine Devices, National Committee on Maternal Health, New York, USA.

^a The number of insertions is shown in brackets beneath the name of the device.

Overall picture

5.6 There are regional and local differences in the reported rates of unintended pregnancies, expulsions and removals of IUDs which may depend on many factors, including completeness of follow-up and method of statistical analysis. There is no evidence that these differences are influenced by such factors as physical environment, ethnic background or socio-economic status.

5.7 When the rates for unintended pregnancies, expulsions and removals are considered together, the total reaches 25% to 30%; in other words, the method can be used successfully by almost 3 out of every 4 women who adopt it.

6. SIDE EFFECTS AND COMPLICATIONS

6.1 The commonest side effects are bleeding and pain. Between them they account for two thirds of the removals of the devices undertaken for medical reasons. Their assessment is complicated because of the use of different types of device, multiplicity of or change in symptoms, and variations in both female fortitude and standards of documentation in different parts of the world. Other important but far less frequent complications are pelvic inflammatory disease and perforation.

Bleeding

6.2 A certain amount of bleeding is so common immediately after insertion that it should be considered as the usual event. Intermittent slight bleeding

("spotting") or a sero-sanguinous discharge frequently continues after the initial period of bleeding associated with insertion. This pattern is thought to be particularly common in women suffering from iron deficiency and requires suitable medication; it can be a serious personal burden. Bleeding may also become manifest as menorrhagia or metrorrhagia. These constitute probably the most troublesome symptoms and may be intense enough to alarm both patient and physician. Severe bleeding requires active treatment and usually calls for removal of the device.

Pain

6.3 Spasmodic uterine pain or low backache may occur as the main symptoms or in combination with others, such as bleeding or discharge. Tolerance of pain is highly variable and is markedly affected by psychological and cultural factors. Discomfort immediately after insertion is not uncommon, but severe uterine cramps or syncope, during or after fitting of a device, are rare. They are most likely to occur in nulliparous patients and in women who have not had a child for a number of years. Continuing dysmenorrhoea and dyspareunia are hardly ever caused by IUDs.

Vaginal discharge

6.4 This is common, and appears to be the direct sequel of the insult to the endometrium associated with insertion of the device. It becomes much less frequent after the first period.

Pelvic inflammatory disease

6.5 The table on page 17 shows an incidence of 2.2-3.5 cases of pelvic inflammatory disease (P.I.D.) per 100 women during the first year after insertion. Only a quarter of these, however, were graded as "severe". Consequently, acute P.I.D., as customarily defined in terms of pyrexia, leucocytosis and a raised erythrocyte sedimentation rate, occurred in less than 1% of these women. Available evidence does not permit a confident statement whether this rate differs significantly from the incidence of P.I.D. in the populations from which these subjects were drawn.

6.6 While most cases of P.I.D. occur soon after insertion of a device some only appear after many months of use. At least half of the total incidence of P.I.D. is considered to be an exacerbation of a condition existing before insertion of the device. Most of these patients can be successfully treated with antibiotics and do not require removal of the device.

Perforation

6.7 Perforation of the uterus occurs in a small proportion of cases, even in the hands of the most careful and competent gynaecologists. Its incidence varies with the type of device (bow : 1 in 200 insertions ; loop, spiral and stainless steel ring, combined : 1 in 2000). In the case of the bow the risk of perforation is far higher if insertion is done less than six weeks post-partum or before the return of menstruation. The number of perforations reported with other types of IUD is too small to permit analysis.

6.8 Most perforations do not produce clinical symptoms and are only discovered at routine follow-up examination. It is therefore impossible to determine with certainty the time and circumstances of their occurrence. It is believed, however, that most perforations take place at insertion and others during attempted removal of a device, especially if this proves difficult. It has been claimed that an IUD can make its way unaided through the wall of the uterus, but this has never been unequivocally demonstrated.

