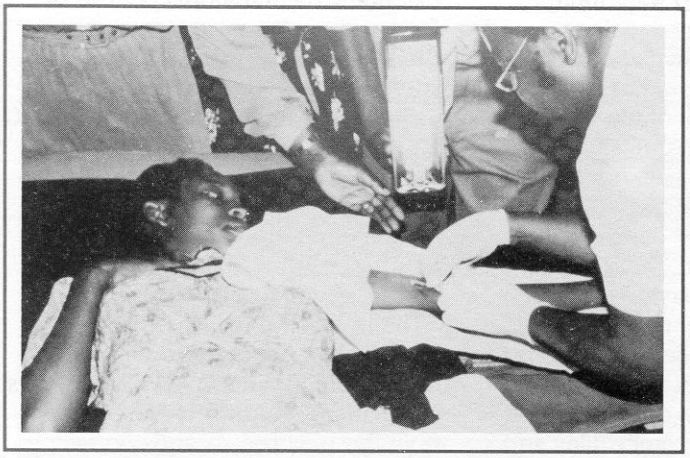
AT ARMS LENGTH



A health worker inserting a NORPLANT capsule at a Kenyan clinic.

In a small rural clinic in Kenya a doctor performs a simple operation on his first patient of the day, a woman of about 30. First, he applies a local anaesthetic to her upper arm; then, using a specially designed instrument, he carefully inserts six thin rubber capsules about the size of matchsticks beneath the skin of her arm. In 10 minutes the procedure is over and the woman is ready to leave. By nightfall the capsules have begun to work — the woman will be protected against pregnancy for the next 5 years.

What the doctor inserted in the woman's arm were NORPLANT capsules, the first contraceptive implants to become available for general use. NORPLANT has been approved in 15 countries and is currently being reviewed by the Food and Drug Administration (FDA) in the United States. It is estimated that close to half a million women are using, or have used, the implant worldwide, and the numbers are increasing rapidly.

The contraceptive part of NORPLANT is not new. The thin rubber capsules contain small doses of a synthetic hormone called levonorgestrel, a substance used in oral contraceptives for years.

What is new is the method by which the contraceptive is delivered: a continuous release of controlled amounts of hormone into the woman's body for a period of up to 5 years.

This small but constant release of hormones from capsules provides full-time protection against pregnancy.

The development of NORPLANT is a fascinating and surprising story; fascinating, because it demonstrates how complex, costly, and fraught with hazards the process of developing a contraceptive can be. It is surprising because, despite the cost of over $20 million and 25 years of research, NORPLANT was not developed by one of the multinational pharmaceutical giants, but by the Population Council, an international nonprofit organization based in New York. The process is also surprising because many of those responsible for developing the implant didn't believe it would be accepted by women.

Wayne Bardin, a vice-president of the Population Council, became involved with the project 10 years after it began. "There was a great deal of opposition to implants from population experts who were convinced that women would never accept the methods," he said. "Even I had some doubts." But the experts were wrong.

From the very beginning, the Council never had difficulty attracting volunteers to test the new contraceptive. Indeed, when the implants were removed at the end of the trials, many women wanted new ones inserted again.

As is often the case in research and development, the creation of NORPLANT required a small measure of chance. It is just possible, for example, that if the Population Council's Dr Sheldon Segal had not had lunch one day in 1965 with a representative of the Dow Corning Corporation, the implant might never have been developed. Over lunch the conversation turned to Silastic, a polymerized silicone rubber material used by Dow Corning in artificial heart valves and other medical implant devices.

To Segal, Silastic material suggested another possibility — a contraceptive implant. If dyes and other liquids slowly dissolved through the Silastic implant, hormones, he reasoned, could also slowly release from the capsules into the body. He began to test his idea that same day in his laboratory on female rats. The concept was workable.

From that simple beginning sprang the NORPLANT contraceptive, a project that would eventually involve thousands of individuals and scores of organizations. Some of the organizations that collaborated with the Population Council included the World Health Organization (WHO), the UN Family Planning Agency (UNFPA), and the International Planned Parenthood Federation (IPPF).

In 1965, Segal and a Chilean colleague, Dr Horacio Croxatto, began to study the idea of a contraceptive implant seriously. Within 2 years, they were able to proceed with testing on a group of 25 women — the first of many such test groups.

The capsules were still at the trial-and-error stage, with the dosages often too low to prevent pregnancy. There were several unplanned pregnancies but the volunteers remained undeterred.

