Copper IUDs
Performance To Date

For the last ten years, intrauterine devices have been used with varying success in clinical practice and in family planning programs throughout the world.

In theory, the IUD is close to an ideal contraceptive method. Although it requires a clinical procedure, the IUD is not related to coitus, usually requires only a single insertion, rarely causes systemic hazards, and provides long-term protection against pregnancy. In practice, the first generation of IUDs posed problems of expulsion, accidental pregnancy, perforation, infection, pain, and bleeding that made them less than ideal for many women. During the first 12 months after insertion, for example, about one-fourth of all women using the Lippes loop experience involuntary expulsion of the device, accidental pregnancy with the device in situ, or removal for excess bleeding or pain.

A decade of international research has focused therefore on improving IUD performance by reducing the incidence of the three most pertinent events in IUD failure. Buttressed by rigorous statistical analysis, IUD research and development has concentrated on three general areas: (1) improved techniques and training for insertion; (2) optimal size and configuration of the device itself; and (3) addition of bioactive substances to reinforce the contraceptive effect or reduce bleeding and pain.

Some progress has been made in the first area. Better insertion techniques plus improved training, more experience, and better patient selection have undoubtedly reduced the incidence of perforation and infection. In the second area—IUD design—little progress has been documented to date despite an amazing array of new IUD sizes, shapes, surface areas, and other physical dimensions. There is some hope, however, that a better theoretical understanding of how IUDs work may soon lead to better devices. Those developments will be covered in detail in a forthcoming report.

In the third area—bioactive devices—research on the addition of copper or the hormone progesterone has now been underway for about five years. The current status of research and development with copper IUDs is reviewed in this report.

Of all the new possibilities, the longest in development, the most rigorously tested, and already the best publicized through collaborative international studies is the copper IUD. A copper IUD resembles other IUDs except that a copper wire is twisted around the plastic device, thus providing a surface area from which copper ions are released.
Dr. Irving Sivin, of the Population Council, has demonstrated that the antifertility effect of the copper combined with continuous release within the uterus. The three configurations that have been tested with copper are the T, the 7 and the Lippes loop. Since Zipper demonstrated the antifertility effects of copper in 1969 (55), the advantages of adding copper have been thoroughly explored.

Early reports on copper IUDs—after six months, nine months and one year of use—were optimistic. It appeared that the antifertility effect of the copper combined with the smaller surface area and uterine-conforming shape of the T or the 7 might indeed result in fewer expulsions and removals for pain and bleeding as well as in fewer pregnancies. Measured against the most widely accepted inert device, the Lippes loop, the first results were promising.

As often occurs with the new devices, however, later data based on an additional year of experience with the copper T suggest that for multiparous women the present models of copper IUDs do not appear to be an important improvement over the inert Lippes loop. Two-year cumulative gross event rates show that although removals for bleeding and pain are slightly lower, pregnancies and expulsions are in the same range for both devices (see Fig. 1 and Table 1).

For young women who have never borne children, the copper T and 7 may offer some advantage over the Lippes loop. Since the inert IUDs have rarely been used in nulliparous women, it is difficult to find a proven basis of comparison, but some one-year studies show rates of pregnancy, expulsion, and removal for bleeding and pain in nulliparas that are at least comparable to the rates in multiparas with inert devices. The copper devices may also be somewhat easier to insert and produce less bleeding than the loop.

Nevertheless some problems remain. Unlike an ordinary IUD which is left in the uterus indefinitely, the copper IUD may need to be replaced when the copper is exhausted, usually after about two years, in order to retain contraceptive efficacy. Dr. Irving Sivin, of the Population Council, suggests that this time limitation precludes the use of copper 200 IUDs “as a preferred device” in most family planning programs where subsequent medical follow-up may be difficult (39).

Further questions can only be answered by additional research. For example,

- What is the ideal IUD configuration to which any biologically active component might be attached?
- What is the optimal quantity, form, and location for copper to be added to the inert carrier?
- Can a copper IUD be used over long periods of time without toxic or other untoward effects?
- If pregnancy occurs and is continued, what effects would copper have on the fetus?
- Can the release of copper ions be sustained at an adequate level beyond two years?
- Can the increased menstrual flow sometimes associated with IUDs—though less so with the copper models—be still further reduced?

Since few of the copper IUDs have been in place longer than two years, it is too soon to know how well they will work over the long run.

Even with the addition of copper, age and parity remain major determinants of IUD effectiveness. Young, low parity women have much higher rates of expulsion and pregnancy than older, high parity women with all devices in use today.

The challenge of IUD development is that improving one parameter of IUD performance as, for example, reducing pregnancies by a larger, more rigid device may adversely affect another parameter by increasing the number of removals for bleeding and pain. An optimal biologically active device might therefore either combine an inert device which minimizes pregnancy with an active ingredient that reduces expulsions, pain, and bleeding or combine an inert device which minimizes expulsions, pain, bleeding with an active ingredient that reduces pregnancies.

The copper IUDs, which belong in the latter category, are useful especially for younger nulliparous women. They have also made a substantial contribution toward better understanding of IUD performance. But they have not, as was once hoped, eliminated the continuing IUD problems of accidental pregnancy, expulsion, or removal for bleeding and pain. For general family planning program use with parous women, the Lippes loop remains the standard.

HISTORY

Modern scientific interest in copper as a contraceptive agent can be traced to Dr. Jaime Zipper and his co-workers in Chile. Zipper demonstrated in 1969 that a small length of copper wire inserted within one horn of the uterus of a rabbit dramatically reduced the number of implantation sites in that horn as compared with the control horn (55) (see Fig. 2). Zipper’s animal studies were followed by clinical trials among Chilean women using copper wire twined around the stem of a plastic T. Whereas without
Table 1—Comparison of Expulsion, Pregnancy, and Removal for Bleeding and Pain in Parous Women with T Cu 200 and Lippes Loop D, One- and Two-Year Gross Rates

<table>
<thead>
<tr>
<th>Type of IUD</th>
<th>Number of Insertions</th>
<th>Woman Months of Use</th>
<th>Expulsions Rate</th>
<th>Pregnancy Rate</th>
<th>Removels</th>
<th>Continuation Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>One-Year Rates</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T Cu 200</td>
<td>9.8</td>
<td>12.1</td>
<td>3.2</td>
<td>8.8</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Lippes loop D</td>
<td>3.2</td>
<td>3.2</td>
<td>8.8</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Two-Year Rates</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T Cu 200</td>
<td>6,801</td>
<td>52,133</td>
<td>13.0</td>
<td>6.1</td>
<td>17.1</td>
<td>7.5</td>
</tr>
<tr>
<td>Lippes loop D</td>
<td>7,419</td>
<td>105,199</td>
<td>14.3</td>
<td>5.5</td>
<td>20.5</td>
<td>6.3</td>
</tr>
</tbody>
</table>

Fig. 1. Comparison of Expulsion, Pregnancy and Removal for Bleeding and Pain in Parous Women with T Cu 200 and Lippes Loop D, One- and Two-Year Gross Rates, Age-parity Adjusted.

NOTE: The data in Fig. 1 and Table 1 were provided in November 1973 by the Cooperative Statistical Program of the Population Council and were presented in part by Dr. Christopher Tietze at the Battelle IUD Workshop in October 1973 (60). Data for the T Cu 200 have been pooled from a number of Western Hemisphere clinics. Data for the loop D are taken primarily from the Ninth Report of the Cooperative Statistical Program (49) and have been adjusted for age and parity of the copper T acceptors. (Graph by Roger Bernard, M.D., The International Fertility Research Program, University of North Carolina, USA.)
copper the T shape produced an unacceptably high pregnancy rate of 18 per 100 woman-years, the addition of 200 sq mm of exposed copper reduced the pregnancy rates to approximately one per 100 woman-years (57,58). Overall results were so favorable that by 1970 plans were underway for international trials of the copper T.

As of late 1973, a number of reports suggest that copper IUDs—either in the T or 7 shape—are effective devices (10, 28, 29, 32, 38, 42, 43, 48, 52). Dr. Jack Lippes is adding copper to the loop that bears his name and experimenting with the amount and placement of the copper (28).

Copper IUDs are now being tested in three shapes, the original T, developed by Dr. Howard Tatum of the Population Council, the copper 7, which is patented and manufactured by G.D. Searle and Co.; and the copper Lippes loop, still being perfected by Dr. Lippes (see Fig. 3). The British Committee on Safety of Medicines has already approved the copper 7, and the United States Food and Drug Administration may also soon grant official approval for distribution of copper 7 and copper T IUDs to physicians, thus ending the present experimental status of the device.

