Session 6
LONG-ACTING CONTRACEPTION

FIRST AND SECOND GENERATION IMPLANTS

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Experience with Norplant has shown it to be an effective 5-year long-term delivery system for contraception [1]. Its introduction to the USA has resulted in a wider choice for women and results are encouraging [2–4], while its introduction to Europe has aroused much interest [5]. Pregnancy rates are low, 0.7 at 4 years [1] and 2.47 per 1000 at 1 year of use [3]. While removal for bleeding problems still remains the major reason for removal, 32.2%; of all removals [3] other side-effects remain low and acceptable. The difficulties of correct insertion, requiring adequate training and removal [6], have prompted the development of second generation implants using fewer covered rods of capsules. The Norplant II implants using two covered rods is also very effective [1,7]. These systems all use levonorgestrel as the active hormone, together with a silastic polymer release system.

An alternative second generation, single rod implant is Implanon, a 3-keto desogestrel release system using a polyvinyl acetate rod. This system is very simple to insert subdermally through a wide bore needle and is equally easy to remove [8]. Our group has completed two detailed studies of Implanon over 5 years. The first relates to a phase II detailed study of release rates, biochemical peripheral hormone analysis and ultrasound monitoring to detect ovarian function and sperm mucous interaction studies. The volunteer also had control cycle monitoring followed by regular periods of intensive monitoring for the four years of the study. The implants were chemically leached to represent the loading of 3 keto desogestrel present at the start of year 2 in an ordinary implant. Effective suppression of ovulation occurred with no confirmed evidence of ovulation on biochemistry or USS monitoring even at 5 years of use. Ovarian activity is evident by follicular growth and some peripheral estradiol activity though less than late follicular level values were seen which tended to increase in year 4. However, progesterone values remained very low throughout. The mucus was strongly progestogenic throughout the study with Insler scores of less than 4 and standardised sperm penetration tests showed no activity or penetration of mucus by sperm. From this study we are able to conclude that Implanon is an effective contraceptive subdermal implant system for at least 5 years. In the second study, Implanon was compared in a random allocation study with Norplant. The results of the first year of this study showed no difference in the incidence of side-effects, e.g.

bleeding, acceptable cycle pattern, removal for medical reasons. However, the ease of insertion of Implanon gave a significant advantage to this second generation implant for use in family planning programs.

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NORPLANT TRAINING IN THE UK: A MODEL FOR SUCCESS

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Norplant is a novel, long-term, hormonal method of contraception consisting of 6 flexible capsules of levonorgestrel for subdermal placement. Successful use of Norplant and high levels of user satisfaction are dependent upon the skill of the service provider. Good counselling skills in association with skillful insertion and removal are required.

Norplant has been introduced into a number of developing countries via training programs designed and implemented by the Johns Hopkins Program for International Education in Reproductive Health (JHPIEGO). These programs involved the use of models designed to provide the trainee with an opportunity to learn and practice the technique of insertion and removal prior to implementing these skills in the clinical situation. The base of clinically trained health care providers is then increased using a cascade system.

Norplant was introduced into the UK in October 1993, the principles of the JHPIEGO approach to training were adopted by the pharmaceutical company responsible for distribution and was the first experience with this approach in a developed country. The training program for Norplant in the UK has proved successful and has followed a similar pattern to that seen in other countries where the JHPIEGO approach was adopted. In one year over 6000 health care providers had attended the sessions utilising the model arm and over 3000 health care providers had

completed clinical training for insertion. The cascade is now being repeated to establish a base of health care providers skilled in the removal procedure.

ACCEPTABILITY OF NORPLANT IN THE UK: ANALYSIS FROM 350 USERS

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Norplant is a novel, long-term, highly effective method of contraception introduced into the UK in October 1993. This prospective five-year parallel group study was designed to investigate the acceptability of Norplant compared to the combined pill amongst 700 UK women. This first analysis reports on acceptability of the Norplant insertion procedure ($n=354$) and is therefore non-comparative. Three hundred and fifty-four patients were recruited from a wide range of ages, family status and previous contraceptive experience. Most subjects reported none or only slight discomfort either during the Norplant insertion procedure (96%) or after the procedure (87.9%). Complications of the procedure were not common and none were of a serious or unexpected nature.