There were other setbacks along the road. One of the more promising materials being tested, megestrol acetate, had to be withdrawn when its British manufacturer reported possible adverse effects in toxicity tests with

animals. Later, the development of a two-capsule version of the implant, known as NORPLANT II, had to be stopped when Dow Corning ceased manufacturing the material used to make the capsule. (A new version of NORPLANT II is currently undergoing trials.)

None of these problems, however, prevented the project from moving forward. By 1975, the Population Council had reached agreement with a commercial manufacturer, Leiras Pharmaceuticals of Finland. The implant was ready for large-scale international trials.

The first of these trials involved 1500 women in six different countries — Brazil, Chile, Denmark, Finland, Jamaica, and the Dominican Republic. Field testing of a contraceptive with a 5-year life span turned out to be a lengthy process, and it was 1980 before the next round of trials began.

This time the volunteers numbered in the tens of thousands of women. Eventually, more than 55,000 women in 44 countries participated in the NORPLANT tests, with developing countries representing a large number of test sites. The trials involved 12 countries in Latin and South America, 7 in sub-Saharan Africa, 3 in North Africa and the Middle East, and 13 in Asia. The United States and 8 countries in Europe also participated in the testing of the implant. The developing countries, many with serious population problems, had perhaps the most to gain from the tests.

The enormous task of organizing and tracking trials of this scale led the Council to another innovation: it created the first global computer database for the introduction of a contraceptive. This global database led to the increased involvement of other organizations like the Association for Voluntary Surgical Contraception (AVSC), Family Health International (FHI), and the Program for Appropriate Technology in Health (PATH). These groups also aided the Council in supervising the trials and preparing training materials for health workers.

An essential component of the project from the first trials was training. One of the disadvantages of the NORPLANT method is that the insertion of the capsules requires skilled medical personnel. Special centres had to be established around the world to provide training for the hundreds of personnel needed just to conduct the trials. By the time NORPLANT was ready to be introduced on a nation-wide scale, a 3-day training program was developed to provide the necessary clinical expertise.

Concern with the users, however, is perhaps the feature that makes the NORPLANT program truly unique. The tone was set by the president of the Population Council in 1966, when he said that "...important as it is to have a satisfactory method, it is equally important that women be given a real understanding of what they can expect."

A large part of IDRC's involvement with the project has been in funding studies of user satisfaction with the implants. Dr George Brown, a Council vice-president and a former director of IDRC's Health Sciences Division, is responsible for the NORPLANT introduction program. He says the IDRC-supported studies have been invaluable in obtaining a better understanding of the attitudes of the users.

Despite the modest success of NORPLANT to date and the increased international scientific cooperation, the question remains whether it was all worthwhile. The implant is still one of the more expensive contraceptive options available — roughly double the cost of the pill and 18 times the cost of an intrauterine device (IUD), according to one study. Was there really sufficient need for a new contraceptive to justify 25 years of effort and millions of dollars?

Dr Beverly Winikoff, a Council physician and public health specialist, says yes. "NORPLANT very definitely fills a need for a long-term method that doesn't require constant attention," she says. "It is a good alternative to sterilization and an excellent way to space children. It works well for women who don't want any more children but still have a decade or two of reproductive potential ahead of them."

Based on United Nations projections, there could be as many as 639 million contraceptive users by the year 2000. Using these projections, it would be expected that there would be between 4–7 million NORPLANT users in developed countries and 15–25 million users in developing countries. In the future, NORPLANT promises to play a large role in birth control.

Winikoff adds that women still need more contraceptive choices to meet their changing requirements. The introduction of each new method increases the chances of reaching the millions of women who still do not use contraception, she says.

Despite these needs, the major pharmaceutical companies have virtually moved out of the field of contraceptive research. This is partly because of high costs and partly because of the fear of litigation should some unforeseen side-effect be discovered in a contraceptive product.

The task, then, falls to nonprofit organizations such as the Population Council to provide women with more choices for birth control. In this sense, the Council's initiation of the new NORPLANT contraceptive and its information cooperation may act as a stepping-stone for increased research into birth control and family planning.

By Bob Stanley.

Choice and Challenge: Global Teamwork in Developing A Contraceptive Implant", IDRC-278e, available from the Communications Division of IDRC, Ottawa, Canada.

Or write to: The Population Council, One Dag Hammarskjold Plaza, New York, New York 10017, USA.