**DESCRIPTION**

Regardless of shape, copper IUDs are made of polyethylene plastic to which barium sulfate is added to make them radio-opaque. The horizontal stem of the T-shaped device is 32 mm in length and the vertical arm 36 mm in length; the surface area is 3.15 sq cm. The 7-shaped device is 35.9 mm long and 28 mm wide. At the junction of the upper and lower arms of the 7 is a small rounded cap which seals the two limbs together and thus helps prevent uterine perforation (see Fig. 3).

The copper wire is usually twined around the vertical arm of the T or 7 and not the horizontal arms (see Fig. 3). With the serpentine Lippes loop, copper is added on the upper horizontal bars (see Fig. 3). Most published reports to date deal with Cu 200 devices where the 200 denotes a surface area of 200 sq mm of copper (Cu).

**New Application Techniques**

Although initially copper wire was simply wound around plastic IUDs, Tatum suggested a new technique in fabricating the copper Lippes loop. Lippes describes it as follows:

> Copper was applied ... by placing copper tubing in the mold before the melted plastic was injected into it. Upon completion of the mold cycle, Loop A had sleeves of copper tubing on the upper ... three arms which totalled ... 200 sq mm of surface area of copper (29).

This method is currently preferred for adding copper to the T also, although with only one exception, all published results deal with wire entwined devices. The great advantage of the “sleeve” technique is that the pharmacologically active metal will last longer. The single long sleeves, however, have been found too rigid. To overcome this, Tatum and Lippes are now experimenting with multiple small-sleeve rings of copper interspersed between equal rings of plastic. Further testing will determine whether using wire on the vertical arms, and small sleeves on the horizontal arms of the T will prove to be the best combination.

Attempts to impregnate devices like the T with metallic copper, copper salts, such as copper carbonate or copper sulfate, have thus far not been successful because the copper is not released from polyethylene and therefore has no effect.

**Amount of Copper Added**

As testing has continued, ever larger amounts of copper have been added to the IUDs. In 1971 Zipper and co-workers demonstrated that 30 sq mm of copper surface resulted in a pregnancy rate of 4.9 per 100 woman-years; 120 sq mm of copper reduced the rate to 2.0 (57). Several double-blind studies, directly comparing Cu 200 devices with either Cu 120 or Cu 135, showed that the larger quantities of copper reduced the pregnancy rate (10,28,57) (see Fig. 4). Extrapolation from this data suggests that adding even more than 200 sq mm of copper might reduce pregnancies still further.

Preliminary results of a nine-month study conducted during the last year appear to corroborate the value of adding...
more copper. With Cu 250 and Cu 300 devices, Zipper found that the pregnancy rates were reduced to near zero (56) (see Table 2). Furthermore, increasing the copper did not increase the incidence of bleeding, pain, or expulsion.

A double-blind study comparing T Cu 200 and T Cu 300 devices which was reported by Dr. Christopher Tietze in October 1973 also showed a slight improvement in pregnancy rates and other pertinent events using the T Cu 300 (see Fig. 5) (60). However, there is no conclusive evidence on this point as yet. Tatum, Zipper, and Mishell are now conducting further studies with T Cu 380 devices. It is possible that more copper may improve contraceptive effectiveness. Additional copper in the form of collars or sleeves may also extend the life of these devices as long as 10 years (18).

Mode of Action

The contraceptive effect of copper apparently results from the release of copper ions into the uterine cavity where they influence various biochemical reactions. These reactions are limited to local changes in the intrauterine environment and little or no copper is found systemically.

Extensive research on both animals and humans suggests that the effects of the copper ion are many and complex. Most likely, the contraceptive action is due to cationic antagonism specifically related to zinc (21,37). One of the most important zinc-containing enzymes in the female reproductive tract is carbonic anhydrase. Copper may compete with zinc and inhibit the carbonic anhydrase reaction, thus resisting implantation. Numerous enzyme systems, however, including that of alkaline phosphatase, may also be implicated (7,13,14,35).

Other recent evidence indicates that copper ions interfere with cellular DNA in the endometrium (15), with glycogen metabolism (38), and with the normal rate of endogenous estrogen uptake by the uterine mucosa (53). Contraceptive effect may be enhanced by one or more of these actions. It appears unlikely that inhibition of sperm motility by copper is an important factor (19). Other scientists, including for example Dr. E. Parr, noted the induction of

Fig. 3. Three copper IUDs now being tested are the copper T on the left, the copper 7 in the center, and the copper Lippes loop on the right. Each of these devices has a surface area of 200 sq mm of copper.

Mode of Action

The contraceptive effect of copper apparently results from the release of copper ions into the uterine cavity where they influence various biochemical reactions. These reactions are limited to local changes in the intrauterine environment and little or no copper is found systemically.

Extensive research on both animals and humans suggests that the effects of the copper ion are many and complex. Most likely, the contraceptive action is due to cationic antagonism specifically related to zinc (21,37). One of the most important zinc-containing enzymes in the female reproductive tract is carbonic anhydrase. Copper may compete with zinc and inhibit the carbonic anhydrase reaction, thus resisting implantation. Numerous enzyme systems, however, including that of alkaline phosphatase, may also be implicated (7,13,14,35).

Other recent evidence indicates that copper ions interfere with cellular DNA in the endometrium (15), with glycogen metabolism (38), and with the normal rate of endogenous estrogen uptake by the uterine mucosa (53). Contraceptive effect may be enhanced by one or more of these actions. It appears unlikely that inhibition of sperm motility by copper is an important factor (19). Other scientists, including for example Dr. E. Parr, noted the induction of

Fig. 4. The antifertility effects of copper are greater with a surface area of 200 sq mm than with lesser areas and may increase still further with additional amounts of copper (44). (Courtesy of Howard Tatum, M.D., The Population Council, New York, USA.)
Table 2—Expulsion, Pregnancy, Removal and Continuation Rates of Copper IUDs in Early Clinical Studies, 6 to 21 months, 1971-1973

<table>
<thead>
<tr>
<th>Author and Date</th>
<th>Reference Number</th>
<th>Country</th>
<th>Type of IUD</th>
<th>Number of Insertions</th>
<th>Women Months of Use</th>
<th>Expulsion Rate</th>
<th>Pregnancy Rate</th>
<th>Removal Rate</th>
<th>Bleeding Rate</th>
<th>Pain Rate</th>
<th>Continuation Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zipper 1971</td>
<td>57</td>
<td>Chile</td>
<td>T Cu 200</td>
<td>233</td>
<td>872</td>
<td>1.2</td>
<td>0.0</td>
<td>0.8</td>
<td>0.0</td>
<td>98</td>
<td></td>
</tr>
<tr>
<td>Tatum 1972</td>
<td>43</td>
<td>USA, Canada</td>
<td>T Cu 200</td>
<td>233</td>
<td>774</td>
<td>7.2</td>
<td>2.2</td>
<td>5.6</td>
<td>77</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sivin 1973</td>
<td>39</td>
<td>Colombia</td>
<td>T Cu 200</td>
<td>945</td>
<td>5,636</td>
<td>3.5</td>
<td>1.8</td>
<td>4.1</td>
<td>2.7</td>
<td>82</td>
<td></td>
</tr>
<tr>
<td>Lewit 1973</td>
<td>26</td>
<td>USA</td>
<td>T Cu 200</td>
<td>1,996</td>
<td>26,760</td>
<td>8.3</td>
<td>2.2</td>
<td>6.4</td>
<td>76</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hong Kong FPA 1972</td>
<td>16</td>
<td>Hong Kong</td>
<td>T Cu 200</td>
<td>100</td>
<td>1,617</td>
<td>6.7</td>
<td>1.2</td>
<td>1.7</td>
<td>0.4</td>
<td>5.7</td>
<td>88</td>
</tr>
<tr>
<td>Newton 1972</td>
<td>32</td>
<td>England</td>
<td>T Cu 200</td>
<td>516</td>
<td>4,127</td>
<td>3.1</td>
<td>2.2</td>
<td>1.4</td>
<td>0.2</td>
<td>91</td>
<td></td>
</tr>
<tr>
<td>Zipper 1972</td>
<td>56</td>
<td>Chile</td>
<td>T Cu 200</td>
<td>516</td>
<td>1,197</td>
<td>2.1</td>
<td>1.1</td>
<td>3.0</td>
<td>0.2</td>
<td>91d</td>
<td></td>
</tr>
<tr>
<td>Zipper 1972</td>
<td>56</td>
<td>Chile</td>
<td>T Cu 200</td>
<td>516</td>
<td>4,127</td>
<td>3.1</td>
<td>2.2</td>
<td>1.4</td>
<td>0.2</td>
<td>91d</td>
<td></td>
</tr>
<tr>
<td>Gibor 1973</td>
<td>39</td>
<td>USA</td>
<td>Lippes loop</td>
<td>333</td>
<td>1,793</td>
<td>5.0</td>
<td>0.9</td>
<td>9.9</td>
<td>81e</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lippes 1973</td>
<td>39</td>
<td>USA</td>
<td>Lippes loop</td>
<td>144</td>
<td>1,793</td>
<td>5.0</td>
<td>2.9</td>
<td>0.7</td>
<td>9.4</td>
<td>86a</td>
<td></td>
</tr>
</tbody>
</table>