6.9 The terminal bead of the transcervical appendage of the spiral is occasionally found embedded in the vaginal mucosa or the cervix uteri.

Effect on pregnancy

6.10 The incidence of abortion among women who have a device inserted while already pregnant or those who conceive later with an IUD *in situ* is higher than the rate of abortion in women conceiving after an unnoticed expulsion. It is impossible to determine what proportion of these abortions are intentionally induced and what proportion are due to the presence of the foreign body within the uterus.

6.11 If gestation continues with the device *in situ* the latter remains outside the amniotic sac, and is usually delivered with the membranes or attached to the placenta. In rare cases it may be expelled during pregnancy. If the IUD is retained *in utero* after delivery, and also after complete abortion, a decision concerning its removal must be made in the light of the circumstances of the case and the medical personnel available. Although there have been no detailed studies of children born following pregnancy with a device *in utero*, no case of congenital malformation or birth injury attributable to an IUD has so far been reported.

6.12 There is no evidence that IUDs can cause a conceptus to become implanted ectopically. They inhibit both tubal and uterine pregnancy, but they prevent the latter more effectively than the former. Among the few pregnancies that occur with the device *in situ* the ratio of ectopic to orthotopic pregnancies is therefore high.

Effect on later fertility

6.13 No adverse effect has been demonstrated. Women who have an IUD removed in order to conceive, usually do so promptly. Reported rates of conception are normal: about two-thirds achieve pregnancy in 6 months, about nine-tenths within one year.

7. CONTRAINDICATIONS

7.1 There appears to be increasing agreement that the only absolute contraindications to the use of IUDs are:

- (a) active pelvic inflammatory disease;
- (b) pregnancy, proven or suspected.

Uterine cancer

7.2 An established malignancy of the body or cervix of the uterus calls for immediate treatment—not for contraception.

7.3 Different considerations apply in the presence of suspicious exfoliative cytology (Papanicolaou smear Class III or higher). As indicated in section 4, there is no evidence that progress of a precancerous lesion is accelerated by an IUD. A good case can therefore be made for not withholding the protection afforded by a device, provided the patient can be kept under constant and close medical supervision. Should it not be possible to maintain such surveillance physicians may consider it more prudent not to insert a device or to remove one already fitted.

Fibroids (fibromyomata)

7.4 Large or submucous fibroids are not likely to be present in a fertile woman in need of conception control. Lesser ones need not interfere with insertion and retention of a device.

Abnormal bleeding

7.5 In all cases of metrorrhagia and other forms of abnormal uterine bleeding the cause must be established and appropriate treatment instituted before an IUD is inserted.

Cervicitis and erosion

7.6 Acute cervicitis and vaginitis must be treated before an IUD can be fitted. Chronic cervicitis and erosion are common in parous women and may occur in nulliparas; they do not constitute contraindications.

Trichomonas vaginalis and *Candida albicans*

7.7 The presence of these infections without clinical signs does not constitute a contraindication.

8. MANAGEMENT

In the management of women who wish to use intra-uterine contraception, many aspects require appraisal and clarification. The more important ones are listed below.

Parity

8.1 Nulliparous women have often been considered unsuitable for IUDs and consequently denied the use of this method. They are undoubtedly more difficult to fit, and may require some dilatation of the cervix and possibly an anaesthetic. These difficulties can be overcome, at least in selected cases, by using smaller devices together with sedation before attempting insertion and by administering adequate analgesics should uterine cramps develop. There are non-parous women who cannot be adequately protected by other contraceptive techniques and for whom IUDs may be the method of choice.

Size of uterus

8.2 Little appears to be known about the relation between body size and the size of the uterus, and the effect variations in the latter have upon the ease with which a given device can be inserted and tolerated. The earlier impression that women in South or East Asia require smaller IUDs than women in North America or Europe has not been confirmed by later experience. This problem should be studied systematically in the countries concerned.

