CONCEPTION AFTER THE PILL: TIME TO CONCEIVE AND BIRTH DEFECTS

A THESIS

SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS

FOR THE DEGREE OF MASTER OF SCIENCE

IN THE GRADUATE SCHOOL OF THE

TEXAS WOMAN'S UNIVERSITY

COLLEGE OF NURSING

BY

CHARLOTTE R. PATRICK, R.N., B.S.N., M.Ed.

DENTON, TEXAS

MAY 1980

ACKNOWLEDGEMENTS

This writer wishes to express her sincere appreciation and gratitude to all those who assisted with this study:

To my husband for his constructive criticism and most of all his love and encouragement;

To my committee chairmen, Gail Watson, M.S., and Cheryl Anderson, M.S. for their guidance;

To my committee members, Judith Ann Erlen, Ph.D., Emile Michel, M.S.N., Jean Stair, Ed.D., Dean Anne Gudmundsen, Ph.D., for their helpful suggestions;

To Britt Canada, M.S. for his statistical assistance;

To Margaret Jordan for her expert typing assistance.

TABLE OF CONTENTS

TABLE OF CONTENTS (Continued)

Chapter

LIST OF TABLES

CHAPTER I

INTRODUCTION

In the United States approximately ten million women are estimated to be using oral contraceptives, some for as long as ten to fifteen years. Many of these women are now concerned about the length of time to become pregnant once they stop taking oral contraceptives. This concern is often expressed to nurses involved in family planning. Among the lay population, misconceptions abound such as continued use of oral contraceptives will result in "sterility" or women who take the pill will still be able to conceive after the age of fifty or sixty. Currently, there is little published research directed toward fertility after discontinuance of oral contraceptives to guide the nurse.

Conflicting data can be found in the literature regarding the length of time to conceive after discontinuing the use of oral contraceptives and the incidence of infertility. Some early research has suggested the possibility that fertility might be enhanced following the use of ovulation inhibitors. Controlled studies have discounted that rebound fertility actually occurs in human

subjects. Other research has indicated that there is no significant difference in the conception time for those women who discontinue oral contraceptives and those who discontinue other methods of conception, although a short delay in the return to maximum fertility has been reported in some studies. Also proposed is that conception occurring during the first few cycles following discontinuance of oral contraceptives poses a risk to the fetus.

Further research is needed so that the nurse may respond intelligently to the concerns expressed by women desiring to use oral contraceptives and to become pregnant following discontinuance. This study retrospectively has investigated two factors: (1) the time for conception to occur after discontinuance of oral contraceptives and (2) the incidence of birth defects in infants born to women who have used oral contraceptives.

Statement of Problem

The questions proposed in this study were:

1. Is there a relationship between the length of time on oral contraceptives and the length of time to conceive after oral contraceptives are discontinued?

2. Is there an increased incidence of birth defects in infants born to women who conceive within the

first two months after discontinuing oral contraceptives compared to women who conceive after the second month?

Purposes

The purposes of this study were to determine the:

1. Length of time on oral contraceptives prior to pregnancy

2. Length of time between discontinuation of oral contraceptives and conception

3. Presence of birth defects in infants of women who conceive within the first two months after discontinuing oral contraceptives

Background and Significance

Man's desire to control his fertility is as old as humanity. Although oral contraceptives are considered a contemporary development, the use of oral preparations to prevent pregnancy has been recorded in earliest history. A prescription from a Chinese book dated 2700 B.C. suggested that a small piece of quick silver which has been fried in oil if taken on an empty stomach will permanently prevent pregnancy (Family Planning 1967). Teas made from roots, weeds, and leaves have been described over the centuries in medical literature as fertility control agents. In Japan, women ate the bodies

of dead bees, and in Egypt, women consumed the seeds of caster oil plants in order to prevent pregnancy (Manisoff 1969).

Oral contraception as practiced today is a recent development. In fact, as late as the 1950s, oral contraceptives were not available for clinical use. Although the potential use of steroids for contraception was known earlier, the first clinical trials did not begin until 1956. Formal approval for the use of the combination pill was given by the United States Food and Drug Administration in 1960 (Chez 1976). Chez suggested that the popularity of the "pill" is undoubtedly related to its effectiveness as a contraceptive. Of all reversible contraceptive methods, oral contraceptives have the lowest failure rate both in theory and actual use.

A 1974 survey estimated that 30 percent of all women in the United States, between the ages of eighteen and forty-four, were using oral contraceptives. Oral contraceptives were used by 24 percent of the married women and by 41 percent of the unmarried women (Mishell 1976). According to data collected by the National Survey of Family Growth, oral contraceptives and surgical sterilization were the main methods of birth control used by married couples in the United States during 1973

and 1976. Ford (1978) reported a slight decline in the use of oral contraceptives between 1973 and 1976, from 25 percent of married women in 1973 to 22 percent by 1976. The National Survey of Family Growth reported that the percentage of women fifteen to forty-four years of age seeking to become pregnant in 1976 was 6.5 percent and those pregnant were 6.9 percent compared to 7.0 and 7.3 percent, respectively, in 1973 (Ford 1978).

Early studies of post-pill fertility suggested the possibility of increased fertility following the use of oral contraceptives. Rebound fertility has been observed in laboratory animals. In early studies, Mears and Grant (1962) reported an 80 percent pregnancy rate by the end of the second cycle following discontinuance of oral contraception, which would be higher than normally expected in the general population. Mears (1968) questioned the validity of the study and suggested that the women who volunteered for the early trials were women who were particularly fertile and had experienced failure with other methods. In 1968 Mears readdressed the question of rebound fertility. She reported that most investigators found that "the first cycle after discontinuing medication is usually prolonged and ovulation postponed because of the lengthening of the

proliferative phase" (Mears 1968, p. 342). Ovulation during the first cycle appears to occur in only 70 percent of women; however, over 90 percent of the women are ovulating by the third cycle. Mears concluded that "there is no convincing evidence of any real increase in fertility in normal or infertile women following inhibition of ovulation, whether short or long term" (1968, p. 344).

Taber (1968) correlated the length of time that patients had been receiving Norinyl-I therapy with the time interval for conception to occur after discontinuance. No attempt was made to control data for factors such as marital status or sexual activity which might influence the fertility rate. Taber (1968) suggested that patients who discontinue oral contraceptives should be counseled to have patience, for the majority of couples will conceive within six to twelve months.

Coital frequency and the time required to conceive after discontinuing the use of oral contraceptives was the focus of a study conducted by Westoff, Bumpass, and Ryder (1969). Analysis of the data revealed women taking oral contraceptives had a mean coital frequency of 9.2 per month compared to 6.6 for women using all other methods of contraception. In the

second portion of their study, Westoff, Bumpas, and Ryder (1969) compared the time required for women to conceive after discontinuance of oral contraceptives with women who had used other methods of contraception. They concluded that there was no significant difference between the two groups.

The need for continued research in fertility after contraception is essential for valid assessment of post-contraception fertility. Tietze observed that

> . . . while clinical observers appear to agree that most women conceive "promptly" after discontinuation of oral contraception and while the fragmentary statistics compiled by several investigators are compatible with this impression, hard data is not available to support it (1968, p. 389).

Menses resumes spontaneously in most women after discontinuance of oral contraception. Amenorrhea and subsequent infertility can be distressing for women who desire to become pregnant. Post-pill amenorrhea is defined as "amenorrhea persisting for at least six months after birth control drugs are discontinued" (Buttram, Vanderheyden, Besch, and Acosta 1974, p. 37). Golditch (1972) reported the incidence of post-pill amenorrhea was 2.2 per one thousand with 90 percent of the women spontaneously resuming menses within six to twelve months. Amenorrhea is often accompanied by galactorrhea, breast

secretion. Galactorrhea may be related to hypothalamic suppression of prolactin-inhibiting factor (Golditch 1972). However, the relationship of amenorrhea and galactorrhea should not be overlooked. Buttram and associates (1974) suggested that if a female is likely to develop post-pill amenorrhea, the length of time on the drug is of little consequence. Golditch stated there is "no sound basis for interrupting oral contraceptives every two to three years to allow a spontaneous menstrual period" (1972, p. 907). However, Buttram and associates (1974) stated that despite this knowledge, they feel compelled to advise those desiring to become pregnant to discontinue the drug after two years. For women with irregular menses, they recommend the use of oral contraceptives for as short a period as feasible, and not more than a year.

Data suggested that women with a history of irregular menstrual cycles appear to be more susceptible to post-pill amenorrhea (Buttram et al. 1974). Golditch (1972) found a correlation with past menstrual dysfunction and/or absence of withdrawal bleeding during pill use. The importance of obtaining a thorough menstrual history prior to prescribing oral contraceptives was stressed.

Zatuchini (1978) emphasized the need for the nurse to obtain a thorough medical and social history as well as to perform a physical examination prior to providing oral contraceptives. The medical history should include a detailed gynecological and menstrual history. The social history according to Zatuchini should include the client's sexual activity--frequency of intercourse and the number of partners.

Studies suggesting an increased incidence of birth defects and spontaneous abortions following oral contraceptive use have elicited concern. The difficulty of obtaining and documenting such reports is well recognized. A retrospective study by Janerich, Piper, and Glebatis (1974) demonstrated a relationship between the use of oral contraceptives during early pregnancy and birth defects, specifically congenital limb-reduction anomalies. In another study, Janerich, Flink, and Keogh (1976) investigated the relationship of oral contraceptive use and the incidence of Down's Syndrome. They concluded that it seemed unlikely that oral contraceptives were responsible for any substantial increase in the frequency of Down's Syndrome among live births. However, they did not rule out the possibility that the "pill" was the cause of an increase in trisomies among

spontaneous abortions. A retrospective study conducted by the New York Department of Health determined there was no significant increase in birth defects of children whose mother used oral contraceptives just before or during early stages of pregnancy (Pill Taken During 1977). Data collected in a prospective study reported that congenital heart malformations were associated with the use of oral contraceptives (Pill Taken During 1977). In view of conflicting data and the difficulty documenting causal relationships between environmental agents and birth defects, Janerich, Piper, and Glebatis (1974) suggested that women, who wish to become pregnant, should use a nonhormonal method of contraception for several months. In December, 1976, the Food and Drug Administration announced plans to require warnings on birth control pill labeling information to include medical complications. Included in this information was the warning that oral contraceptives may increase the risk of birth defects, including heart defects and limb defects. The literature recommends that oral contraceptives be discontinued two to three months before a woman tries to become pregnant (Huxall 1977).

In summary, oral contraceptives are the most popular form of reversible contraception used by women

in the United States. In recent years, the nurse has assumed an increasingly important role in caring for women using oral contraceptives. In order to assist the client, the nurse needs to be well informed of the effects of oral contraceptives. As more women are using oral contraceptives for longer periods of time, there is an increased concern about the effects of long-term use of oral contraceptives on postcontraceptive fertility. Studies have indicated that the majority of women conceive within six months after discontinuing oral contraceptives. However, further research in this area is needed. For the few women who do not establish normal menses after discontinuing oral contraceptives, the phenomenon can be distressing. For those who conceive immediately after discontinuance of oral contraceptives, the possibility of birth defects is a cause for concern.

Conceptual Framework

The concept of homeostatis formed the conceptual framework for this study. Oral contraception affects the homeostatic mechanisms governing ovulation. A woman's ability to conceive after discontinuance of oral contraceptives is dependent upon the body's ability

to adapt and restore normal homeostatic balance of the hypothalamic-anterior pituitary-ovarian feedback system.