ACCEPTABILITY OF NORPLANT – IN-DEPTH INTERVIEWS WITH NORPLANT USERS

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Thirty-three patients involved in a 5-year study to evaluate the continuation rates and acceptability of Norplant in a UK population ($n=354$) were selected for face to face (1:1) interviews to provide in-depth information about acceptability of the method. Patients were interviewed in their homes or at hotels in 9 different centers across the UK by an independent interviewer. Interviews were carried out after each patient had completed between 3–6 months of use of Norplant (further interviews will be held after 12–18 months of use at a later date).

Patients report the advantages of Norplant to be convenience, reliability, reversibility, light/no periods and the fact that it is long term. The insertion procedure was pain free, quick and not perceived as a problem by the patient. There is a high level of acceptability of the method despite changes in menstrual bleeding pattern and some other minor side effects.

EXPERIENCES WITH LONG-ACTING HORMONAL IMPLANTS FOR CONTRACEPTION IN A GERMAN GYNECOLOGICAL PRIVATE PRACTICE

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Between 1986–1995 two studies as part of multicenter trials have been performed with Norplant II (5 years) and the desogestrel-containing Implanon (one rod, 2 years) in 50 patients.

The aim of these studies was the evaluation of acceptability and tolerance of long-acting contraceptives in a developed and highly industrialized country where more than 50% of women in the fertile age are using various methods of contraception.

The overall continuation rate was 60%. The drop-outs were due to irregular bleeding pattern from the medical point of view. But behind these understandable reasons we found substantial psychosocial problems such as broken partnerships, new life planning, wish for another pregnancy, troubles at work, giving up extramarital relationship, disappointment and broken career. Most women in both studies presented similar bleeding patterns as 173 regular, 173 irregular and one-third amenorrhoic. The acceptance of bleeding irregularities are widely influenced by the primary motivation for contraception and the stability of the sexual relationship as well as being conscious to use a safe, effective and reversible method of family planning with simple and easy handling.

CROSS-NATIONAL COMPARISON OF 17 PRE-INTRODUCTORY CLINICAL TRIALS OF NORPLANT

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(1) Family Health International; (2)Population Council

This report summarizes the data collected in pre-introductory Norplant clinical trials in 17 countries in Latin America, Asia and Africa that were coordinated by either The Population Council or Family Health International (FHI) between 1984 and 1991. A total of 16 282 women between the ages of 18 and 40 participated in the studies with semiannual or annual follow-up visits for up to 5 years.

Gross cumulative pregnancy rates were <0.6 per 100 women in the first year and <1.5 in the second year in all countries. Significant differences in cumulative 5-year pregnancy rates were observed between weight groups 40–49 and 50–59 kg and between 50–59 and 60–69 kg body weight but not between 60–69 kg and those >70 kg. Total cumulative discontinuation rates after five years of Norplant use ranged from 35.8 to 60.0 per 100 women. Younger age and low parity were associated with a higher discontinuation rate. Cumulative discontinuation rates for menstrual reasons more than doubled between the end of the first and second year of use in 13 of 17 countries.

This analysis and one previous review provide the only comparison of Norplant study results across a wide diversity of countries; thus allowing an appreciation of the range of clinical experience with Norplant and the regional differences in that experience.

A COHORT STUDY OF NORPLANT IMPLANT: SIDE-EFFECTS AND ACCEPTANCE

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Objectives: Menstrual irregularity is the main cause of termination of Norplant, and a study of its safety and level of acceptance is needed.

Study methods: A cohort study using medical records of Dr Kariadi Hospital Semarang, Indonesia and comparison interviews between Norlant and IUD users who had in 1990 been followed up for 5 years. Expulsion rate, removal rate, level of acceptance and satisfaction were examined.

Results: From 170 Norplant and 168 IUD acceptors, the net cumulative pregnancy rates by month 36 of the Norplant and the IUD groups are 0.0% and 1.19%, respectively ($p>0.05$). The net cumulative expulsion rates are 0.61% and 1.32% ($p>0.05$). The net cumulative rates of removal for medical reasons are 2.37% and 1.97% ($p>0.05$). The net cumulative removal rates for non-medical reasons are 1.80% and 10.38% ($p<0.001$); the net cumulative continuation rates are 95.29% and 85.60% ($p<0.002$). The net cumulative acceptance rates are 97.04% and 93.83% ($p>0.05$). The Norplant users experienced less menstrual and inter-menstrual bleeding and more amenorrhea than the IUD group. The psychological satisfaction scores among Norplant and IUD users are high ($p>0.05$). The Norplant contraceptive is well accepted.

Conclusions: The findings could be very useful for further steps in promoting Norplant as a contraceptive which is long-acting with good efficacy, acceptance and safety.