Optimal time for insertion

8.3 In women with normal menstrual cycles, the best time for insertion is at or just after the end of a period. It must be realized, however, that this is not always possible, particularly in large clinics and public health programmes. The risk of inserting a device into a pregnant uterus is greatly increased during the second half of the cycle, and should always be kept in mind. It has, of course, to be weighed against the inconvenience and possible risk of impregnation as the result of postponing insertion until the next cycle. The inadvertent introduction of an IUD into the pregnant uterus is not necessarily followed by abortion.

8.4 In the case of post-partum insertion, a period of at least six weeks is considered appropriate by many investigators and has, in fact, been adopted as a fixed policy by some clinics and in national programmes. IUDs have, however, been inserted on the delivery table or within a few days after childbirth. These early insertions have been associated with high expulsion rates, and patients fitted in this way should be carefully checked at short intervals until the retention of the device appears assured.

8.5 After caesarean section, a delay of eight weeks is recommended. Caution is urged with the immediate post-abortum insertion of IUDs, because of the risk of infection.

Choice of device

8.6 As can be seen in the table on page 17, no single type of IUD is superior to all others in every respect. In choosing a device for general use it is important to consider not only the advantages but also the disadvantages of each type (pregnancies, expulsions, need for removals, pelvic inflammatory disease, perforations, etc.). It is preferable to select a device associated with a good all-round performance rather than one that is excellent in some features but seriously deficient in others.

Size of device

8.7 For each of the IUDs that have been studied intensively, the larger sizes have been found to be associated with significantly lower pregnancy and expulsion rates than the smaller sizes of the same type of device.

Clinical procedures

8.8 Desirable steps before any woman is fitted with a device include (a) an adequate medical history; (b) a cervical (Papanicolaou) smear; (c) a pelvic examination made by trained personnel and sufficiently thorough to exclude the principal contraindications to the use of IUDs (see section 7).

8.9 Women must be instructed and prepared for the likelihood of some bleeding and discomfort immediately after insertion and during the next one or two cycles. It must be ensured that they and, if necessary, physicians and paramedical personnel, know how to deal with such complaints. Apprehension concerning possible adverse effects, such as genital cancer and permanent sterility, should be anticipated and undue fears dispelled.

Use of paramedical personnel

8.10 It is preferable that the physical examination and insertion should be carried out by a qualified medical practitioner. It is, however, recognized

that rigid insistence on this would seriously diminish possibilities of the use of intra-uterine devices in many countries. Consequently, it is suggested that the modifications in fertility control programmes needed to permit the inclusion of intra-uterine contraception be decided by the Governments concerned in the light of national, regional and local circumstances. Considerations should include the possibility of the utilization of paramedical personnel for all aspects involved in application of the method, realizing that where such persons are employed, they should be properly instructed and supervised. In several countries field programmes are in progress to determine the feasibility of using paramedical personnel at all levels in the implementation of the method. Decisions on this matter can be made in the light of growing experience.

Loss of device

8.11 This is most likely to occur during menstruation. Pads or tampons should therefore be examined. Some women may also be taught to examine themselves vaginally and determine the presence and length of the thread attached to the loop or the cervical appendage of a spiral. It must, however, be realized that in various parts of the world women may be reluctant to carry out self-examinations, and the value of this procedure is doubtful. It is also not uncommon for rotation of the device within the uterus to cause retraction of the appendage. This makes detection of the device by inspection or palpation impossible.

Anaesthesia

8.12 Except for some nulliparous women, anaesthesia is not normally required. Most of the women requesting IUDs are multiparous, and have essentially normal pelvic organs. The cervix rarely needs to be dilated. Very nervous women may be given suitable premedication.

Follow-up examinations

8.13 In the absence of complaints, it is desirable that women should be examined one or two months after insertion to check that the device has not been expelled. Subsequently, they should be examined at approximately yearly intervals. The annual examination offers the opportunity to take a Papanicolaou smear; suspicious ones should be repeated and, if confirmed, a careful cervical biopsy performed.