NOTE: Net cumulative closure and continuation rates are given per 100 women after 12 months of use except where otherwise stated. In some cases figures have been rounded off to the nearest decimal point.

a—six months of use
b—nine months of use
c—plus other medical causes
d—excludes patients whose devices were removed for planned pregnancy; thus, these figures are higher than and not directly comparable with continuation rates quoted from other sources
e—twenty-one months of use

For singularity, data on removals for planned pregnancy, for other personal reasons and for medical reasons other than pain or bleeding are omitted from this table. Therefore, the sum of closure rates for expulsions, pregnancies, and removals, for bleeding and pain only, does not reflect true rate of discontinuation.

an inflammatory response similar to that provoked by inert IUDs (60).

**INSERTION AND REMOVAL**

Insertion procedures for copper and inert IUDs are basically similar. The ideal time for insertion is during the last day or two of the menses. At that time, the patient is rarely if ever pregnant; the cervix is softer and more open, thus reducing discomfort. The small amount of bleeding which sometimes accompanies insertion is not obvious to the patient. With postpartum patients, many physicians wait 4-8 weeks after delivery to avoid higher rates of expulsion and perforation.

**Packaging of Device and Inserter**

Copper IUDs, like other IUDs, may either be packaged in sterile containers together with individual inserters and plungers, or be bulk-packed in nonsterile condition. Instructions for insertion are usually enclosed. Sterile containers with inserter invariably cost more but are more convenient and safer to use. During the current investigational period of use, prepacked sterile units of the copper 7 and the copper T have been used (see Fig. 6).

Evidence suggests that should bulk-packed units be used, sterilizing agents (such as iodine) would have no deleterious effects on the copper.

**Techniques of Insertion**

In general, the smaller and more flexible the device, the easier the insertion, particularly for nulliparous women. The maximum outside diameter of the folded 7 is 2 mm which is less than that of the T. Inserting a 7 is thus easier than inserting a T, which, in turn, is easier to insert than a Lippes loop (10,23).
The insertion procedure for the copper T is described as follows:

Following physical examination, a tenaculum was attached to the cervix and a uterine sound inserted into the endometrial cavity. The sound was left in the uterine canal while the IUD was loaded in a retrograde fashion by flexing the horizontal arms until they touched the vertical copper-bearing arm. The sound was then removed from the uterus and the IUD properly positioned in the uterine fundus by placing the loaded inserter into the uterus . . . (30).

The copper T insertion technique is different than that for most plain IUDs, such as the Lippes loop. The device within the insertion tube is placed high in the fundal cavity and then the tube is withdrawn slightly over the plunger. This allows the lateral arms to extend free of the insertion tube. The plunger and the tube are then removed, leaving the T in the uterine cavity. Thus the insertion is made by a withdrawal technique rather than a forcing out* (see Fig. 7).

This “withdrawal” technique is intended to minimize the likelihood of perforating the uterus. The Searle Company also is advising this “withdrawal” technique in inserting a copper 7 (see Fig. 8). The technique was first applied with the Majzlin spring and M device in the late 1960s.**

Insertion of the copper Lippes loop is identical with that of the inert Lippes loop.

After insertion, patients are taught how to feel the nylon threads in the vagina, are instructed to call the clinic if any problems arise, and are given appointments to return.

If recommended procedures are followed, the insertion of a copper IUD is generally easy and painless. Prior to insertion, anesthesia or analgesics are rarely given. For postinsertion cramps, less than 10 percent of 471 copper T acceptors required mild analgesics such as aspirin (30). In a study of 342 copper 7 acceptors, 10 percent had postinsertion uterine cramps which lasted less than five minutes, and two percent had cramps which lasted five to 10 minutes; the rest experienced no insertion pain at all (32).

In another study comprising 3,457 multiparous copper 7 acceptors, approximately seven percent had difficult insertions (cramps, bleeding, fainting, and other reactions) (59). Of this seven percent, 1.9 percent suffered moderate reactions and 0.3 percent suffered severe reactions; the rest had slight reactions.

*Personal communication, Howard Tatum, M.D., July 26, 1973.
** Personal communication, Roger Bernard, M.D., November 12, 1973.
Step 1
Do not bend the T until immediately before insertion.
Fold the arms of T into inserter tube can be accomplished in partially opened package, thus preserving sterility. Open package halfway. Place package on flat surface. Place thumb and index finger on top of package at ends of the horizontal arms. Push inserter tube against arms of T as indicated by arrow in Fig. 1 to start arms folding. Complete the bending by bringing thumb and index finger together while using the other hand to maneuver the inserter tube to pick-up the arms of the T (Fig. 2). Insert them no further than 1/4 inch (6mm).

Introduce the plunger into the inserter tube from the bottom alongside the threads until it touches the bottom of the T.

Step 2
Adjust the movable flange so that it indicates the depth to which the device should be inserted and the direction in which the arms of the T will open. Introduce the loaded inserter through the cervical canal and upwards until the T lies near the top of the fundus cavity.

Step 3
Withdraw the outer sheath more than 1/2 inch while the plunger is not permitted to move. This releases the arms of the T.

Step 4
Withdraw the plunger while holding the outer sheath in place.

Step 5
Withdraw outer sheath.

Difficult insertions occur more frequently with nulliparous than with multiparous IUD acceptors. Of 1,704 nulliparous copper T acceptors, approximately 14 percent had difficult insertions (59).

Sovera and Goldsmith recommend avoiding sexual intercourse for 24 hours after insertion and making a follow-up visit to the physician 4-6 weeks after insertion. Most problems occur during this initial period (41).

Postabortal Insertion
With abortion now legal for 58 percent of the world population, more and more practitioners are now inserting IUDs immediately after such operations. Copper IUDs inserted while the patient is still under anesthesia are well retained and do not add to postabortal complications, according to a recent Swedish study of two matched groups of patients who had first trimester legal abortions (33). The Swedish investigators suggest that expulsion or removal for medical reasons may be somewhat lower with the copper T than with the Lippes loop (33).

Problems of Insertion
Improper insertion may lead to expulsion of the device, to ineffective contraceptive action, or to uterine perforation. The frequency of such complications has declined in recent years for all IUDs as insertion techniques have improved. Although insertion has not been a major problem with copper IUDs to date, nevertheless, for all three models, high placement of the device in the fundus is essential.

In a U.S. cooperative study involving nine clinics, for example, the results from one clinic were quite out of line with those of the other eight. The explanation was offered that in this clinic, insertion techniques were faulty. The copper T was inserted too low in the uterine cavity, thus causing an expulsion rate twice as high as that found in the other eight clinics and consequently, a much higher pregnancy rate. Net cumulative pregnancy rates of 11.8 per 100 users were reported for this one clinic in comparison with 0.3 for the other eight (43).

In another study, in which expulsion rates were exceptionally low, Lippes attributes his success in part to a different insertion technique which emphasizes careful placement of the device high in the uterine fundus (27).

With copper IUDs such as the 7 and the T, the incidence of uterine perforation at time of insertion is low. As with all IUDs, the perforation rate varies according to the experience and skill of the professional. In contrast to what must surely have been an all-time high perforation rate—one per 100 insertions with the now outmoded Birnberg bow (17)—no uterine perforations at all occurred in more than 4,000 insertions of copper T IUDs (47). The latest tabulations indicate a perforation rate of one per 20,000 insertions for the copper T device.