Homeostasis

The term homeostasis was coined by Cannon (1939) from the Greek words "homios," meaning "like" and "stasis," meaning "standing" to describe the equilibrium that the internal environment maintains while adapting to change. Homeostasis as defined by Guyton means "maintenance of static, or constant, conditions in the internal environment" (1976, p. 3). A constant environment is maintained by all homeostatic mechanisms of essentially all organs and tissues. Some authorities have not regarded reproduction as homeostatic function. However, Guyton (1976) proposed that all body structures are organized to maintain continuity of life. The homeostatic function of reproduction is to "generate new beings to take the place of ones that are dying" (Guyton 1976, p. 5). The concept of homeostasis as originally defined by Cannon was limited to specific self-regulatory physiological processes. Today, the concept of homeostasis has taken on a broader focus of application. Homeostatic principles may be applied to all processes that are self-regulatory.

Homeostatic mechanisms depend on a negative feedback system and are self-regulatory. Regulation by negative feedback is defined by Beland and Passos as a "change in one direction is counteracted or opposed by a change in the opposite direction" (1975, p. 58). Negative feedback mechamisms control almost all biological systems in maintaining optimum function. On the other hand, positive feedback enhances rather than counteracts a change. Unless positive feedback is controlled or reversed by the negative feedback system, optimum function cannot be maintained and death or illness may result. Adjustment to change in the external and internal environment is required to maintain a state of equilibrium. The normal menstrual cycle is dependent upon feedback mechanisms as well as influences from the external and internal environment. The menstrual cycle is controlled by a complex feedback system involving the hypothalamus, anterior lobe of the pituitary, and the ovaries.

The administration of oral contraceptives directly alters the homeostatic balance of the hypothalamic-anterior pituitary-ovarian feedback system. The primary action of estrogen in oral contraceptives is to suppress the production of follicle stimulating hormone (FSH)

by the inhibiting of the FSH-releasing factor from the hypothalamus. Progesterone also has a direct effect on the endometrium and cervical mucus becomes thick and viscuous acting as a barrier to sperm (Chez 1976).

When a woman discontinues the use of oral contraceptives, homeostatic mechanisms must re-establish normal functioning. Faulty or inadequate adaptation may result in prolonged amenorrhea and infertility. Amenorrhea is believed to be caused by oversuppression of the hypothalamic-pituitary-ovarian axis (Chez 1976).

Hypotheses

Two hypotheses were investigated:

1. There is no significant relationship between the length of time taking oral contraceptives and the length of time to conceive

2. There is no significant increase in the incidence of birth defects in infants born to women who conceive within the first two months after discontinuing oral contraceptives and those born to women who conceive after the second month

Definition of Terms

For the purposes of this study, the following terms were defined:

1. Oral contraceptive--a hormone pill of synthetic estrogen and synthetic progesterone in combination form, sequential form, or a low dose progestin only pill which prevent ovulation

2. Conceive--impregnation of the ovum by the spermatozoon marking the beginning of pregnancy. For this study, conceive refers to that time the woman becomes pregnant as estimated by the date of the last normal menstrual period after discontinuing oral contraceptives plus two weeks

3. Length of time taking oral contraceptives--The interval measured in months and/or years that the woman had continuously taken oral contraceptives prior to this pregnancy

4. Length of time to conceive--the interval measured in months from the time oral contraceptives were discontinued to the time conception occurred. In cases where the client used an alternate method of contraception after discontinuing oral contraceptives, the interval was measured in months from the discontinuance of contraceptive practice to the time of conception

5. Infants with birth defects--the presence of malformations or congenital anomalies in infants at the

time of birth, occurring singularly or in combination with other defects.

Limitations

Limitations of this study were:

1. Sample was not randomized and the sample size was small so that conclusions cannot be generalized to a larger population

2. Retrospective design of study required the use of memory to recall past events

3. Limited time of the researcher for data collection

4. Reliability and validity of the questionnaire was not established because this was its initial use

Delimitations

The delimitations of this study were:

1. The women had used oral contraceptives prior to this pregnancy

2. All women were able to speak, read, and understand English

3. The women, who were under eighteen, had to be married in order to consent to be in the study

4. The infant had been assessed for physical defects by a physician and/or nurse in the newborn nursery

5. The women had no prior history of genetic or infectious disorders

Assumptions

The following assumptions were made:

1. Oral contraceptives were prescribed by a physician for the purpose of contraception

2. All women were assumed to be normal, healthy women during pregnancy and up to and through delivery

3. All subjects received counseling regarding the proper use and side effects of oral contraceptives

4. All subjects responded truthfully to the questionnaire

Summary

Oral contraceptives are widely used by women in the United States. Concern has been expressed in the literature regarding the effects of oral contraceptives on a woman's ability to become pregnant as well as the possibility of bearing an infant with birth defects if conception occurs within the first two months after discontinuance. So that nurses may respond intelligently to these concerns, additional nursing research is needed.

Chapter I has provided an overview of the retrospective study undertaken to investigate conception after discontinuance of oral contraceptives. Homeostasis has formed the conceptual framework for this research study. Two hypotheses have been stated. Limitations, delimitations, and assumptions have been described.

Chapter II includes a review of current literature on the effects of oral contraceptives on post-contraceptive fertility, and the incidence of birth defects and spontaneous abortions following oral contraceptive use. Overviews of the concept of homeostasis and the alteration of the menstrual cycle by oral contraceptives are included.

Chapter III, Procedure for Collection and Treatment of Data, describes the setting, population, and sample. The procedures for protecting human subjects and collecting data are explained. A description of the pilot study and an explanation of the treatment of data are included in this chapter.

Chapter IV is the Analysis of Data. The statistics used to analyze the data are described and the findings are reported.

Chapter V, Summary of the Study, includes a review of the study and a discussion of the meaning of the

findings. Conclusions and implications drawn from the findings of the study are stated. Suggestions for further study are offered in this final chapter.

CHAPTER II

REVIEW OF LITERATURE

In the review of literature the concept of homeostasis is presented. The menstrual cycle and the effects of oral contraceptives are discussed. Current studies concerned with post-pill fertility, amenorrhea, and the teratogenic effects of oral contraceptives are reviewed.

Homeostasis

The concept of homeostasis had its origin in early history. According to Langley (1965) Hippocrates' teachings embraced aspects of the concept and recognized the presence of an internal environment. The teachings of Hippocrates and later Galen contended that man was composed of four humours; when these humours were in correct balance, man was healthy. Disease was the result of imbalance of the humours (Beland and Passos 1975). Hippocrates believed that disease was cured by natural powers (mechanisms) within the living organism and these were capable of returning the body to a normal state of health when an imbalance occurred (Langley 1965).

Bernard is acknowledged as the first to emphasize the role of the inner environment in the establishment and maintenance of steady states in the body. In 1878, Bernard introduced the proposition that cells lived in the fluids (blood, lymph, and tissue fluid) which he called the "milieu interieur." The maintenance of stability of this fluid was the objective of all vital activities (Beland 1975).

Cannon (1939) created the term homeostasis to describe the equilibrium that the internal environment maintains while adapting to change. Homeostasis implied a dynamic equilibrium rather than a statis state. Cannon stated:

> The coordinated physiological processes which maintain most of the steady states in the organism are so complex and so peculiar to living beings--involving, as they may, the brain and nerves, the heart, lungs, kidneys and spleen, all working cooperatively--that I have suggested a special designation for these states, homeostasis (1939, p. 24).

Homeostasis as originally conceptualized was limited to specific self-regulatory physiological processes.

Homeostasis is described as a process working through a system of specific and complimentary mechanisms by Peterson (1972). The biological activities that take place are controlled to a large extent by the

neuroendocrine system. The body fluids, according to Peterson, are ". . . the essential internal environment for the integration of homeostatic events" (1972, pp. 304). All living organisms are open systems which maintain themselves by the continuous and dynamic exchange of materials within their environment. The biological systems are markably constant in states of health. The normal biologic states are never in true equilibrium, but are instead in a balance within measured limits (Peterson 1972). Internal adaptation of the system occurs when the function of a body part is altered in response to change in another body part (Murray 1971). The ability of the human body to adapt to changes in the external and internal environment is required to maintain or establish a state of equilibrium. Homeostatic mechanisms maintain the internal environment in a steady state. The capacity to adapt to change is essential to optimum functioning of body system and health. If adaptation is faulty or inadequate, homeostatic balance is disrupted and illness might occur (Murray 1971).

Four features are characteristic of homeostatis mechanisms. First, homeostatic mechanisms are self-regulatory. If an imbalance occurs, mechanisms are activated automatically to restore equilibrium. The

autonomic nervous system and the endocrine system regulate homeostasis. These systems are generally involuntary, but they are also responsive to input from the external environment. Respiratory function is an example of the self-regulatory mechanism of homeostasis. In illness or disease, the self-regulatory function of homeostasis decreases or fails (Beland and Passos 1975, Guyton 1976).

Secondly, the mechanisms of homeostasis are compensatory in that body systems are capable of compensating for change and stress. For example, the cardiovascular system compensates for a drop in blood pressure with an increase in heart rate (Guyton 1976).

A third feature of homeostasis is that almost all physiologic functions are controlled by closed-loop negative feedback systems. If some factor increases or decreases, the negative feedback system is initiated to return the factor towards normal. Negative feedback is defined as when ". . . a change in one direction is counteracted or opposed by a change in the opposite direction" (Beland and Passos 1975, p. 58). Positive feedback, on the other hand, results in more of the same. The menstrual cycle is governed by a complex system of positive and negative feedback systems.

The fourth feature of homeostasis is that several negative feedback systems may be initiated to correct imbalances of homeostasis. An interrelationship of body systems exists. A change occurring in one system may be under the control of several negative feedback systems which function to compliment each other. Regulation of blood pH is an example of this homeostatic feature (Cannon 1939, Guyton 1976).

Peterson (1972) cautioned that disturbances in homeostasis may result from artificial control and manipulation of normal life processes. Exposure of the fetus to teratogens was cited by Peterson (1972) as an example of disrupting homeostasis. The action of teratogens depends on the genetic make-up of the mother and fetus. The extent of the effect by a teratogen ranges from no effect to fetal death. According to Peterson,

> a fundamental principle of teratology is the concept that congenital defects relate to interferences and injury to highly specific enzyme-substrate-inhibitor functions at the biochemical level of embryonic development (1972, p. 66).

Menstrual Cycle

Cannon (1939) did not include the reproductive system in his discussion of homeostasis; however, both Guyton (1976) and Langley (1965) proposed the

applicability of the concept of homeostasis to the reproductive processes. According to Langley (1965), complex mechanisms control the cyclic pattern of the female sex hormones; thus the concept of homeostasis was applicable. Guyton (1976) took a different view of the reproductive system stating the homeostatic function of reproduction was to ". . . generate new beings to take the place of ones that are dying" (p. 5).

Complex feedback systems control the menstrual cycle involving the hypothalamus, anterior pituitary and ovaries. The hypothalamus monitors the levels of ovarian hormones (estrogen and progesterone) in the blood stream. In response to low levels of ovarian hormones due to the shedding of the endometrial lining, a positive feedback action on the hypothalamus is believed to occur (Hatcher et al. 1978). The positive feedback action on the hypothalamus results in the production of luteinizing hormone-releasing factor (LH-RF) and follicle stimulating hormone-releasing factor (FSH-RF). These releasing factors act in turn on the cells of the anterior pituitary to secrete follicle stimulating hormone (FSH) and some luteinizing hormone (LH).

Follicle stimulating hormone (FSH) and luteinizing hormone (LH) are carried by the blood stream to the

ovaries where they stimulate the development and maturation of the graafian follicle. The secretion of estrogen is initiated in the follicle by the luteinizing hormone. The estrogen produced by the maturing follicle acts upon the endometrium to stimulate proliferation of the endometrium (proliferative phase). Cervical mucus changes also occur to permit the penetration of sperm. The liquid cervical mucus becomes increasingly abundant with high spinnbarkheit and ferning characteristics (Hatcher et al. 1969, Moghissi 1973, Guyton 1976).