8.14 If the appendage of a loop or spiral is not visible, the presence or absence of the device can usually be determined by sounding the uterus. An X-ray examination should rarely be necessary; if it is, it should preferably be done immediately after a menstrual period. It should be noted

that a single film does not always permit a distinction between the intra-uterine and extra-uterine location of a device.

Replacement of device

8.15 In the present state of knowledge, there seems to be no valid reason why an IUD should not be left *in utero*, at least until the menopause. This view is supported by 15 years' experience with stainless steel rings and 4 years' experience with the modern plastic devices. The above statements may require re-evaluation and modification during the coming years.

9. RESEARCH NEEDS

As indicated in the body of the report there are numerous aspects of intra-uterine contraception that require clarification and additional research.

The following items are selected from the many discussed by the Scientific Group as being in particular need of study. The references in parenthesis relate to the relevant sections of the report.

9.1 Laboratory research on the effects of IUDs in sub-human primates and lower mammals

- (a) Ovulation and fertilization mechanisms (3.7, 3.16-3.20).
- (b) Ovum and sperm transport and sperm capacitation, particularly in primates and ruminants (3.6, 3.7)
- (c) Tubal and uterine motility, throughout the menstrual cycle (3.9-3.11)
- (d) Decidualization processes, particularly in rodents and primates (3.26-3.28)
- (e) Histochemistry, vascularization and neurogenic stimuli of the female reproductive tract (3.29, 3.32-3.34)
- (f) Qualitative and quantitative changes in intraluminal secretions (3.21).

9.2 Clinical research on the effects of IUDs in women

(g) Recovery, at elective hysterectomy, of ova at the most suitable stages of the menstrual cycle and determination of their fertilization (or fertilizability) and normal development; sperm transport and capacitation (3.8).

- (h) Motility patterns of the Fallopian tubes and uterus (3.9-3.11).
- (i) Tubal patency and the tubo-uterine sphincter (3.3-3.5).
- (j) Chemistry and enzymology of the tubal and uterine fluids (3.21).

(k) Establishment and abolition of the contraceptive effect following insertion or removal of IUDs at accurately known stages of the cycle (3.4, 3.5, 6.13).

9.3 *Bio-statistical and allied studies*

(l) Comparative evaluation, preferably under "double-blind" conditions, of rates of pregnancy, expulsion, removals, and pelvic inflammatory disease (P.I.D.) after first insertion of IUDs (5).

(m) Systematic and controlled evaluation of pregnancies with device *in situ*, including the incidence of congenital malformations and subsequent child development (6.10-6.13).

(n) Study of menopausal women following long-continued use of an IUD or deliberate insertion of a device in volunteers approaching the menopause (8.15).

(o) Long-term evaluation (15-20 years or longer) with reference to endometrial and cervical cancer and exfoliative cytology, using adequate controls (4.5-4.11).

(p) Comparative studies, in different parts of the world, of blood factors, state of nutrition, etc., before and after insertion of an IUD (6.1, 6.2).

9.4 *Clinical aspects*

(q) Systematic studies of women who have not conceived (nulligravid) or who have conceived but not delivered a child (nulliparous) before insertion of an IUD (8.1).

(r) Treatment of side-effects, especially bleeding, without removal of IUD (6).

(s) Systematic studies of women following insertion of a device immediately post-partum or during the first few days after delivery and post-abortion (8.3-8.5).

9.5 *Research on devices*

(t) Study of new devices with regard to design and consistency; physical changes in IUDs after long use (2.3-2.6, 8.6, 8.7).

(u) Development of prepacked devices and disposable inserters.

(v) Comparative studies, in different parts of the world, of optimal size of devices, and of criteria used in selection (8.6, 8.7).

(w) Detection of IUDs *in utero* other than by X-rays (8.11, 8.13).

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