In the nine-clinic study mentioned above, three cervical perforations were reported in a series of 945 patients (43). It is believed that these occurred because the inserter was not introduced far enough into the uterus (25). Instead of
entering the uterine cavity, the two arms of the T perforated the proximal portion of the cervical canal. A new insertion technique has been developed by the Population Council to remedy this situation (see Fig. 7).

Removal
Removal of copper IUDs is in most cases not difficult. The tails of the IUD are grasped with an appropriate forceps and pulled with steady force. Dr. Lise Fortier of Canada has now removed about 150 copper T devices two years after insertion and all devices came out easily (9).

**EFFECTIVENESS**

Throughout the 1960s, the effectiveness of IUDs has been measured in terms of continuation rates, that is, how long an IUD remains in situ without being involuntarily expelled, without a pregnancy occurring, or without voluntary removal for medical or personal reasons. The life table method, originally used to calculate life expectancy, was modified to assess the rates of IUD expulsion, pregnancy, and removal over differing periods of time. This technique allows information to be pooled even though individuals are constantly entering or leaving the studied population of IUD acceptors. Also it permits information gathered throughout the world to be compared on a uniform basis.

For a comprehensive evaluation of copper IUDs and inert Lippes loops, gross and net event rates from double-blind studies and also from data adjusted for age and parity are desirable. Gross rates record the incidence of each event—expulsion, pregnancy or removal—without regard to other intervening events, but gross rates cannot be totalled to

| Step 1. Determine the axis of and sound the uterus. |
| Step 2. Load the Cu—7 in the tube until only the mushroom tip protrudes. The end of the plunger should touch the Cu—7. **(Do not leave it in the tube longer than two minutes or the plastic will lose its memory.)** |
| Step 3. Set the cervical stop at the depth the uterus was sounded and remove the clip holding the thread. |
| Step 4. Gently slide the tube through the cervical canal until the fundus is felt. The cervical stop should be at the cervix at this time. |
| **Note:** If resistance is felt before the fundus is reached, DO NOT FORCE; withdraw and reinsert. |
| Step 5. Holding the plunger handle firmly, slide the tube back over the rod until it reaches the handle, depositing the Cu—7 in the uterine cavity. |
| Step 6. Remove the insertion instrument. |
| Step 7. Pull about one inch of excess thread from the cervical canal and cut it approximately two inches from the external os. |

![Fig. 8. Details of insertion technique for the copper 7. (Courtesy of G.D. Searle and Co., Chicago, Illinois, USA.)](image-url)
achieve an overall continuation rate. Net rates may somewhat overemphasize those events such as expulsion which tend to occur soon after insertion but net rates are necessary to calculate the continuation rate. Net rates are given in this report except where gross rates are specifically mentioned.

Pregnancy Rates

No IUD is 100 percent effective. Accidental pregnancies do occur with all models. The number of pregnancies is related to the type of device used. With copper IUDs, pregnancy rates range from zero to 3.0 per 100 women after one year of use, as expressed in the net cumulative rate calculated by the life table method (see Table 2). In the largest study, comprising 26,760 woman-months of use of the copper T, the net cumulative pregnancy rate was 2.2 per 100 women after one year, and 3.5 after two years (26). These figures are not markedly different from pregnancy rates found with some inert IUDs.

The pregnancy rate for Lippes loop A with 200 sq mm of copper added is not statistically different from that of the T Cu 200 (28,29). Thus, Lippes' figure for the pregnancy rate for copper loop A 200 is 0.7 (S.E. ± 0.6) and for that of T Cu 200 is 0.8 (S.E. ± 0.3) after six months of use (28).

Copper T devices have been compared directly with inert Lippes loops on the basis of a common protocol to evaluate their efficacy. Controlled, double-blind studies (which reduce the possibility of the experimenter's personal bias) were sponsored by the Population Council in the United States and Canada. The Lippes loop was selected for comparison with the new copper T because the loop has been the most popular, best-tested, and best-accepted of all IUDs throughout the past decade. In some clinics, a roll of dice or use of a random table of numbers determined which IUD would be used for each patient. In other clinics, all women coming to the clinic on a particular day were given the same device.

Reports by Tatum in 1972 and a subsequent report by Lewit in 1973, both of whom combined US and Canadian data, showed a pregnancy rate of 2.2 for the T Cu 200. For the inert Lippes loop, Tatum found a 3.0 rate, and Lewit a 2.6 rate (26,43).

Another Population Council study was conducted in Colombia, Iran, Korea, Taiwan and Thailand (39). These trials were not double-blind studies, but in a meticulous statistical analysis, Irving Sivin concluded from them that "the net 12-month cumulative pregnancy rates for copper T users are either consistent with or below those for loop users." The 12-month data indicated that the range of pregnancy rates for the copper T was 0.3 to 3.2, whereas the range for the Lippes loop was 1.3 to 4.5. Although Sivin noted that reporting errors may account for some of the statistically significant differences, his review demonstrated that the pregnancy rates for the copper IUDs are among the lowest encountered for any IUD, or indeed for any other contraceptive.

Expulsion

Expulsion of the device, especially in younger, low parity women, has heretofore been a major problem with non-copper IUDs. At best, expulsion means another trip to the clinic; at worst, it means unwanted pregnancy. The rate of expulsions varies according to the type of device used. Population Council studies by Lewit and Tatum show that after one year, copper T devices were better retained than the inert Lippes loop (26,43) (see Table 3). After two years, however, gross rates of expulsion in age-adjusted data for parous women differed very little—14.3 for the loop, 13.0 for the T Cu 200 (see Fig. 1).

The most marked difference in expulsion rates between the copper T and the non-copper inert Lippes loop was documented by Lippes himself. He achieved remarkably low expulsion rates for both devices but the copper T was expelled less often than the inert loop—1.3 (S.E. ± 0.4) closure rate for expulsion per 100 woman-years of use compared with 2.9 (S.E. ± 1.2) for the inert Loop D (28) (see Table 3). Pooled data from other clinics, although showing more expulsions for both devices, showed a closure rate for expulsions of 7.3 for the copper T, compared with 13.0 for the loop (43) (see Table 3).

Reporting on the cooperative Asian study, Sivin (39) found no statistically significant differences in rates of expulsion between the two devices in Colombia or Iran, but in Taiwan, Korea, and Thailand he noted that expulsion rates among T acceptors were lower than the corresponding rates among loop users.

In further well-controlled comparative studies of two copper devices, it was found that the Lippes Loop A with 200 sq mm of copper added is more likely to be expelled than the T Cu 200 (28). After six months of use, Lippes found that 2.9 per 100 women had expelled the copper loop A whereas only 1.3 per 100 women had expelled the T Copper 200 (28). After 12 months of use, Lippes concluded that the difference in expulsion rates between these two copper devices was statistically significant (29).

The age of the woman may affect the expulsion rate even more than parity (26). Girls between the ages of 15-19 have an expulsion rate of 15.0 per 100 copper T users, but the rate falls to 8.5 and 8.7 for women between the ages of 20-24 and 25-29. For older women, the rate is even lower: 6.0 for women 30-34 and 3.1 for women 35-39.
Table 3—Comparison of Expulsion, Pregnancy, Removal, and Continuation Rates with Copper IUDs and Inert Lippes Loops D, 1972-1973

<table>
<thead>
<tr>
<th>Author and Date</th>
<th>Reference Number</th>
<th>Country</th>
<th>Type of IUD</th>
<th>Number of Insertions</th>
<th>Woman Months of Use</th>
<th>Expulsion Rate</th>
<th>Pregnancy Rate</th>
<th>Removal Rate 'Bleeding and Pain</th>
<th>Continuation Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fortier 1973</td>
<td>10</td>
<td>Canada</td>
<td>T Cu 200</td>
<td>250</td>
<td>1,504^a</td>
<td>7.1^a</td>
<td>1.9^a</td>
<td>9.2^a</td>
<td>76</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>inert Lippes loop D</td>
<td>60</td>
<td>1,021</td>
<td>0</td>
<td>22.0</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>Lewit 1973</td>
<td>26</td>
<td>USA</td>
<td>T Cu 200</td>
<td>4,127</td>
<td>26,760</td>
<td>8.3</td>
<td>2.2</td>
<td>6.4</td>
<td>76</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>inert Lippes loop D</td>
<td>7,533</td>
<td>86,777</td>
<td>10.8</td>
<td>2.6</td>
<td>11.8</td>
<td></td>
</tr>
<tr>
<td>Lippes 1972</td>
<td>28</td>
<td>USA</td>
<td>T Cu 200</td>
<td>820</td>
<td>4,322^b</td>
<td>1.3^b</td>
<td>0.8^b</td>
<td>5.6^b</td>
<td>91^b,c</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>inert Lippes loop D</td>
<td>175</td>
<td>975^b</td>
<td>2.9^b</td>
<td>0.6^b</td>
<td>9.2^b</td>
<td>87^b,c</td>
</tr>
<tr>
<td>Tatum 1972</td>
<td>43</td>
<td>USA</td>
<td>T Cu 200</td>
<td>945</td>
<td>7,740</td>
<td>7.2</td>
<td>2.2</td>
<td>6.6</td>
<td>77</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>inert Lippes loop D</td>
<td>750</td>
<td>5,760</td>
<td>13.0</td>
<td>3.0</td>
<td>9.0</td>
<td></td>
</tr>
</tbody>
</table>

a—nine months of use  
b—six months of use  
c—excludes patients whose devices were removed for planned pregnancy and personal reasons; thus, these figures are higher than, and not comparable with continuation rates quoted from other sources.