As estrogen hormone levels increase with the development of the follicle, a negative feedback action on the hypothalamus and the anterior pituitary is initiated to suppress follicle stimulating hormone (FSH). A surge of luteinizing hormone (LH) occurs at mid-cycle in response to the high estrogen level. Ovulation occurs as a result of this surge. The release of the ovum from the mature graafian follicle marks the end of the proliferative phase of the menstrual cycle and the onset of the secretory phase. Following ovulation, the follicle stimulating hormone (FSH) level declines while the luteinizing hormone (LH) level remains constant. Under the influence of the luteinizing hormone (LH), the follicle transforms into the corpus luteum and begins

to secrete progesterone along with the continuing production of estrogen (Yen 1973, Guyton 1976, Hatcher et al. 1978).

Progesterone stimulates the continued thickening of the endometrium. Changes in the cervical mucus also occur under the influence of progesterone to decrease the ability of sperm to penetrate the cervical os. Cervical mucus becomes scant and viscous. Spinnbarkheit is low and ferning does not occur. If fertilization of the ovum does not take place, a negative feedback mechanism is initiated by the increased levels of progesterone and estrogen to suppress gonadotropin secretion. Progesterone inhibits luteinizing hormone-releasing factor (LH-RF) and luteinizing hormone (LH) while estrogen suppresses follicle stimulating-releasing factor (FSH-RF) and follicle stimulating hormone (FSH). Without the production of gonadotropins, the corpus luteum regresses and deteriorates. Decreasing progesterone and estrogen levels result in the necrosis of the endrometrium and the onset of menses (Moghissi 1973, Yen 1973, Guyton 1976, Hatcher et al. 1978).

If conception occurs, the corpus luteum does not degenerate. Instead, the corpus luteum is maintained by the luteotrophic hormone of pregnancy, human chorionic

gonadotropin (HCG). Human chorionic gonadotropin is secreted by the placenta eight days after conception. Luteal function continues until the placenta takes over the complete production of progesterone and estrogen. After eleven weeks, pregnancy can be maintained without the corpus luteum and luteal function gradually declines and the corpus luteum degenerates (Guyton 1976).

The menstrual cycle is influenced by the external as well as the internal environment. Langley stated

> . . . a wide variety of psychological stresses impinge upon the individual which can influence the input to the hypothalamus and thus importantly alter the endocrine balance (1965, p. 106).

According to Guyton (1976), dysfunction or cessation of the menstrual cycle as a result of emotional factors is not unusual. Thorn (1977) emphasized the effect of systemic disorders such as those with neurologic and endocrine causes (thyroid, adrenal, and diabetes mellitus), obesity and malnutrition in altering the menstrual cycle.

Oral Contraceptives

Oral contraceptives have become a widely accepted and popular method of contraception since 1960 when formal approval for the combination pill was given

by the United States Food and Drug Administration (Chez 1976). Two types of oral contraceptive formulations are currently used in the United States. A third type, the sequential pill, is no longer manufactured and distributed in the United States. The combination pill contains both estrogen and progesterone and is the most reliable contraceptive, almost 100 percent effective. The vast majority of women use the combination type pill (Mishell 1976b, Hatcher et al. 1978). The combination pill is taken once a day starting on the fifth day after the onset of menses for three weeks, with one week pill free. Mishell (1976b) stated that the combination pills containing 50 mcg of estrogen or less should be prescribed initially. The dosage of the pill should be the lowest effective dose and with an acceptable level of side effects (Mishell 1976b).

The second type of pill is the progestogen-only pill or minipill. The minipill contains a combination of progestogens and is without estrogen. The pill is administered everyday without pill-free intervals. According to Mishell (1976b), the minipill has fewer adverse metabolic effects common to pills containing estrogen. A disadvantage of the minipill is the high frequency of amenorrhea and irregular bleeding associated

with the lack of estrogen (Mishell 1976b, Hatcher et al. 1978). In relation to its effectiveness "the actual use/pregnancy rates are 2 to 8 percent" (Mishell 1976b, p. 15).

The sequential pill contained only estrogen for the first two weeks and for the third week, the pill contained a combination of estrogen and progesterone. In 1976 all pharmaceutical companies in the United States agreed to discontinue the production of the drug and the drug is no longer prescribed as a contraceptive (Mishell 1976b).

Oral contraceptives are believed to act directly on the hypothalamus-anterior pituitary-ovarian axis by suppressing gonadotropin secretions (Good and Kempers 1974). According to Guyton (1976), the surge of luteinizing hormone which occurs about thirteen days after the onset of menstruation is essential for ovulation to occur. The administration of either progesterone or estrogen or both is believed to inhibit the normal surge in the secretion of luteinizing hormone-releasing factor (LH-RF) and luteinizing hormone (LH), thus preventing ovulation (Guyton 1976). The primary action of estrogen in oral contraceptives is to suppress the production of follicle stimulating hormone (FSH) by

inhibiting the follicle stimulating hormone-releasing factor (FSH-RF) from the hypothalamus. Progesterone reduces the production of luteinizing hormone-releasing factor (LH-RF) in the hypothalamus as well as the secretion of luteinizing hormone (LH) (Chez 1976, Guyton 1976, Hatcher et al. 1978). Oral contraceptives act directly on the endometrium and cervical mucus. The progesterone component of the pill produces growth of the uterine lining and decreases the permeability of cervical mucus by sperm. The cervical mucus becomes thick and exhibits decreased ferning and spinnbarkheit (Bennett 1974, Chez 1976, Hatcher et al. 1978).

The minipill (progestogen only pill) does not inhibit ovulation as the estrogen containing pill does, rather ovulation and ovum fertilization may occur (Bennett 1974, Hubbard 1977). According to Mishell (1976b), ovulation is inhibited in only a third of the cycles. Pregnancy is prevented by the accelerated transport of the ovum and inhibition of implantation. Hostile cervical mucus produced by the action of progestins also prevents pregnancy (Bennett 1974, Hubbard 1977, Hatcher et al. 1978).

A woman's ability to conceive after discontinuing oral contraceptives is affected by adaptation to hormonal

changes and restoration of normal homeostatic balance. Adequate physiological adaptation should promptly return gonadotropin secretion to normal levels and restore homeostasis. Inadequate adaptation occurs occasionally and the return of fertility is delayed.

Post-Pill Fertility

Initial studies of post-pill fertility suggested a possible rebound effect following discontinuance of oral contraceptives (Mears and Grant 1962). Later studies by Mears (1968) and Taber (1968) refuted the rebound effect. Taber (1968) compared the fertility patterns following oral contraception and pregnancy. Taber (1968) proposed that because hypothalamic-ovarian axis is suppressed in both instances, a gradual return of ovulatory function can be expected to correspond with that following pregnancy.

A retrospective study by Peterson (1969) determined the length of time to conceive after oral contraception. Four hundred forty-two patients who had used oral contraceptives were compared with a control group of 699 women who had used another method of contraception. Among the 442 women studied, the length of oral contraceptive used ranged from 1 to 72 months.

Peterson (1969) reported that by the end of the first month, 30 percent of the women became pregnant, 46 percent by the second month, and 62 percent by the third month. Eleven percent required in excess of ten months to conceive, while 18 percent of the control group required longer than ten months. The range of the length of time to conceive for these women was ten to thirty-eight months and ten to seventy months, respectively (Peterson 1969).

Lefebvre (1970) reported that studies by Watts and Diddle concluded that the mean conception time is from 5.8 to 6.5 months with a range of 1 to 42 months following cessation of oral contraception. A retrospective study conducted by Robinson (1971) of 1,250 births noted that over 90 percent of the women under 30 years of age and 80 percent of those over 30 conceived in less than a year.

According to Tyler (1973), normal menstrual cycles should start within a few months after discontinuing oral contraceptives. The delay may be longer if prior to the use of oral contraceptives, the relationship between the hypothalamus-pituitary-ovarian axis is not normal. Tyler (1973) cautioned that once the oral contraceptives are discontinued, menses may be delayed

or irregular; therefore, those women with abnormal hypothalamus-pituitary-ovarian axis are not good candidates for the pill.

Korba and Heil (1975) investigated the return of fertility after discontinuance of Ovral in 6,806 women over an eight-year period. Seventy-eight percent of the women had regular menstrual periods with a mean length of 28.2 days prior to taking Ovral. The time to conceive was reported by cumulative percentages for the third, sixth, and twelfth menstrual cycles following cessation of contraception. According to Korba and Heil (1975), 38.5 percent conceived within three cycles, 85.4 percent within six cycles, and 95 percent within twelve cycles. The longest duration was eighty-five cycles.

Janerich, Lawrence, and Jacobson (1976) reviewed the data from the prospective study of the Royal College of General Practitioners to determine post-pill fertility patterns. A tri-modal pattern was noted after discontinuing oral contraceptives. Wolfers (1970) had previously reported observing a bi-modal pattern of fertility after analyzing data generated from studies by Westoff, Bumpass, and Ryder (1969). Wolfers (1970) noted that pregnancy appears more likely in the third month than the second and more likely in the fourth

month than the third. He assumed that there are two populations of pill users. One that is unaffected by the use of the pill and the other which experiences a carry-over of contraceptive effects of the pill for two or three months. Janerich, Lawrence, and Jacobson stated ". . . the results show that monthly conception-rates follow a consistently oscillatory pattern" (1976, p. 1052). A pattern with distinct peaks of conception-rates occurred every four months. The reason for the multi-modal pattern was unexplained. Janerich, Lawrence, and Jacobson (1976) speculated that the pattern may be a natural but unrecognized pattern or possibly a post-pill rebound phenomenon. A comparison of the monthly conception-rates among post-pill users and post-IUD users by Janerich, Lawrence, and Jacobson (1976) revealed no significant difference. The findings support those of Westoff, Bumpass, and Ryder (1969) that the time required for women to conceive after discontinuing oral contraceptives did not differ from women who had used other methods of contraception.

Amenorrhea

Amenorrhea has been defined as the absence of menses for one year. Post-pill amenorrhea has been

defined by Halbert and Christian (1969) as the absence of menses for three months; whereas Buttram et al. (1974) used six months as the determinant of amenorrhea after oral contraceptive use. Post-pill amenorrhea is presumed to be caused by over-suppression of the hypothalamic gonadotropin releasing-factors (Golditch 1972). Galactorrhea often accompanies amenorrhea. Buttram and associates (1974) viewed galactorrhea as an ominous sign of hypersuppression of the hypothalamus-pituitary-ovarian axis.

A retrospective study by Halbert and Christian (1969) investigated the relationship between the length of oral contraceptive use and amenorrhea after discontinuance. Thirty-five women with amenorrhea for three months or longer were studied. The most striking finding according to Halbert and Christian (1969) was a history of menstrual abnormality in twenty-five of the thirty-five women. Galactorrhea was present in ten women. Halbert and Christian (1969) concluded that women with a history of menstrual dysfunction may be predisposed to developing amenorrhea.

A comparison of women with amenorrhea after oral contraceptive use and women with secondary amenorrhea was initiated by Friedman and Goldfien (1969). Nineteen

women with amenorrhea and two women with oligomenorrhea were followed for up to four years. Nine of the women had galactorrhea. Friedman and Goldfien (1969) contended that the incidence of breast secretions was less in those women who had taken oral contraceptives, and that there was no evidence of a causal relationship between oral contraceptives and galactorrhea.

Lefebvre (1970) reported on an investigation by Sherman, who studied twenty-two women with secondary amenorrhea of at least twelve months duration following discontinuance of oral contraceptives. The endogenous gonadotropins were assayed. A majority of the women had low endogenous production of estrogens. A satisfactory response to treatment with clomiphene indicates that the cause of secondary amenorrhea was in the hypothalamus (Lefebvre 1970).

Golditch (1972) reported an incidence of post-pill amenorrhea of 2.2 percent per 1,000 among 20,000 oral contraceptive users. Forty-one women with post-oral contraceptive amenorrhea were followed. Ovulatory status was determined by basal body temperature and endometrial biopsy. The women were screened for pituitary tumor and adrenal and thyroid function measures. Gonadotropin levels were assayed. A high incidence of

menstrual dysfunction was noted in the group of women studied (Golditch 1972). Twenty-five percent of the women had taken oral contraceptives to regulate menses. Golditch (1972) cautioned that taking oral contraceptives to regulate menses does not insure that normal menstrual function will resume after discontinuing the pill. Hypothalamic suppression of prolactin-inhibiting factors was suggested by Golditch (1972) as a possible cause of galactorrhea.

Tyson, Andreasson, Huth, Smith, and Zacur (1975) reported a low incidence of galactorrhea (.89 percent) in 5,597 unselected gynecoloic patients. Analysis of the galactorrhea secretion samples for fat concentration demonstrated a ten times increase (35 percent) in fat content as compared with breast milk. Tyson et al. (1975) treated thirteen women with post-pill amenorrhea/ galactorrhea (PPAG) with ergocryptine. In all but one case cyclic gonadotrophin secretion resumed.

Successful treatment of post-pill amenorrhea was reported by Dickey (1977) with daily injections of human menopausal gonadotrophins (menotropins) for nine to twelve days followed by injections of human chorionic gonadotropin (HCG). Dickey (1977) warned that the treatment was expensive and may result in multiple

gestations. An investigation of fifty patients with post-pill amenorrhea and galactorrhea (PPAG) revealed no relationship to the length of time oral contraceptives were used. Dickey concluded that there was no benefit in taking women off the pill for a month or two every two or three years. Women who had used a pill with a high progestational potency had a greater incidence of PPAG; however, estrogen dosage was not related to PPAG. Dickey supported earlier studies suggesting women with menstrual dysfunction prior to oral contraception were at greater risk for PPAG.

A prospective data file is maintained by the Menstrual and Reproductive History (MRH) Research Program at the University of Minnesota. Berger, Taylor, and Treloar (1977) studied the records of 245 cases from the data file to investigate the duration of post-pill amenorrhea. Criteria for inclusion in the study were use of oral contraceptives between 1965 and 1969, recorded dates for discontinuance, and resumption of menses. Berger, Taylor, and Treloar found that 25 percent of the women resumed menses by day thirty-two, and 50 percent by day thirty-eight. Only seven women (2.9 percent) had not resumed menstruation by ninety days. Six women started menstruation between 90 and 120 days. One

woman resumed menses on day 220. Berger, Taylor, and Treloar (1977) estimated an incidence of post-pill amenorrhea as 1.1 to 1.7 per 100 women.

Teratogenic Effects of Oral Contraceptives

Teratogenic effects have been described by Peterson (1972) as a disturbance of homeostasis as a result of artificial control and manipulation. The extent of the effect of teratogens on the developing fetus depends on the genetic makeup of the mother and the fetus (Peterson 1972). Questions have been raised about the teratogenic effects of oral contraceptives. Ambani, Joshi, Vaidya, and Devi (1977) cautioned that teratogenic effects are difficult to document. As proposed by Ambani and associates, women who are genetically predisposed may have abnormal infants as the result of using oral contraceptives through two possible mechanism which are:

1. The contraceptive hormones or their metabolic products may act in conjunction with the pool of abnormal genes to trigger the development of a specific malformation.
2. Low metabolic clearance of the hormones in some women may lead to abnormal accumulation of hormones and/or their metabolic products (p. 795).

Ambani and associates (1977) hypothesized vitamins crucial to fetal growth may be deficient as a direct or indirect response to oral contraceptives. Decreases in the levels of vitamin B_{12}, folic acid, and pyridoxal phosphate are related to oral contraceptive use. A deficiency of folate has been known to cause abnormalities in experimental animals.

An early retrospective study by Robinson (1971) compared 1,250 births occurring in women who had previously used estrogen-progesterone contraceptives with a matched number of births occurring in women who had not used oral contraceptives. The results did not suggest an association between birth defects and oral contraceptive use. By 1974, a gradual accumulation of clinical reports and retrospective studies, according to Nora and Nora (1974), suggested the potential teratogenic effects of progesterone and estrogen. Nora and Nora concluded that if oral contraceptives did produce birth defects, it was at a low frequency in predisposed persons.

Nora and Nora (1974) described a pattern of multiple congenital anomalies that were associated with the use of oral estrogen and progesterone by the mother. The acronym used to describe these anomalies is VACTERAL, which stands for: V, vertebral; A, anal; C, cardiac;

T, tracheal; E, esophagus; R, renal; and L, limb. A retrospective study of children with esophageal atresia conducted by David and O'Callaghan in South-West England ". . . did not support the suggestion that oral contraceptives or oral pregnancy test hormones caused esopageal atresia alone or as part of the VACTEL association" (1974, p. 1236). The acronym VACTEL was used rather than VACTERAL. VACTEL association was not found in 345 cases of esophageal atresia, although 55 percent of the cases had other malformations (David and O'Callaghan 1974).

Janerich, Piper, and Glebatis (1974) retrospectively studied children with congenital limb-reduction comparing them with a corresponding number of normal children. An association between exposure to exogenous sex steroids during gestation and congenital limb-reduction was reported. The mothers of affected children tended to become pregnant while on a combination-type of oral contraceptives or immediately after discontinuation of the pill. An interesting finding reported by Janerich, Piper, and Glebatis (1974) was the sex-specificity effect in cases in which the hormones were taken during pregnancy. The affected infants of mothers who had become pregnant while on the pill and those who had taken

other types of orally administered sex steroids during pregnancy were all males. Janerich, Piper, and Glebatis (1974) raised the question as to whether the association of limb-reduction and the sex-specific effect are causal or secondary. Maternal predisposition was suggested as probably necessary since the great majority of pregnancies preceded by the use of oral contraceptives do not result in defective infants.

Heinonen, Slone, Monson, Hook, and Shapiro (1977) conducted a prospective cohort study of 50,282 mother-child pairs. Data obtained from the study on cardiovascular defects and use of female sex hormones were thoroughly analyzed. Among the 1,042 women who had taken female sex hormones during early pregnancy, 19 of their children had cardiovascular defects (18.2 per 1,000). In the 49,240 children not exposed to exogenous female hormones in utero, 385 had cardiovascular malformations (7.8 per 1,000). Heinonen et al. (1977) concluded that the association between in utero exposure to female sex hormones and cardiovascular malformation was significant ($P < .05$). According to Heinonen et al., exposure during the second and third lunar months of pregnancy was associated with congenital heart defects. No evidence of cardiovascular malformation was associated

with female sex hormone if initial exposure occurred after the fourth lunar month (Heinonen et al. 1977).

A five-year prospective study was conducted by Nora, Nora, Blu, Ingram, Fountain, Peterson, Lortscher, and Kimberling (1978) to investigate the possible teratogenicity of exogenous female hormones. The investigation included three case-control studies and one cohort study. Nora and associates (1978) reported that two of the prospective studies provided evidence of an association between maternal exposure to exogenous female hormones and congenital heart disease. The third prospective study, however, did not support the previous findings. The cohort study was conducted as a controlled single-blind prospective study during a three-year period. One hundred and eighteen women with documented first-trimester exposure to oral contraceptives were matched and paired with a control group. Eleven of the 118 women had infants with major malformations compared with 4 infants in the control group. The eleven infants had sixteen malformations, including three in one infant, which were consistent with the definition of VACTERAL.

Janerich (1975) scrutinized the findings of the prospective study by the Royal College of General

Practitioners and noted that 20.98 percent of pregnancies among ex-pill users resulted in abortions compared with only 12.28 percent among non-pill users. The adjusted rate, excluding induced abortions, was 13.37 for ex-pill users. Janerich (1975) observed that the abortion rate had not been adjusted for the non-pill users. The effects of oral contraceptives on subsequent pregnancies were retrospectively evaluated by Rothman (1977). According to Rothman (1977), lower rates of miscarriage and stillbirth were recorded for women who became pregnant within three years after oral contraceptive use. Among 3,221 pregnancies that occurred prior to pill use, there were 412 miscarriages and 12 stillbirths, while 163 miscarriages and 3 stillbirths occurred among 2,136 pregnancies within 3 years of oral contraception. Rothman (1977) cautioned that these findings should not be construed to mean oral contraceptives prevent stillbirths or miscarriages; rather the findings support the premise that oral contraceptive use prior to pregnancy does not threaten fetal life.

Studies by Alberman, Creasy, Elliott, and Spicer (1976) suggested a slight increase in chromosome abnormalities among early spontaneous abortions after discontinuing oral contraceptives. Alberman and

associates (1976) compared the karyotype of aborted fetuses of women who had and those who had not used oral contraceptives. The proportion of abnormal fetuses of women who had used oral contraceptives for more than eighteen months exceed 20 percent ($P = .01$).

A study of newborn infants and medically-induced abortions conducted by Klinger, Glasser, and Kava (1976) did not support a relationship between oral contraceptive use by the mother and chromosomal birth defects. No significant difference between age-adjusted rates of chromosome abnormalities and contraceptive history was found ($P > .10$ in all cases) (Klinger, Glasser, and Kava 1976).

Janerich, Flink, and Keogh (1976) reporting on a controlled study of pill use and Down's Syndrome, concluded that there is no increased incidence of Down's Syndrome in mothers who had taken oral contraceptives. The retrospective study included a group of 104 mothers of infants with Down's Syndrome and a matched group of mothers of normal infants. Janerich, Flink, and Keogh noted that fewer infants with Down's Syndrome were conceived during the first three months following discontinuation of oral contraceptives which they

attributed to an increased abortion rate of defective fetuses conceived after pill use.

An increased incidence of twinning was supported by a retrospective study conducted by Rothman (1977). A substantial increase in the risk of giving birth to twins exists when pregnancy follows pill use of at least six months and conception occurs within one month after discontinuance of pill use. According to Rothman (1977), of the 1,609 mothers in his study who conceived within one month after discontinuing oral contraceptives, 25 gave birth to twins (1.6 percent). A rate of 1.1 percent was recorded for the 2,614 women who had not used the pill.

Studies by Nora and Nora (1973); Janerich, Piper, and Glebatis (1974); Ambani et al. (1977); and Nora et al. (1978) raised the question as to the advisability of using hormonal tests for pregnancy. They contended the risks of inadvertent exposure is too great in comparison to the benefits from such tests. Ambani and associates (1977) implied the use of hormones for pregnancy testing is unjustified and may be unwise legally.

Although the association between congenital anomalies and oral contraceptive use by mothers is

difficult to document, investigators tend to view the higher rates of defects to be clinically significant especially for congenital cardiac malformations (Pill Taken During 1977). The Food and Drug Administration in 1977, required a warning of possible risks of birth defects on labeling information for the pill. In April 1978, the FDA required that detailed information for patients be given with each supply of pills (Hatcher et al. 1978). The literature warned that:

> Oral contraceptives should not be taken by pregnant women because they may damage the developing child. An increased risk of birth defects including heart defects and limb defects has been associated with the use of sex hormones, including oral contraceptives in pregnancy (Birth Control With 1978, p. 10).