NOTE: Net cumulative closure and continuation rates are given per 100 women after 12 months use except where otherwise indicated. In some cases figures have been rounded off to the nearest decimal point.

For simplicity, data on removals for planned pregnancy, or other personal reasons, and for medical reasons other than pain or bleeding are omitted from this table. Therefore, the sum of closure rates for expulsions, pregnancies, and removals, for bleeding and pain only, does not reflect true rate of discontinuation.

**Bleeding**

As with other IUDs, increased bleeding remains the problem most frequently associated with copper IUD use. With the addition of copper, the incidence of spotting, or of profuse or painful menstruation has been reduced but by no means eliminated.

Fortier, for example, reported that 25 percent of Canadian women with Cu 200s experienced spotting in comparison to 38 percent with inert Lippes loops (10). Furthermore, using the copper device, 11 percent of the women experienced increased menstrual bleeding compared with 27 percent using the Lippes loop. In some cases spotting and painful or profuse menstruation were sufficiently severe to warrant removal of the IUD. The removal rate for the copper T was considerably lower than that for the inert Lippes loop—3.8 as compared to 12.4. Similarly, in another study, the termination rate due to bleeding was lower for copper Ts (6.4 percent) than for inert Lippes loops (11.8 percent) (26).

In the studies included in this report, the 9-month rate of copper IUD removals due to bleeding ranged from 0.5 to a large Thai study of approximately 2,000 women, to 7.9 in an Iranian study of 700 women (39) (see Tables 2 and 3).

At one year, age-adjusted data from US and some Western Hemisphere studies of multiparous women showed removals for bleeding and pain with the copper devices were 8.8 for the T Cu 200 and 13.3 for the Lippes loop D. Gross removal rates for bleeding and pain at two years were 17.1 for the T Cu 200, and 20.5 for the loop D (60) (see Fig. 1 and Table 1).

Preliminary quantitative data from current US studies suggest that increased blood loss for a woman with a copper IUD may not be so great as for a woman with an inert Lippes loop (45). Drs. E.C. Laufe, Y. Gibor, B.J. McClanahan and R.F. Wheeler compared the total volume of menstrual flow in groups of women using no contraceptive method with those using inert or copper IUDs. Patients collected all tampons used during each menstrual period and hemoglobin levels were estimated. Women with either copper 7, Saf-T-Coil, or Dalkon Shield devices all showed an increase in menstrual blood flow. Compared with women using no contraceptive method, blood flow with copper 7 devices was somewhat elevated, that with the Saf-T-Coil was about twice as high, and that with the Dalkon Shield was about three times as high. Thus, women using no contraceptive method had menstrual hemoglobin levels of 2.9 gm (S.E. ± 0.59); those with copper 7 devices—4.1 gm (S.E. ± 0.79); those with Saf-T-Coil devices—6.0 gm (S.E. ± 1.4); those with Dalkon Shields—8.3 gm (S.E. ± 1.1).

Excessive or painful blood flow does not seem to be influenced by the age of the woman (26), nor is post-abortion insertion of the device an influencing factor (24). Some evidence, however, indicates that bleeding and pain are more prevalent in nulliparous than in multiparous women (30) (see section on “Nulliparas”).

Problems associated with bleeding tend to diminish with time. Thus, 10 percent of 342 women with copper 7 devices experienced greater bleeding during the first menstruation after insertion, but only 3 percent during the second menstruation (32).

*Personal communication, Leonard E. Laufe, M.D., September 28, 1973. This work was presented at the 11th Annual Meeting of the American Association of Planned Parenthood Physicians held in Houston, Texas, April 11-13, 1973.
Pain

On the whole, pain is not as serious a problem as bleeding, but current methods of data collection make analysis difficult. Pain and bleeding are often linked and therefore many investigators pool the data. As a result, it is often impossible to evaluate the importance of pain as an independent factor either in the frequency of occurrence (event rate) or in the effect upon termination (closure rate). Fortier is exceptional in providing such information (10). Her results suggest that the termination rate because of pain is lower with the copper T (5.4 per 100 woman-years of use) than with the Lippes loop (9.6). It should be noted that Fortier’s 5.4 termination rate due to pain is higher than that found by most other investigators using copper devices. The only higher figure was that of 12.2 reported in a Population Council study in Korea (39).

All other figures on removals for pain fall below three percent (see Table 2). Zipper, for example, reported no medical removals at all for pain in one study (57), and only 0.2 per 100 woman-years in another (56). Newton in England also reports a relatively low incidence of pain (32). Thus, out of a total of 342 insertions, medical removal was necessary in only 5 patients, including one case of pain associated with increased bleeding (32).

As with bleeding, pain, when it does occur, tends to diminish with continued IUD use (32).

Infection

During the 1960s, infection following IUD insertion was commonly reported. Nowadays, however, serious infection is uncommon. It has been greatly reduced by sterile prepackaged devices, by aseptic insertion procedures, and by screening patients to eliminate those with existing pelvic inflammatory disease (PID). Thus, in a typical study comprising 945 patients, eight copper Ts were removed because of infection, a rate slightly less than one percent (43). In another study involving 516 patients with copper T s in situ for 21 months, both the event and removal rate due to PID was 0.2 per 100 users (56).

Most cases of PID can be treated rapidly and effectively by antibiotics with the IUD in situ. In Landesman’s study of 396 women in New York City, for example, ten women were treated successfully by antibiotics with the copper T 200 in situ. In only two other cases was it necessary to remove the device because of PID (24). In this urban community, the incidence of PID (3.0 per 100 woman-years of use) was higher than that reported elsewhere.

Unlike a condom which offers protection against venereal disease, an inert IUD offers no such protection. Recent studies, however, suggest that copper IUDs may offer some indirect prophylaxis against gonococcal infection. In vitro research has demonstrated that copper ions kill or inhibit growth of Neisseria gonorrhoeae (8). This effect has not yet been demonstrated in vivo, but comparative studies of the incidence of gonorrhea in patients with copper IUDs and those with inert IUDs might yield valuable information.

Displacement and Embedding

The idealized picture of an IUD set into an anatomically perfect position within the uterus is not always achieved in practice (see Fig. 9). Reports now available suggest that, at least in some clinics, displacement is not infrequent. Thus, x-ray studies of the uterus undertaken by Dr. I. Kamal and co-workers at Cairo University more than three months after insertion of T Cu 200s indicated that anatomical harmony between the device and the uterus was achieved in only 7 out of 39 cases (20) (see Fig. 9).

In the remaining 32 cases, either one or both transverse arms of the T penetrated the myometrium (uterine wall), even though only three of these patients experienced increased bleeding and none felt pain (see Fig. 9). Whether Kamal’s photographs were in any way affected by inadequate filling with the contrast medium or other cause is not known as yet but is under current investigation. Kamal concluded that myometrial penetration was the primary factor in fixing the device in situ.

Landesman found displacement primarily in the nulligravid and the postpartum patients (24). In his opinion, displacement is the primary cause of unwanted pregnancies. In 75 of 1500 patient (5 percent) the copper devices were displaced into the cervix where, of course, they would have little contraceptive effect (23). Displacement occurred even though a new insertion technique was being used, and great care was exercised to insert the T into a high fundal position.

In addition to displacement and penetration, embedding sometimes occurs soon after insertion. Fifteen randomly selected patients using the copper T 200 were examined x-ray graphically (by x-ray) by Timonen and co-workers in Finland (50) from 4 to 14 months after insertion. Six of their IUDs had been inserted immediately after therapeutic abortion. In 13 of the 15 women (87 percent), one or both tips of the transverse arms of the T were embedded in uterine tissue and one IUD was found in the cervix. (By comparison, 70 percent of patients with inert Lippes loops showed embedding of the tips of the device (50)). In the most extreme case, 11 mm penetration and embedding was observed on one arm and 13 mm penetration on the other—a total of 24 mm. The length of both arms together is 36 mm. Nevertheless, none of Timonen’s patients suffered bleeding, pain, or other symptoms. All had a normal shaped uterus.

Embedding, although a major factor in anchoring the device does not appear to complicate removal, and most physicians do not recommend removal for asymptomatic embedding. Dr. Lise Fortier of Canada, for example, has encountered “no adhesions” and “absolutely no problems” in 150 or so copper IUD removals 2 years after insertion (9).

Koetswong, however, described a case in which removal was essential because of continuous pain from the time of insertion, six months earlier (22). The copper T perforated the uterus at the time of insertion and was located in the
abdominal cavity. Dense adhesions had formed between the copper portion of the copper T 200 and the omentum (tissue which connects the pelvic organs). Removal using a laparoscope was “relatively difficult.” He now recommends that copper-bearing devices which are outside the uterus be removed as early as possible.

**Replacement**

Because copper is constantly released from the device, it is eventually exhausted and pharmacological action ceases. Hence, replacement of old copper devices with new ones may be necessary to maintain protection against pregnancy.

To determine the rate of copper release, Hagenfeldt removed T Cu 200s from patients at various intervals after insertion (12). She determined that during the first year, the daily release of copper was about 45 mcgm. After one year a T Cu 200 device had lost a total of 10.3 mgm.

The rate of release of copper diminishes over time. Thus, Gibor and his co-workers have estimated that, immediately after insertion, a single copper 7 device released on average, 55.5 mcgm copper per day. At six months, the device released 33.0 mcgm per day; at 12 months, 19.6 mcgm per day; at 18 months, 11.6 mcgm per day, and at 21 months, 8.9 mcgm per day (59) (see Fig. 10).
Since the rate of release diminishes over time, Cu 200 IUD is estimated to provide up to four years of effective copper release. During the current experimental phase, however, it is recommended that copper devices be changed every two or three years (31). This time limitation precludes the use of Cu 200 IUDs in some national family programs in less developed countries where subsequent medical follow-up may be difficult. The time limit may be revised if further experience warrants.

**Continuation**

The continuation rate reflects the percentage of women who retain their IUDs after one and two or more years of use. Discontinuation is normally caused by pregnancy, expulsion, or removal for medical or personal reasons. If the age and parity of the patients and the circumstances of the clinic are similar, continuation rates provide a reasonable test of the relative efficacy of different IUD configurations.

![Graph showing average daily release rate of copper from the copper 7 device from time of insertion to 21 months.](image)

**Fig. 10.** Average daily release rate of copper from the copper 7 device from time of insertion to 21 months.

**NOTE:** If these rates are calculated on a cumulative basis, it can be seen that the major part of the copper release occurs during the first six months after insertion and that thereafter only relatively small quantities of copper are released. Gibor suggests that continuing contraceptive action of copper devices beyond six months may be due to catalytic action of copper on various enzyme systems (60). (Data courtesy of G.D. Searle and Co. Chicago, Illinois, USA.)

In some of these studies, IUDs with copper produced slightly higher continuation rates than inert Lippes loops. Double-blind studies showed that use of copper devices for one year resulted in continuation rates of 76 and 77 as compared with continuation rates of 68 and 70 for inert Lippes loop D (26,43) (see Table 3). Sivin's report on the International Postpartum Family Planning Program in 11 countries which involved 188,527 contraceptive acceptors showed that the continuation rate after one year for all models of inert IUDs tested averaged 78 percent (40).

Combining data from a number of clinics, Tietze calculated a continuation rate of 74.4 per 100 women after one year for parous women using the T Cu 200. After two years and taking account of age and parity distribution, Tietze found continuation rates of 52.7 for T Cu 200 users and 53.9 for loop D users. The small difference in continuation rates might be accounted for by personal reasons for removal (see Table 1).

Summarizing a detailed analysis of continuation rates in five Asian countries, Sivin concludes:

- For women with one, two or three living children at the time of acceptance, Copper T acceptors had higher continuation rates than Lippes loop acceptors in the same countries.
- For women with four or more living children at acceptance, continuation rates for the T device were only slightly higher or the same as those for the Lippes loop (39).

### NULLIPARAS

The experience of the 1960s showed that nulliparous women do not tolerate inert IUDs as well as multiparous women. High expulsion rates for inert IUDs in nulliparous of up to 20 per 100 woman-years cause high rates of unwanted pregnancy. Nulliparas report more pain and bleeding. Thus, many physicians still recommend IUDs only for multiparous or high parity women.

Several recently published studies of the copper IUDs, however, suggest that these new devices may be "a very suitable method of contraception for nulliparous women" (30), and one which produces retention and pregnancy rates "encouragingly different" from those with inert IUDs (2) (see Table 4). In separate analyses by Bernstein, Gibor, Lewis, and Mishell, including one study of over 2000 nulliparas (26), expulsion rates of copper IUDs ranged from 4.1 to 10.7 per 100 woman-months of use; pregnancy rates ranged from 0.8 to 1.7 per 100 woman-months; and removals for bleeding, pain or other medical reasons ranged from 11.0 to 12.9 per 100 woman-months (see Table 4).

These expulsion and pregnancy rates in nulliparas are low compared to earlier experience using inert IUDs. But removals for bleeding and pain with copper IUDs are still about twice as high in nulliparas (9.4-10.7 per 100 woman-years after one year's use, Table 4) as in multiparas (5.6 per 100 woman-years) (43). Mishell observes that...
Although the 10.7 one year removal rate for bleeding and pain (for nulliparous women) is not ideal, this rate is similar to the 11.7 rate for these events reported in the Cooperative Statistical Program for multiparous women with the (inert) Loop D . . . (30).

Unfortunately for purposes of precise comparison, comprehensive one-year data on Lippes loop D by age and parity are not available nor have two-year data for the copper IUDs yet been fully analyzed on an age and parity basis. Moreover, because the loop D was so little used in nulliparous women, comparative data is inadequate.

Nevertheless, one-year data on the T Cu 200 from the Cooperative Statistical Program of the Population Council comprising more than 65,000 woman-months of use show the strong effect of age and parity on the pertinent events of IUD performance (see Table 5 and Fig. 11). Pregnancy and expulsion are strongly related to age. Expulsion is also clearly related to parity. Removals for bleeding and pain decline somewhat more with increasing parity than with increasing age whereas pregnancies decline in a linear relation with age.

A more serious problem for nulliparous women is possible displacement of the device from the uterus. It is difficult, in nulliparas, to place the 7 or T IUDs in a high fundal position and occasionally the vertical bar protrudes into the cervical canal (24). In order to accommodate the smaller uterine cavity in the nulliparas, Landesman recommends fabricating a shorter arm segment on the T device. He notes that there is also more vaginal discharge in nulliparous acceptors of copper IUDs than in multiparous ones (24).

Mishell's group of 471 nulliparous patients included 143 (41 percent) younger than 21 years of age. He concluded that the copper T device "is easily inserted and well tolerated by the adolescent girl" (30). Less than 10 percent of these patients required mild analgesic drugs, usually aspirin, for postinsertion cramps. Only five slight vaginal reactions were noted and no syncopal episodes (30). Mishell suggests that the copper T IUD be used as "an effective alternative means of contraception to the oral steroids."

On the whole, copper IUDs seem to present fewer difficulties for the nullipara than do inert IUDs. Where follow-up care is available, copper IUDs may be increasingly used for childless and low parity women. On the other hand, in his comprehensive evaluation of copper IUDs in five countries, Sivin concluded that there seems to be no strong advantage to introducing the copper T among women of parity four or higher (39). For these women, the Lippes loop D may be more suitable since it becomes more effective (i.e., has a lower pregnancy rate) the longer it remains in place.