The labeling information cautions of the risks of cancer in female children following the use of DES, an estrogen, as well as possible abnormalities of the urinary and sex organs of male offspring. The information booklet for Lo/Ovral also cautions the pill-taker of an increased incidence of miscarriage if pregnancy occurs soon after stopping the pill and suggests that the doctor may recommend the use of an alternate method of contraception for a short period after discontinuance. The booklet also reassures the woman that if she should become pregnant soon after stopping the pill and does not have

a miscarriage ". . . there is no evidence that the baby has an increased risk of being abnormal" (Birth Control With 1978, p. 11).

Summary

Homeostatic mechanisms are governed by complex feedback systems which are self-regulating and compensatory in nature. Disruption of homeostatic balance in a living organism may result from artificial control and manipulation of normal processes (Peterson 1972). The menstrual cycle is a self-regulatory process governed by a complex system of positive and negative feedback systems. Oral contraceptives alter the homeostatic equilibrium by acting directly on the hypothalamus-anterior pituitary-ovarian axis causing the suppression of gonadotropins. When oral contraceptive use is discontinued, adaptive processes restore the normal menstrual cycle and re-establish homeostasis. If the adaptive processes are inadequate or fail, disruption of homeostasis occurs resulting in infertility.

Studies of post-pill fertility suggest that most women conceive within a year after discontinuing oral contraceptives (Robinson 1971, Peterson 1972, Korba and Heil 1975). The mean conception time was 5.8 to 6.5

months (Lefebvre 1970). An unexplained cyclic pattern of fertility was noted by Wolfers (1970) and Janerich, Lawrence, and Jacobson (1976). Comparison studies of the time to conceive for pill users and those who use other methods of contraception did not differ significantly (Westoff, Bumpass, and Ryder 1969; Janerich, Lawrence, and Jacobson 1976).

Amenorrhea is believed to be caused by oversuppression of hypothalamic gonadotropin-releasing factors (FSH-RF and LH-RF). Galactorrhea may accompany amenorrhea. Studies by Halbert and Christian (1969), Golditch (1972), and Dickey (1977) suggested that women who have a history of menstrual dysfunction prior to oral contraceptive usage have an increased risk for amenorrhea and galactorrhea.

The effects of oral contraceptive usage prior to and during pregnancy on the developing fetus are difficult to document (Nora and Nora 1974, Ambani et al. 1977). A significant association between oral contraceptive usage and congenital heart disease (Heinonen et al. 1977) and an increased incidence of limb-reduction (Janerich, Piper, and Glebatis 1974) has resulted in warnings that hormonal pregnancy tests not be used, and

that an alternate method of birth control should be used for several months after discontinuing oral contraceptives.

CHAPTER III

PROCEDURE FOR COLLECTION AND TREATMENT OF DATA

The design of this study was retrospective. In a retrospective study, recall is used to find the relationship between phenomenon. The independent variable or variables are investigated after an event has occurred in an attempt to identify a causal relationship (Polit and Hungler 1978). Retrospective studies, according to Polit and Hungler, are ex post facto investigations. An ex post facto investigation differs from an experimental design in that the researcher is unable to control and manipulate the independent variables.

This study was a retrospective investigation to determine if the length of time a woman has taken oral contraceptives was related to the length of time for conception to occur after discontinuance. A questionnaire developed by the investigator was used to elicit data from the subjects (appendix A). The incidence of birth defects in infants whose mothers conceived during the first two months after discontinuance was also investigated. Data obtained from the infant's chart

regarding the presence of birth defects at the time of birth was recorded on the Infant Data Collection Sheet (appendix B).

Setting

This study was conducted in three general hospitals in a Southwestern metropolitan area of over one million in population. By using these three hospitals, the study involved clients from a wide range of socio-economic backgrounds, race, and age. The first, a large nonfederal government hospital, located in an inner city area with a capacity of approximately 800 beds and 100 bassinets; the second, a nonproprietary hospital located in a suburban area having a bed capacity of approximately 213 with 29 bassinets; and the third, a proprietary hospital with approximately 275 beds and 25 bassinets, situated in a residential area, were the sites of data collection. The postpartum units of the three hospitals have a patient capacity of approximately 140, 30, and 32 patients, respectively.

Population and Sample

The sample was selected from postpartum women and their infants in three metopolitan hospitals during November and December 1979. Convenience sampling was

utilized for the pilot and major research investigation. A criterion for inclusion in the study was that the women had used oral contraceptives prior to pregnancy. All eligible women were considered for inclusion in this study. Written permission of all participants in the study was obtained after the women had been given an explanation of the purpose and methodology of the study. A sample of ninety women and their infants was obtained for the study.

Protection of Human Subjects

Approval was obtained from the Human Research Committee at Texas Woman's University to conduct this study (appendix C). The research proposal was presented to the Directors of Nursing at the three general hospitals selected for the study. Written permission was granted to collect data on the obstetrical units of the three hospitals (appendix D).

A verbal and written explanation of the study and the rights of research subjects was given to all women who participated in the pilot or research study (appendixes E and F). The participant was assured that all information was confidential and that no names or other form of identification would be used. The woman

was informed that she could withdraw from the study at any time even though a consent form had been signed. If the woman agreed to voluntarily participate in the study, written permission was obtained. Additional consent was obtained from the mother for her infant to act as a subject for the research investigation. A copy of the written permission forms was retained by all women participating in the research study.

Instrument

A questionnaire developed by the investigator was used to obtain data for this study (appendix A). The information elicited from the questionnaire included age, menstrual history, age oral contraception was first initiated, length of continuous use of oral contraceptives, length of time until conception occurred, coital frequency, and use of another method of contraception after discontinuance of oral contraceptives. Information obtained from questions seven and ten provided data for nominal level measurement. Ordinal level data were provided by questions one, two, three, and nine. Interval level measurement data were obtained from questions four through six, eight, and eleven.

An Infant Data Collection Sheet was used to record data from the infant's chart regarding the presence of birth defects (appendix B). In order to correlate the data obtained from the mother with that of the infant, the questionnaire was coded with a number. The same number was placed on the Infant Data Collection Sheet. No record of the woman's and her infant's name was retained and anonymity was maintained.

In order to determine "face validity," the questionnaire was reviewed and critiqued by a panel of nurses knowledgeable in family planning. The panel included two Master's prepared Maternal Child Health Nursing graduate faculty members, a Master's prepared Medical-Surgical undergraduate nursing faculty member, and a Maternal Child Nursing graduate student.

A pilot study was conducted to establish the validity of the tool, the methodology of collecting data, as well as the statistical treatment of data. Based on the results of the pilot study, two revisions of the questionnaire were made. Question two was reworded to improve clarity and sentence structure. In order to obtain additional information as to the reason the woman discontinued oral contraceptives, question seven was changed from a multiple-choice to an open-ended question.

Key words such as "prior," "first," and "last," were underlined to give emphasis and improve clarity. The revised questionnaire (appendix A) was reviewed and approved by a panel of experts. The panel of experts included two Master's prepared Maternal Child Health graduate nursing faculty and a Master's prepared statistician.

Data Collection

The procedure followed during this retrospective study was, first, the interviewer introduced herself to the woman and determined if she had used oral contraceptives prior to pregnancy. If the woman had used oral contraceptives, an oral explanation of the purposes of the study was given. If the woman indicated a willingness to voluntarily participate in the study, written permission was obtained. The questionnaire was completed in the presence of the researcher. The completed questionnaire was immediately placed in a manila envelope to ensure confidentiality. The researcher then reviewed the chart of the woman's infant to determine the birth date and the presence of any birth defects.

Pilot Study

A pilot study was conducted during a one-week period in October 1979 at the three general hospitals selected for the research investigation. Fifteen postpartum women who met the stated criteria, five from each setting, participated in the pilot study. The purposes of the pilot study were to (1) validate the questionnaire, (2) rehearse the method of selecting subjects and the procedure for explaining the study, and (3) test the statistical treatment of data.

As a result of the pilot study, minor revisions in the questionnaire were made to clarify and improve sentence structure (appendix A). The proposed procedure for selecting subjects and explaining the study proved to be satisfactory without revision (appendix E). Data obtained from the pilot study were tabulated and analyzed in order to test the statistical treatment of data. The results of the findings for the pilot study were not included in the final research report.

The data from the pilot study were summarized. An age distribution of fifteen women participating in the pilot study ranged from 17 to 32 years with a mean age of 22.4 years. The age when subjects first used oral contraceptives ranged from 15 to 22 years with a mean of

17.9 years. The mean length of time the subjects in the pilot study had taken oral contraceptives was 30.2 months with a range of 2 to 72 months. The length of time to conceive ranged from 0 to 36 months with a mean of 10.3 months. The Pearson product-moment correlation was used to determine if a significant association existed between the independent variable, length of time oral contraceptives were used and the dependent variable, time to conceive. The length of time to conceive was adjusted for the three women who had used an alternate method of contraception following discontinuance of the pill. The Pearson product-moment correlation gave an $\underline{r}^2$ value of -.2520 (P = .0473) which was significant and indicated a negative linear relationship.

Data were insufficient to test the relationship between the incidence of birth defects and the time of conception. All of the women in the pilot study gave birth to normal infants. No infant was born with a defect as defined for this study.

Treatment of Data

Computer analysis of the data was performed by a statistician. A .05 level of significance was used in the analyses. Descriptive statistics for age,

menstrual frequency and regularity, and coital frequency of the women participating in the study was presented in tabular form. Descriptive statistics relating to usage of oral and alternate methods of contraception were presented. The Pearson product-moment coefficient of correlation was used to determine the relationship between the length of time taking oral contraceptives and the length of time to conceive. The length of time to conceive was adjusted for those subjects using an alternate method of contraception after discontinuing oral contraceptives. Correlations were obtained for the unadjusted and the adjusted length of time to conceive. Scatter diagrams of the data were plotted to graphically represent the correlations and were included in appendixes G and H. A multiple-regression analysis was used to further investigate the relationship between time to conceive with age of initial use of oral contraceptives, menstrual frequency and regularity, and coital frequency.

A comparison was made of the incidence of birth defects in infants born to women who conceive within two months of discontinuing oral contraceptives and those who conceive after the second month. The age of mother, age of initial use of oral contraceptives, menstrual frequency and regularity, and length of time on

oral contraceptives were described. A comparison between the mothers of infants with birth defects and those having infants without defects was made using the mean values and range of the descriptive variables.

CHAPTER IV

ANALYSIS OF DATA

A retrospective study was conducted to determine the relationship between the length of time on oral contraceptives and the time to conceive after discontinuance. The presence of birth defects in infants born to women who have used oral contraceptives was also investigated. The findings are reported in chapter IV. The statistics used to analyze the data are included.

Demographic data of age, menstrual history, and oral contraceptive usage were determined. The relationships between time to conceive, coital frequency, menstrual frequency and regularity, and age of initial use of oral contraceptives were analyzed. The incidence of birth defects in infants of women who conceived within two months after discontinuance of oral contraceptives was compared with infants of women who conceived after the second month.

The data collection period was from November 6, 1979 through December 4, 1979. Questionnaires were completed by ninety postpartal women. Data regarding the presence of birth defects were obtained from the

charts of infants whose mothers had completed the questionnaire. This chapter will present the statistical analysis of the data.

Description of Sample

The sample was composed of ninety women and their infants. The women were patients on the postpartum unit of one of the three general hospitals, and the infants were in the newborn nursery at the same hospital. The age distribution of the postpartum women who participated in the study ranged from seventeen to thirty-four years. The mean age of the women was 23.6 years, the median was 22.4 years, and the mode was 21 years. Table 1 shows the age distribution of postpartum women in the sample.