LONG-TERM SAFETY

Because copper IUDs are so new, data on their long-term effects are still being collected and assessed. To be judged safe, researchers must demonstrate that copper IUDs do not:

- cause or stimulate cancer;
- allow deleterious levels of copper to accumulate in any body tissue;
- produce teratological (fetus-deforming) effects if pregnancy occurs and continues with the IUD in place;
- impair later fertility;
- produce other conditions hazardous to life or health.

<table>
<thead>
<tr>
<th>Author and Date</th>
<th>Type of IUD</th>
<th>Number of Insertions</th>
<th>Women Months of Use</th>
<th>Expulsion Rate</th>
<th>Pregnancy Rate</th>
<th>Removal Rate</th>
<th>Continuation Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bernstein a 1972</td>
<td>T Cu 200</td>
<td>186</td>
<td>1,693</td>
<td>4.1</td>
<td>1.1</td>
<td>0.12</td>
<td>0.03</td>
</tr>
<tr>
<td>Gabor b 1972</td>
<td>T Cu 200</td>
<td>1,278</td>
<td>8,093</td>
<td>6.5</td>
<td>1.1</td>
<td>0.11</td>
<td>0.07</td>
</tr>
<tr>
<td>Lewit b 1973</td>
<td>T Cu 200</td>
<td>1,585</td>
<td>8,658</td>
<td>8.7</td>
<td>0.8</td>
<td>0.6</td>
<td>0.3</td>
</tr>
<tr>
<td>Lewit c 1973</td>
<td>T Cu 200</td>
<td>2,099</td>
<td>11,436</td>
<td>10.7</td>
<td>1.3</td>
<td>0.6</td>
<td>0.3</td>
</tr>
<tr>
<td>Mishell a 1973</td>
<td>T Cu 200</td>
<td>421</td>
<td>6,044</td>
<td>5.4</td>
<td>1.7</td>
<td>0.12</td>
<td>0.03</td>
</tr>
</tbody>
</table>

a-Fifty-nine percent of acceptors had either never been pregnant or had never given birth (nulliparous). Forty-four percent had never been pregnant and 15 percent had had one pregnancy terminated in abortion. Forty-one percent were nulliparas.

b-All acceptors were never-pregnant.

c-All acceptors were nulliparas—that is, their first pregnancy had been terminated by spontaneous or induced abortion, but no never-pregnant women were included.

d-All acceptors were nulliparas (73 percent were never-pregnant and 27 percent had at least one prior pregnancy terminated by abortion).


NOTE: Net cumulative closure and continuation rates are given per 100 women over a period of 12 months. In some cases, figures have been rounded to the nearest decimal place.

The figures from different sources presented in this table are not fully comparable since the populations have different characteristics. Furthermore, the figures for never-pregnant women may be misleadingly low because an unknown number may be infertile, subfertile or less frequently exposed to risk of pregnancy. Thus, the pregnancy rate for never-pregnant women of 0.8 per 100 women is lower than the rate for nulliparas of 1.3—which in turn is lower than the rate for multiparas of 2.2.
Table 5—Gross and Net Cumulative Termination Rates per 100 Women Using T Cu 200, by Parity, Age, and Interval Since Last Pregnancy, One Year of Use

<table>
<thead>
<tr>
<th>Termination</th>
<th>Parity</th>
<th>Age (years)</th>
<th>Late post-partum</th>
<th>Interval</th>
<th>Never pregnant</th>
<th>Previously pregnant</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3 or 4</td>
<td>5 or more</td>
<td>15-19</td>
</tr>
<tr>
<td>Gross rates</td>
<td>Pregnancy</td>
<td>2.4</td>
<td>3.5</td>
<td>3.7</td>
<td>3.0</td>
<td>2.8</td>
</tr>
<tr>
<td></td>
<td>Expulsion</td>
<td>10.6</td>
<td>12.7</td>
<td>8.8</td>
<td>9.8</td>
<td>8.9</td>
</tr>
<tr>
<td></td>
<td>Removals</td>
<td>10.4</td>
<td>9.6</td>
<td>5.0</td>
<td>8.8</td>
<td>5.5</td>
</tr>
<tr>
<td></td>
<td>Bleed/pain</td>
<td>3.3</td>
<td>3.8</td>
<td>2.8</td>
<td>4.5</td>
<td>3.4</td>
</tr>
<tr>
<td></td>
<td>Plan pregnancy</td>
<td>2.6</td>
<td>4.7</td>
<td>1.4</td>
<td>0.8</td>
<td>0.0</td>
</tr>
<tr>
<td></td>
<td>Other personal</td>
<td>2.3</td>
<td>2.2</td>
<td>2.0</td>
<td>2.1</td>
<td>3.6</td>
</tr>
<tr>
<td>Net rates</td>
<td>Pregnancy</td>
<td>2.0</td>
<td>2.9</td>
<td>3.2</td>
<td>2.7</td>
<td>2.4</td>
</tr>
<tr>
<td></td>
<td>Expulsion</td>
<td>9.1</td>
<td>11.2</td>
<td>8.4</td>
<td>6.4</td>
<td>4.9</td>
</tr>
<tr>
<td></td>
<td>Bleed/pain</td>
<td>9.3</td>
<td>7.6</td>
<td>5.3</td>
<td>7.9</td>
<td>5.2</td>
</tr>
<tr>
<td></td>
<td>Other medical</td>
<td>2.8</td>
<td>3.3</td>
<td>2.5</td>
<td>4.1</td>
<td>3.2</td>
</tr>
<tr>
<td></td>
<td>Plan pregnancy</td>
<td>1.6</td>
<td>3.9</td>
<td>1.2</td>
<td>0.7</td>
<td>0.0</td>
</tr>
<tr>
<td></td>
<td>Other personal</td>
<td>2.6</td>
<td>1.6</td>
<td>1.6</td>
<td>1.6</td>
<td>3.3</td>
</tr>
<tr>
<td>Total termination rate</td>
<td>27.4</td>
<td>30.6</td>
<td>22.6</td>
<td>23.6</td>
<td>15.9</td>
<td>33.1</td>
</tr>
<tr>
<td>Continuation rate</td>
<td>72.6</td>
<td>69.4</td>
<td>77.5</td>
<td>76.4</td>
<td>81.0</td>
<td>66.9</td>
</tr>
<tr>
<td>Insertions</td>
<td></td>
<td>4,591</td>
<td>7,716</td>
<td>2,170</td>
<td>1,472</td>
<td>443</td>
</tr>
<tr>
<td>Woman-months of use</td>
<td></td>
<td>24,103</td>
<td>15,942</td>
<td>13,876</td>
<td>9,690</td>
<td>3,076</td>
</tr>
</tbody>
</table>

NOTE: These figures exclude insertions during the first four weeks since the last pregnancy. Age and parity distributions exclude “not stated” categories. “Late post-partum” covers insertions from four weeks to one year after delivery and “interval” covers all insertions more than three months after last pregnancy.

Fig. 11. Pregnancy, expulsion and removal rates for bleeding and pain with copper T 200 by age and parity, one-year gross rates.

NOTE: Gross rather than net event rates are used in the figure to illustrate the relationship of each event separately. These rates therefore cannot be used to calculate overall termination or continuation rates. Data have been pooled for 11,404 T Cu 200 acceptors from a number of clinics in the USA and Canada. (All data courtesy of The Cooperative Statistical Program, The Population Council, New York, USA. Graph by Roger Bernard, M.D., The International Fertility Research Program, University of North Carolina, USA.)
No Carcinogenic Effects

Current research indicates that copper has had no carcinogenic effects up to four years after insertion. Among 6,000 women with copper IUDs who were checked annually with Papanicolaou smears over a period of four years, there has been no evidence of either premalignant or malignant cervical or endometrial lesions (42,44,54). Serial endometrial biopsies from a randomly selected group of these women showed no pathological changes other than infiltration by leukocytes (6). There were no neoplastic changes. Longer periods of testing will be needed, however, to establish long-term effects since four years may be too short a latent period.

Accumulation of Copper

Okereke and his co-workers in New York City have urged that additional studies be undertaken to determine whether there is an excessive accumulation of copper in the body over time (34). Although Hagenfeldt found no change in plasma copper levels in 16 women after insertion of T Cu 200 (12), Okereke, using a more sensitive means of detecting copper in rats, found that some copper was absorbed and transported from the uterus via the blood, producing elevated copper levels in serum, liver, kidneys, and broad ligaments. Okereke’s technique involved tracing radioactive copper, a method that cannot normally be used in human beings.

Hagenfeldt has shown that in humans the T Cu 200 device releases about 50 mcg/day of copper for a period of at least one year (14). This is estimated to be from 1/30 to 1/50 of the adult minimum daily requirement. Hagenfeldt’s study was cited by Tatum as evidence that systemic poisoning from copper IUDs need not be feared (42). Nevertheless, further long-term toxicity studies appear warranted.

Pregnancy with Device In Situ

Animal studies have shown that blastocysts are not harmed by the presence of copper in the uterus. Blastocysts which have been recovered and transplanted showed normal embryological development (24). Furthermore, when a blastocyst was permitted to implant and copper then introduced into the uterus, the pregnancy continued normally (3,42). In animals, neither parturition nor lactation were affected by intrauterine copper and no macroscopic anatomical deformities were encountered through two successive generations (3).

For those few human cases in which a copper IUD has failed to prevent pregnancy, no deformities have been found in the newborn (54).

If a woman does become pregnant while using an IUD, however, the risk of spontaneous abortion is greater than in a normal pregnancy. About 50 percent of pregnant women with inert IUDs have spontaneous abortions (5). With copper IUDs the percentage may be even higher, according to preliminary data (45). Still, it is doubtful that such spontaneous abortions would cause great psychological trauma inasmuch as a woman with an IUD is obviously trying to avoid immediate pregnancies.

Ectopic Pregnancies

There is no evidence that ectopic pregnancies are caused by copper or inert IUDs. Nevertheless, since IUDs markedly reduce the incidence of intrauterine but not ectopic pregnancies, the ratio of intrauterine to ectopic pregnancies is altered in women using IUDs. Normally, ectopic pregnancies occur once in 200 pregnancies, but with an IUD in situ ectopic pregnancies occur once in about twenty pregnancies (46,51), or ten times as often. With an overall rate of three pregnancies per 100 woman-years using copper IUDs, an ectopic pregnancy would occur only once in every 700 woman-years of copper IUD usage, a rate considerably lower than the rate of one in 200 pregnancies for women not using any form of contraception.

Subsequent Fertility

Often the IUD is considered a temporary method of fertility control. Women selecting copper IUDs as a temporary method want to be certain that fertility will return after the device is removed. To date, information is incomplete on pregnancies occurring after copper IUDs were removed. Testing reversibility, Zipper and co-workers reported that of 35 patients who requested removal of T Cu 30 and T Cu 120 IUDs for another pregnancy, 25 or more than 70 percent, became pregnant within the following six months (54). Of these, three aborted. The remaining ten did not return to the clinic. Zipper concluded that with these small amounts of copper, endometrial function returned to normal immediately after the device was removed. Comparable studies with Cu 200 devices are not yet available.

Biopsy studies indicated that copper levels in the myometrium, which are elevated when the copper IUD is in situ, fall to normal levels soon after the device is removed (11). Thus no residual contraceptive action would be expected, but conclusive long-term evidence is not yet available.

Mortality

Although over 10,000 copper IUDs have been inserted, there have been no deaths reported (46). In 1968 when only inert IUDs were available, Dr. Roger Scott identified 10 deaths among women with IUDs in situ (38). In only four of these instances was there a causal relationship between the death and the insertion of the IUD.

Dr. Louise Tyrer of the American College of Obstetricians and Gynecologists placed IUD-related mortality in perspective, noting that in the United States (where maternal death rates are approximately 20 per 100,000 births) “the risk of death from pregnancy far exceeds the risk associated with the IUD...” (51) In developing countries, where maternal
death rates can run as high as 500 per 100,000 births, the mortality risks from IUDs are minute compared with the risks from pregnancy.

**INTERNATIONAL DISTRIBUTION**

More copper IUDs are being distributed each year. The Finnish manufacturer of copper Ts estimated that during 1973, 270,000 devices will be distributed. Through March of 1973, about 200,000 copper 7 units have been sold in Europe.

Legal restrictions in some countries require that copper IUDs be approved for safety and efficacy before marketing. These countries include Australia, New Zealand, Sweden, United Kingdom, Canada, and the United States. No such legal restrictions exist in Austria, Finland, Switzerland, and South Africa, among others.

The British government's Committee on Safety of Medicines licensed the copper 7 for sale in 1973. The US Food and Drug Administration may license the copper 7 and copper T for distribution to US physicians late in 1973 or early in 1974. Such official sanction would result in greatly increased use of these devices.

To date, there are reports on the use of copper IUDs in experimental studies from Chile, Colombia, Mexico, United States, Canada, Korea, Taiwan, Hong Kong, Japan, Australia, Thailand, Iran, UAR, Turkey, Sweden, and England. In addition, copper IUDs are being used in Pakistan, India, Yugoslavia, Indonesia, Israel, France and the Netherlands among others, and are reportedly available in most European countries. Manufacturers and family planning organizations are intending to make copper IUDs available soon in the Philippines, Australia, South Africa, Rhodesia, Jamaica, Senegal and Paraguay.

Copper IUDs are not currently being supplied by the US Agency for International Development since they do not have official sanction of the Food and Drug Administration.

The introduction of copper IUDs into national family planning programs should be approached with caution. The need for replacement when the active copper is exhausted places an additional demand on medical care facilities. In developing countries, the capability for this kind of attention is limited.

Additional research and clinical evaluation programs are needed throughout the world to determine the best configuration for the copper IUDs, the optional amount of copper, the length of time the device can effectively remain in situ and the best procedures for insertion and follow-up.

Whether copper devices offer any clear advantage for family planning programs also remains to be proven.

*Outokumpu Oy, Pori Works, 28100 Pori 10, Finland.

**Manufactured by G. D. Searle and Co., Box 51001, Chicago, Illinois 60680, USA.

Researchers, physicians, or family planning organizations who wish to use these devices should contact the manufacturers or the following organizations for guidance:

- The Population Council
  The Rockefeller University
  York Ave. and 66th St.
  New York, N.Y. 10021, USA

- The International Planned Parenthood Federation
  18-20 Lower Regent Street
  London SW1Y 4PW, England

- The Canadian International Development Research Centre
  P.O. Box 8500, Ottawa, Canada K1G 3H9

**CONFERENCE AND RESEARCH**

At a Workshop in Advances in IUD Contraception for Developing Countries, held October 18-20, 1973, at the Battelle Population Study Center in Seattle, Washington, some fifty outstanding investigators gathered to discuss current and future research and methods for improving IUDs. Among the principal points which emerged with respect to copper IUDs were the following:

- The range of differences between results from various clinical centers are of more significance than differences between various models of IUDs. As the size and diversity of the tested population is increased, the performance differences between many devices, including copper ones, virtually disappear.

- Bleeding remains the most widespread problem of IUD use and is particularly damaging for both medical and cultural reasons in developing countries. Copper IUDs tested thus far have not solved this problem although some improvements in reducing the quantity of blood loss have been achieved. Until the etiology of bleeding is better understood, improved performance in this parameter will be difficult.

- The copper T and copper 7 are superior IUDs for nulliparous patients. Less copper is required to effect long-term contraceptive action than was originally thought, thus, this removes part of the objection of copper IUD use in developing countries since frequent replacement no longer appears to be essential. Copper IUDs with life spans of 15-20 years are now being tested.

- Testing of copper should be continued with other configurations, such as the flat, leaf-like shape which already has been shown to have low expulsion and bleeding rates, as well as the present T and 7.

- More attention should be devoted to the selection of appropriate IUD configurations for different women, including postpartum patients, lactating women, women of different ages, parities, physical characteristics, as well
as ethnic and cultural backgrounds. A more individual approach to both patients and devices may eventually be necessary.

Apart from Research at Battelle, several public and private non-profit agencies are supporting research in copper IUDs. From mid-1971 to the end of 1973, the International Committee for Contraception Research of the Population Council expended over one million dollars for research on the copper T device. This work will continue. The US Agency for International Development, The Pathfinder Council expended over one million dollars for research on Committee for Contraception Research of the Population Apart from Research at Battelle, several public and private non-profit agencies are supporting research in copper IUDs.

The addition of copper may stimulate greater interest in IUDs in general. Lena Hammarberg of the Swedish Association for Sex Education observes that "... on the whole the use of (the) copper IUD has meant an increase in the use of IUDs in Sweden."

Many countries may find during the 1970s that copper IUDs are an acceptable form of contraception. Data and evaluation so far suggests that nulliparous or low parity women in countries where follow-up medical care is available will be the principal beneficiaries.

**BIBLIOGRAPHY**