The menstrual histories of the women are summarized in tables 2 and 3. All of the women in the sample reported the establishment of menstrual periods prior to starting oral contraceptives; although sixteen women (17.8 percent) indicated their periods were unpredictable or irregular. The majority of women, as shown in table 2, described their menstrual periods prior to oral contraception as regular (45.6 percent) or usually regular (36.7 percent). Prior to taking birth

control pills, the mean length of time between periods was twenty-eight days (see table 3).

TABLE 1

AGE DISTRIBUTION OF PARTPARTUM WOMEN IN SAMPLE

Age in Years	Number	Percentage of Sample
17 - 18	6	6.7
19 - 20	18	20.0
21 - 22	22	24.4
23 - 24	14	15.6
25 - 26	6	6.7
27 - 28	9	10.0
29 - 30	7	7.7
31 - 32	4	4.4
33 - 34	4	4.4

N = 90; Mean = 23.6; Mode = 21; Median = 22.4; Range = 17-34.

The age when the women in the sample first started taking oral contraceptives ranged from 14 to 29 years, with the mean age of 18.7 years. Eighty women (89 percent) had taken oral contraceptives prior to the age of twenty-two years. Table 4 reflects the age distribution of the women in the sample for initial use of oral contraceptives.

TABLE 2

REGULARITY OF MENSTRUAL PERIODS PRIOR TO TAKING ORAL CONTRACEPTIVES

Menstrual Regularity	Number	Percentage of Sample
Always regular	41	45.6
Usually regular	33	36.7
Unpredictable	16	17.8
No periods	0	0.0

N = 90.

TABLE 3

INTERVAL BETWEEN MENSTRUAL PERIODS PRIOR TO TAKING ORAL CONTRACEPTIVES

Interval	Number	Percentage of Sample
Less than 28 days	19	21.1
28 - 30 days	59	65.6
31 - 35 days	5	5.6
36 - 90 days	5	5.6
Greater than 90 days	2	2.2

N = 90; Mean = 28 days.

TABLE 4

AGE ORAL CONTRACEPTION FIRST INITIATED

Age in Years	Number	Percent of Sample
14 - 15	8	8.9
16 - 17	25	27.8
18 - 19	31	34.5
20 - 21	16	17.8
22 - 23	3	3.3
24 - 25	3	3.3
26 - 27	1	1.1
28 - 29	3	3.3

N = 90; Mean = 18.7; Median = 18.02; Mode = 18; Range = 14-29.

The frequency distribution for the length of time oral contraceptives were taken by the women in the sample is summarized in table 5. The duration of oral contraceptive usage ranged from one month to ninety-six months. The mean length of time the women took oral contraceptives was 28.9 months, the median was 22.2 months, and the mode was 24 months.

The reasons stated by the women for discontinuing oral contraceptives are categorized in table 6. Oral contraception was discontinued by forty-three women

TABLE 5

LENGTH OF TIME ORAL CONTRACEPTIVES WERE TAKEN BY THE SAMPLE

Months	Number	Percentage of Sample
1 - 12	28	31.1
13 - 24	21	23.3
25 - 36	21	23.3
37 - 48	5	5.6
49 - 60	7	7.8
61 - 72	3	3.3
73 - 84	1	1.1
85 - 96	4	4.5

N = 90; Mean = 28.9; Mode = 24; Median = 22.2; Range = 1-96.

(47.8 percent) in order to become pregnant, eight women became pregnant while on the pill (8.9 percent). Sixteen women (17.8 percent) stopped because of side effects experienced while taking birth control pills. Other reasons given for discontinuing oral contraception were concern about the safety of the pil, two women; forgot to take their pills, four women; unable to obtain pills, five women; quit for no specific reason, nine women; and sexual inactivity, one woman. Two women did not respond to the question.

TABLE 6

REASONS STATED BY THE WOMEN FOR DISCONTINUING ORAL CONTRACEPTIVES

Reason	Number	Percentage
Desired to become pregnant	43	47.8
Became pregnant on the pill	8	8.9
Developed side effects	16	17.8
Nausea	5	
No periods/irregularity	5	
Headache/migraine	3	
Loss of hair	1	
Low libido	1	
Infection	1	
Concerned about safety	2	2.2
Forgot to take pills	4	4.4
Unable to obtain pills	5	5.6
No specific reason	9	10.0
Sexual inactivity	1	1.1
No reason given	2	2.2

N = 90.

The frequency of coitus for women in the sample population ranged from less than four to more than

eighteen times per month (see table 7). Fifty-two percent of the women had coitus ten or more times a month.

TABLE 7

COITAL FREQUENCY AFTER DISCONTINUANCE OF ORAL CONTRACEPTIVES

Frequency	Number	Percentage
Less than 4	14	15.6
4 - 6	15	16.7
7 - 9	14	15.6
10 - 12	12	13.2
13 - 15	9	10.0
16 - 18	11	12.2
Over 18	15	16.7

N = 90.

Table 8 summarizes the length of time for the women in the sample to conceive after discontinuing oral contraceptives. The mean time for conception to occur after the women stopped taking birth control pills was 5.5 months. The length of time for conceiving ranged from less than a month to twenty-four months. Eight women became pregnant while still taking birth control

pills, and one woman became pregnant within two weeks of discontinuance.

TABLE 8

TIME TO CONCEIVE AFTER DISCONTINUING ORAL CONTRACEPTIVES

Months	Number	Percentage of Sample
Less than 1	9	10.0
1 - 3	38	42.2
4 - 6	19	21.2
7 - 9	7	7.7
10 - 12	6	6.7
13 - 15	6	6.7
16 - 18	1	1.1
19 - 21	0	0.0
22 - 24	4	4.4

N = 90; Mean = 5.5; Median = 3.3; Mode = 2.0; Range = 0-24.

Alternate methods of birth control were used by sixteen women (18.9 percent) after discontinuing oral contraceptives. Seventy-four women (81.1 percent) did not use an alternate form of contraception. The length of time each of the women used an alternate form of contraception ranged from 1 month to 13 months with the mean

length of 4.2 months (see table 9). Fifty percent of the women (eight) used an alternate method two or less months. Table 10 illustrates the type of contraceptive method employed by the sixteen women who used an alternate form of birth control after discontinuing the pill.

TABLE 9

LENGTH OF TIME AN ALTERNATE METHOD OF CONTRACEPTION WAS USED AFTER DISCONTINUING ORAL CONTRACEPTIVES

Months	Number	Percentage of Sample
1 - 2	8	50.0
3 - 4	2	12.5
5 - 6	2	12.5
7 - 8	0	0.0
9 - 10	2	12.5
11 - 12	1	6.25
13 - 14	1	6.25

N = 16; Mean = 4.2.

Eighty-six women in the sample gave birth to infants without birth defects. Two sets of twins were included in this group. Infants with birth defects, as defined for this study, were born to four women in the sample (4.4 percent). Subject one gave birth to an

TABLE 10

TYPE OF ALTERNATE METHOD OF CONTRACEPTION USED AFTER DISCONTINUING ORAL CONTRACEPTIVES

Method	Number
Foam	6
Condom	4
Foam and Condom	1
Suppository	2
Douche	3
Rhythm	1

N = 16.

infant with hip dysplasia. Metatarsus adduction was assessed in the infant born to subject two. The third subject's infant had an extra digit of the left foot. Multiple defects which included cleft lip, clef palate, and hydrocele were present in the fourth subject's infant. No incidence of cardiac disorders or limb-reduction were found in the infants assessed for this study.

Table 11 provides a comparison of descriptive data for the four subjects in the sample who gave birth to infants with birth defects. The age of the mother, the age oral contraceptives usage was first initiated, the length of time to conceive after discontinuing oral contraceptives, and the length of time an alternate

TABLE 11

COMPARISON OF DATA FOR THE FOUR SUBJECTS IN THE SAMPLE WHO BORE INFANTS WITH BIRTH DEFECTS

Variable	Subjects				Mean
	1	2	3	4	
Age	19 years	20 years	28 years	31 years	24.5
Age initially used oral contraceptives	17 years	19 years	16 years	25 years	19.3
Length oral contraceptives used	10 months	3 months	12 months	60 months	21.5
Time to conceive	3 months	3 months	2 months	14 months	5.5
Used alternate method	1 month	0 month	0 month	10 months	

N = 4.

method of birth control was used after discontinuing oral contraceptives are shown in table 11.

The age distribution of women who gave birth to infants with birth defects ranged from 19 to 31 years; the mean age was 24.5 years. The age oral contraceptives were first used ranged from 16 to 25 years; the mean age was 19.25. The length of time oral contraceptives were used by these subjects ranged from 3 to 60 months with a mean length of 21.25 months. The length of time to conceive for those women who had infants with birth defects ranged from two to fourteen months. One woman conceived during the second month after discontinuing oral contraceptives, while two women conceived during the third month. An alternate method of birth control was used by two women after discontinuing oral contraceptives for one and ten months, respectively.

Findings

Time to Conceive After Oral Contraceptive Use

Hypothesis one stated that there is no significant relationship between the length of time taking oral contraceptives and the length of time to conceive. To test hypothesis one, frequency distributions of the variables were determined and Pearson product-moment

correlation was used to determine if significant association existed between the variables. For analysis, significance was declared at the .05 level ($P < .05$). A regression analysis was used to further investigate the relationship between the time to conceive with the length of time taking oral contraceptives, the age of initial usage, menstrual frequency and regularity, coital frequency, and time on an alternate method of contraception.

The Pearson product-moment correlation was employed to determine the relationship between the dependent variable, length of time to conceive (see table 5), and the independent variable, length of time on the pill (see table 8). The means for these variables were computed, 5.47 months and 28.86 months, respectively. Computation using the Pearson product-moment correlation gave an r^2 value of .0223 and an F value of 2.05 ($P = .156$), which is not significant. The coefficient of determination, r^2, is the portion of variance in one variable which may be said to be predictable from another variable. Thus only 2.3 percent of the time it takes to conceive can be explained by the length of time on oral contraceptives.

The scattergram (appendix G) shows a slight positive linear relationship of the variables, length of time on the pill, and time to conceive (slope = .0377), although not a significant ($P > .05$) relationship. A regression line was drawn to show the estimate of predicted relationship between the length of time on the pill and the time to conceive.

Sixteen women had used an alternate form of birth control from one to thirteen months after discontinuing oral contraceptives (see table 9). The time to conceive was adjusted for those women who had used an alternate method of birth control. The interval was measured in months from the time of discontinuance of contraceptive practice to the time of conception. The relationship between the adjusted time to conceive and the length of time on oral contraceptives was then determined by the use of the Pearson product-moment correlation. The adjusted mean for the variable, time to conceive, was 4.68 months. A r^2 value of .003 and an F value of 0.29 were obtained. These values were not significant and were less significant than the unadjusted time to conceive.

The scatter diagram indicated a linear relationship which was not significant (appendix H). A

horizontal regression line implied that the adjusted length of time to conceive did not depend on the length of time on oral contraceptives. The null hypothesis one was not rejected.

Stepwise multiple regression analysis was employed to determine the effect of several independent variables on the length of time to conceive. The predictor variables used in the analysis were (1) age of initial usage of oral contraceptives, (2) frequency of menstrual periods prior to oral contraceptive usage, (3) regularity of menstrual periods prior to oral contraceptive usage, and (4) coital frequency. The length of time to conceive was adjusted for those women who used an alternate method of contraception after discontinuing oral contraceptives.

Stepwise multiple regression analysis provides a mechanism by which to make predictions about phenomena. Table 12 shows the $\underline{R}^2$ and $\underline{F}$ values from the analysis of the predictor variables. The multiple coefficient of determination value ($\underline{R}^2$) shows the percent of the variance of the adjusted length of time to conceive that is accounted for by the predictor variables. In stepwise multiple regression, predictors are entered into the regression equation sequentially in the order which

TABLE 12

STEPWISE MULTIPLE REGRESSION ANALYSIS OF THE PREDICTOR VARIABLES ON THE ADJUSTED LENGTH OF TIME TO CONCEIVE

Variable	R^2	F Value	Significance
Coital frequency	.0506	6.886	P < .01
Frequency of menstrual periods	.1042	4.83	P < .031
Age of initial use of oral contraceptives	.1059	0.163	N.S.
Regularity of menstrual periods	.1060	0.012	N.S.

N = 90.

produce the greatest increment in R^2 (Polit and Hungler 1978). The first variable entered was coital frequency (R^2 = .0506). The second variable was frequency of menstrual periods prior to use of oral contraceptives, which increased the R^2 to .1042. The next two variables, age of initial oral contraceptive usage and regularity of menstrual periods, increased the R^2 to .1060. The F value for coital frequency was 6.886 (P < .01). Frequency of menstrual periods prior to oral contraceptive use had an F value of 4.83 (P < .031), which was significant. The last two variables had F values of

.163 and .012, which were not significant. Using the two significant variables, the regression equation is:

$$\text{Adjusted Length of Time to Conceive} = -.7074 \times (\text{coital frequency}) + .1566 \times (\text{frequency of menses})$$

Using the regression equation with the two predictor variables, only 10 percent of variation in the length of time to conceive can be explained.

Birth Defects

Hypothesis two stated that there is no significant increase in the incidence of birth defects in infants born to women who conceive within the first two months after discontinuing oral contraceptives and those born to women who conceive after the second month. The relationship between the variables, incidence of birth defects and time of conception, was compared.

Infants with birth defects were born to four women in the sample population (see table 11). Eighty-six women gave birth to infants without defects as defined for this study. The two sets of frequencies, the time to conceive and the incidence of birth defects, were compared (see table 13). The time to conceive was divided into three time periods: (1) less than one month, (2) one to two months, and (3) greater than two

months. There was no significant increase in the incidence of birth defects in infants born to women who conceive within the first two months after discontinuing oral contraceptives, and the null hypothesis was not rejected.

TABLE 13

COMPARISON OF THE TIME OF CONCEPTION WITH THE FREQUENCY OF BIRTH DEFECTS IN THE SAMPLE

Time of Conception	Without Birth Defects	Birth Defects
Less than 1 month	9	0
1-2 months	24	1
Greater than 2 months	53	3
Total	86 (95.6%)	4 (4.4%)

N = 90.

A comparison was made between the mothers of infants with birth defects and those with infants without defects using the mean values and range of the variables (see table 14). The mean age of mothers with birth defects was 24.5, which was slightly older than the mothers without defects, 23.5 years. The mean age when oral contraceptives were first initiated by the group of

TABLE 14

COMPARISON OF VARIABLES FOR MOTHERS OF INFANTS WITH BIRTH DEFECTS AND WITHOUT DEFECTS USING MEAN VALUES AND RANGE

Variable	With Defects N = 4		Without Defects N = 86	
	Mean	Range	Mean	Range
Age	24.5 years	19-31	23.5 years	17-34
Age of initial use	19.3 years	16-25	18.6 years	14-28
Length of oral contraceptive use	21.5 months	3-60	29.2 months	1-96
Time to conceive	5.5 months	2-14	5.5 months	0-24

N = 90.

mothers of infants with birth defects was 19.3, and for the mothers of infants without defects was 18.6, with a range of 16 to 25 and 14 to 28, respectively. The length of time on oral contraceptives ranged from 3 to 60 months with a mean time of 21.5 months for the group with birth defective infants. The no defect group used oral contraceptives for 1 to 96 months with a mean of 29.2 months. The time to conceive ranged from 2 to 14 months for the birth defect group and 0 to 24 months for the other group. The mean time to conceive for both groups was the same, 5.5 months.

Summary of Findings

The relationship between the length of time taking oral contraceptives and the length of time to conceive was determined using the Pearson product-moment correlation. An F value of 2.05 was obtained, which was not significant ($P = 1.56$). When the length of time to conceive was adjusted for those subjects who used an alternate method of birth control after discontinuing oral contraception an r^2 value of .003 and an F value of .29 were obtained, which were not significant ($P < .05$). The null hypothesis was not rejected.

A stepwise multiple regression was employed to determine the effects of four independent variables. These predictor variables were stepped in order of greatest increment in R^2 as follows: (1) coital frequency, (2) frequency of menstrual periods prior to use of oral contraceptives, (3) age of initial usage, and (4) regularity of menstrual periods prior to use of oral contraception. The F values for coital frequency ($F = 6.886$) and frequency of menstrual periods ($F = 4.83$) were significant at $P < .01$ and $P < .03$, respectively. The predictor values, age of initial usage, and regularity of menses, were not significant.

The relationship between the incidence of birth defects in infants born to women who conceive within the first two months after discontinuing oral contraceptives and those infants born to women who conceive after the second month was compared. The null hypothesis was not rejected.

CHAPTER V

SUMMARY OF THE STUDY

Oral contraceptives are the most popular form of reversible contraception used by women in the United States. As more women are using oral contraceptives for longer periods of time, concern has been voiced as to the effect of long-term use on post-conception fertility and possible risks to the fetus.

Summary

Two questions were proposed in this retrospective study. First, was there a relationship between the length of time oral contraceptives were used and the time to conceive? Second, was there an increased incidence of birth defects in infants of women who conceived within the first two months after discontinuing oral contraceptives compared to those who conceive after the second month?

Permission to conduct the study was obtained from Texas Woman's University Committee for Human Research and from the agencies participating in the study. The obstetrical units at three general hospitals located in a Southwestern metropolitan area were the sites

for data collection. Convenience sampling was utilized. The sample for the study was comprised of ninety women and their infants. All of the women were admitted to the post-partum unit following delivery.

Each woman who participated in the study was given an oral and written explanation of the study. Written permission was obtained from each woman for herself and her infant to participate in the study.

A questionnaire developed by the investigator was used to elicit data. Information regarding the presence of birth defects was recorded from the infant's chart. A pilot study comprised of fifteen subjects and their infants, five from each hospital, was conducted to validate the questionnaire and test the interview procedures and statistical treatment of data. Minor revisions of the questionnaire were made following the pilot study. The revised questionnaire was reviewed and approved by a panel of experts. Data were collected over a six-week period of time.

Descriptive statistics were presented in tabular form. The Pearson product-moment correlation was used to determine the relationship between the length of time oral contraceptives were used and the length of time to conceive. A stepwise multiple regression analysis

was employed to determine the relationship of the time to conceive and the predictor variables: coital frequency, frequency and regularity of menstrual cycle prior to oral contraceptive use, and the age of initial use of the pill. A comparison of frequencies was used to analyze the relationship between the time of conception and the incidence of birth defects. Mean values and ranges were used to compare the mothers of infants with defects and those with infants without defects.

Discussion of the Findings

Analyses by the Pearson product-moment correlation shows a low correlation ($P > .05$) between the time to conceive and the length of time oral contraceptives were used. The predictor variable, length of time oral contraceptives were used, explains only 2.3 percent of the time to conceive. Sixteen women in the sample had used an alternate method of contraception for one to fourteen months. When the time to conceive was adjusted for the use of an alternate method of contraception, the relationship was found to be less significant ($P > .10$). As a predictor variable the adjusted length of time to conceive would account for less than 1 percent of the time to conceive. A horizontal

regession line was plotted on the scatter diagram (appendix H) which implied that the adjusted length of time to conceive was not related to the length of time oral contraceptives were used. The data from this study supported the findings of other studies that conception time is not related to the length of time of oral contraceptive usage (Tabers 1968, Halbert and Christian 1969, Peterson 1969, Robinson 1971, Korba and Heil 1975, Dickey 1977). Eighty-eight percent of the women in the present study conceived within one year after discontinuing oral contraceptives which also supports these earlier studies. The mean time to conceive for the women in the present study was 5.5 months, which supports the findings reported by Lefebvre (1970) that the mean conception time is 5.8 to 6.5 months.

A stepwise multiple regression was employed to determine the effects of the variables, coital frequency, regularity and frequency of menstrual cycle prior to oral contraceptive use, and the age of the initial use of the pill on the length of time to conceive. The variables, coital frequency, and frequency of menstrual periods were found to be statistically significant, and as predictor

variables they explain 10 percent of the length of time to conceive. Applying the variables to the predictor equation, it is apparent that the greater the frequency of coitus, the less time to conceive and conversely, an increase in the interval between menstrual periods increases the time to conceive. The variables, age of initial use, and the regularity of menstrual periods were not significant ($P < .05$).

Fifty-two percent of the women in the sample had coitus ten or more times per month. The median was seven to nine times per month. These findings are similar to those reported in a study by Westoff, Bumpass, and Ryder (1969) who reported an increased frequency of coitus in pill users with a mean frequency of 9.2 times per month compared with 6.6 times per month for women using other methods of contraception. Coital frequency of the four women who took twenty-two to twenty-four months to conceive ranged from less than four to seven to nine times per month. The woman who used an alternate method of contraception had the highest frequency of coitus (seven to nine times). One woman did not respond to the question of coital frequency. Fourteen women had a coital frequency of less than four times per month. The length of time to conceive ranged from less than

1 month to 24 months with a mean of 8.8 times. Two women became pregnant while on the pill. None of the women used an alternate method of birth control.

The mean interval between menstrual periods prior to taking oral contraceptives was twenty-eight days. A significant relationship was determined between the frequency of menstrual periods and the length of time to conceive. As the interval between periods increased, the time to conceive increased. This finding concurs with the studies of Dickey (1977) and Golditch (1972), which show a relationship between menstrual dysfunction prior to oral contraceptive use and increased risk of a delay in the return of menses and fertility.

The relationship between the time of conception and the incidence of birth defects was not found to be significant ($P > .05$). Eight women in the study conceived while on the pill. No birth defects were assessed in the infants born to the eight women. As Ambani et al. (1977) and Nora and Nora (1974) have cautioned, the teratogenic effects of oral contraceptives are difficult to document. According to Nora and Nora the "available data suggest that, if progesterone/estrogen produces malfunctions, it is at a low frequency rate probably acting on predisposed persons" (1974, p. 732). Because of the

the small sample size of this study, one cannot conclude that oral contraceptives are not teratogenic.

Two pairs of twins were born to the women in the sample (2.2 percent). No data were ascertained as to family history of twinning. One mother of twins conceived one month after discontinuing oral contraceptives and the other mother of twins conceived four months after discontinuance. The data from this study supports the findings of Rothman (1977) that there is an increased risk for twinning after discontinuing oral contraceptives. The incidence of twins in women who conceived one month after discontinuance of the pill had a twinning rate of 1.6 percent compared to 1.1 for women who had used another method of contraception.

Conclusions and Implications

The following conclusions resulted from this study:

1. There is no relationship between the length of time to conceive and the length of time of oral contraceptive usage

2. There is a relationship between the frequency of coitus and the length of time to conceive, the greater the frequency, the less time to conceive

3. There is a relationship between the frequency of menstrual periods prior to the use of oral contraceptives and the length of time to conceive, the longer the interval, the greater the time to conceive

4. The sample size was too small to draw conclusions as to the teratogenic efforts of oral contraceptives prior to and during pregnancy

Several implications for nursing practice may be concluded from this study. The nurses need to be aware of their responsibility in assessing and counseling women regarding family planning and more specifically in the use of oral contraceptives. Another implication related to the nurse is the need for increased knowledge and understanding of various methods of birth control in order to give adequate counseling; therefore, basic nursing education and continuing education need to emphasize this area.

A detailed history and complete physical examination should be performed prior to providing oral contraceptives. The history should include a detailed gynecological and menstrual history. Women with a history of amenorrhea, oligomenorrhea, or irregular menses should be cautioned of possible delay in the return of menses and fertility after oral contraceptive

use. Prolonged amenorrhea and infertility may result from faulty or inadequate adaptation of homeostatic mechanisms.

The nurse should assess a woman's knowledge of anatomy and physiology and adapt the teaching to the social and educational background of the woman. Women who desire to use oral contraceptives should be given a detailed explanation of the action of the pill, its use, and possible side effects. Post-pill conception should also be discussed at this time as many women discontinue use of the pill without consulting the nurse or physician.

All women using oral contraceptives should be encouraged to return to the clinic or physician's office when desiring to discontinue use of the pill. Women desiring to become pregnant should be counseled to use an alternate method of contraception for three to six months after discontinuance of the pill because of the possible increased incidence of abortion, twinning, and birth defects in infants conceived during this time. The use of alternate and effective methods of contraception should be discussed by the nurse in order that women avoid unwanted pregnancies or immediate conception.

Recommendations for Further Study

Recommendations for further study include:

1. Replicate this study using a larger sample to further document the findings

2. Conduct a longitudinal study to follow subjects from initial usage of oral contraceptives through subsequent pregnancy to determine the relationship of oral contraceptive use to the time to conceive and the incidence of birth defects

3. Conduct a study to determine knowledge and use of labeling information (drug insert) for oral contraceptives

4. Conduct a comparative study of the length of time to conceive for those women who have used oral contraceptives and those who have used an intrauterine device

5. Initiate a retrospective study over a five-year period to determine the relationship of birth defects and oral contraceptives by reviewing the charts of mothers of infants with birth defects for a history of oral contraceptive use during or prior to pregnancy

6. Conduct a study to investigate knowledge of alternate and effective methods of birth control

7. Conduct a retrospective study to determine the relationship of twinning and oral contraceptive use during and prior to pregnancy

APPENDIX A

QUESTIONNAIRE

Code #_____

This questionnaire is designed to determine the use of oral contraceptives (birth control pills) prior to pregnancy. Please check the appropriate space or fill in the blank.

1. Age_____

2. How would you describe the regularity of your menstrual periods prior to taking birth control pills?

   ___ Always regular
   ___ Usually regular
   ___ Unpredictable (irregular)
   ___ No periods

3. Prior to taking birth control pills, what was the average number of days between your menstrual periods?

   ___ Less than 28 days
   ___ 28-30 days
   ___ 31-35 days
   ___ 36-90 days
   ___ Greater than 90 days

4. How old were you when you first started taking birth control pills? _____years

5. When was the last time you took birth control pills? (Approximate date: month/day/year) _____/_____/_____

6. How many years and/or months did you take birth control pills prior to this pregnancy?
   _____years, _____ months

7. What was the reason for stopping birth control pills prior to this pregnancy?_____
   _____

8. After stopping birth control pills, how long did it take you to become pregnant?
_____ years, _____ months

9. After you stopped taking birth control pills, how many times per month on an average did you have sexual intercourse?

__ Less than 4 times
__ 4-6 times
__ 7-9 times
__ 10-12 times
__ 13-15 times
__ 16-18 times
__ over 18 times

10. Did you use any other form of birth control after you stopped taking the pill?
_____ yes _____ no

If yes, which method did you use? (Check all methods used)

__ Foam
__ Diaphragm
__ Withdrawal
__ Rhythm
__ Condom (rubber)
__ Douche
__ Suppository
__ Other (specify)
_____

11. How long did you use the above method(s) of birth control? _____ months

APPENDIX B

INFANT DATA COLLECTION SHEET

Birth Date_____ Code_____

Birth defect present_____ Yes_____

If yes, describe:

APPENDIX C

TEXAS WOMAN'S UNIVERSITY

Human Research Committee

Name of Investigator: Charlotte Patrick Center: Dallas

Address: 1814 Waterwood Drive, Arlington, Texas 76012 Date: 9/7/79

Dear Ms. Patrick:

Your study entitled Conception After the Pill: ~~Time to Conceive and Birth~~ Defects has been reviewed by a committee of the Human Research Review Committee and it appears to meet our requirements in regard to protection of the individual's rights.

Please be reminded that both the University and the Department of Health, Education and Welfare regulations require that written consents must be obtained from all human subjects in your studies. These forms must be kept on file by you.

Furthermore, should your project change, another review by the Committee is required, according to DHEW regulations.

Sincerely,

Estelle D. Kurtz

Chairman, Human Research
Review Committee

at Dallas.

APPENDIX D

TEXAS WOMAN'S UNIVERSITY
COLLEGE OF NURSING
DENTON, TEXAS 76204

DALLAS INWOOD CENTER
1810 INWOOD ROAD
DALLAS, TEXAS 75235

DALLAS PRESBYTERIAN CENTER
8194 WALNUT HILL LANE
DALLAS, TEXAS 75231

HOUSTON CENTER
1130 M.D. ANDERSON BLVD.
HOUSTON, TEXAS 77025

AGENCY PERMISSION FOR CONDUCTING STUDY*

THE _____

GRANTS TO Charlotte R. Patrick
a student enrolled in a program of nursing leading to a Master's Degree at Texas Woman's University, the privilege of its facilities in order to study the following problem.

Conception After the Pill:

Time to Conceive and

Birth Defects

The conditions mutually agreed upon are as follows:

1. The agency (may) (may not) be identified in the final report.
2. The names of consultative or administrative personnel in the agency (may) (may not) be identified in the final report.
3. The agency (wants) (does not want) a conference with the student when the report is completed.
4. The agency is (willing) (unwilling) to allow the completed report to be circulated through interlibrary loan.
5. Other _____

Date: 10 4 71

Charlotte R Patrick
Signature of Student

Signature of Agency Personnel

Signature of Faculty Advisor

* Fill out and sign three copies to be distributed as follows: Original - Student; First copy - agency; Second copy - TWU College of Nursing.

GP:GEN 13
07026074 cd

TEXAS WOMAN'S UNIVERSITY
COLLEGE OF NURSING
DENTON, TEXAS 76204

DALLAS INWOOD CENTER
1810 INWOOD ROAD
DALLAS, TEXAS 75235

DALLAS PRESBYTERIAN CENTER
8194 WALNUT HILL LANE
DALLAS, TEXAS 75231

HOUSTON CENTER
1130 M.D. ANDERSON BLVD.
HOUSTON, TEXAS 77025

AGENCY PERMISSION FOR CONDUCTING STUDY*

THE _____

GRANTS TO Charlotte R. Patrick Rn, BSN, MEd.
a student enrolled in a program of nursing leading to a Master's Degree at Texas Woman's University, the privilege of its facilities in order to study the following problem.

Conception After the Pill:
Time to Conceive and
Birth Defects

The conditions mutually agreed upon are as follows:

1. The agency (may) (may not) be identified in the final report.
2. The names of consultative or administrative personnel in the agency (may) (may not) be identified in the final report.
3. The agency (wants) (does not want) a conference with the student when the report is completed.
4. The agency is (willing) (unwilling) to allow the completed report to be circulated through interlibrary loan.
5. Other _____

Date: 10-1-79

Charlotte R Patrick
Signature of Student

Signature of Agency Personnel

Signature of Faculty Advisor

* Fill out and sign three copies to be distributed as follows: Original - Student; First copy - agency; Second copy - TWU College of Nursing.

GP:GEN 13
07026074 cd

TEXAS WOMAN'S UNIVERSITY
COLLEGE OF NURSING
DENTON, TEXAS 76204

DALLAS INWOOD CENTER
1810 INWOOD ROAD
DALLAS, TEXAS 75235

DALLAS PRESBYTERIAN CENTER
8194 WALNUT HILL LANE
DALLAS, TEXAS 75231

HOUSTON CENTER
1130 M.D. ANDERSON BLVD.
HOUSTON, TEXAS 77025

AGENCY PERMISSION FOR CONDUCTING STUDY*

THE Parkland Memorial Hospital

GRANTS TO Charlotte R. Patrick Rn, BSN, MEd.
a student enrolled in a program of nursing leading to a Master's Degree at Texas Woman's University, the privilege of its facilities in order to study the following problem.

Conception After the Pill:
Time to Conceive and
Birth Defects

The conditions mutually agreed upon are as follows:

1. The agency (may) ([redacted]) be identified in the final report.
2. The names of consultative or administrative personnel in the agency (may) ([redacted]) be identified in the final report.
3. The agency ([redacted]) (does not want) a conference with the student when the report is completed.
4. The agency is (willing) ([redacted]) to allow the completed report to be circulated through interlibrary loan.
5. Other Would appreciate copy of the findings

Date: 9-20-79

[illegible] 9-20-79
Signature of Agency Personnel

Charlotte R Patrick
Signature of Student

Gail Watson
Signature of Faculty Advisor

* Fill out and sign three copies to be distributed as follows: Original - Student; First copy - agency; Second copy - TWU College of Nursing.

GP:GEN 13
07026074 cd

APPENDIX E

EXPLANATION OF STUDY TO SUBJECTS

I am Charlotte Patrick, a graduate nursing student at Texas Woman's University, conducting a research investigation of pregnancies occurring after the use of birth control pills. If you took birth control pills before you had this baby, I would like to discuss my study with you. (If the subject replies yes, the following explanation will be given.)

I would appreciate your participation in this study. Participation involves filling out a brief (eleven-question) questionnaire. This will only take about five to ten minutes. I will also need your permission to observe your infant in the nursery and his/her chart.

No physical discomfort is expected from filling out the questionnaire or from the observation of your infant. Participation in the study will have no effect on your care or that of your infant. If the questions asked in the questionnaire should cause you embarrassment, you need not continue and may withdraw from the study even though you have signed a consent form. Counseling will be provided by myself should participation in the study cause you embarrassment or concern. All data will

remain confidential to protect you from risk of embarrassment and improper release of data. Your identity and that of your infant will remain anonymous. No name will appear on the questionnaire. You and your infant will be assigned a number to correlate data and facilitate analysis. No record will be retained of your name or the assigned number.

The benefit from this study is to increase knowledge concerning conception which occurs after the use of oral contraceptives. The information obtained through the study is expected to assist nursing personnel in counseling women who desire to become pregnant after taking birth control pills.

Participation in this study is voluntary. If you agree to participate in the study, please read and sign the consent forms for you and your infant. These consent forms will be kept on file by the investigator. You have the right to refuse to participate in the study, and the right to withdraw from the study at any time. If you withdraw, all information obtained from you as a subject will be destroyed. If you have any questions regarding the study, I will be glad to answer them.

APPENDIX F

CONSENT FORM

Texas Woman's University

Human Research Review Committee

Consent to Act as a Subject for Research and Investigation

1. I hereby authorize Charlotte R. Patrick, R.N., B.SN., M.Ed. to perform the following investigation.

   Charlotte Patrick, a graduate nursing student at Texas Woman's University, is conducting a research investigation of pregnancies occurring after the use of birth control pills.

   Participation involves filling out a brief (eleven-question) questionnaire. This will take about five to ten minutes. Your infant and his/her chart will be observed in the nursery.

   No physical discomfort is expected from filling out the questionnaire or from the observation of your infant. Participation in the study will have no effect on your care or that of your infant. If the questions asked in the questionnaire should cause you embarrassment, you need not continue and may withdraw from the study even though you have signed a consent form. Counseling will be provided by Charlotte Patrick should participation in the study cause you embarrassment or concern. All data will remain confidential to protect you from risk of embarrassment and improper release of data. Your identity and that of your infant will be assigned a number to correlate data and facilitate analysis. No record will be retained of your name of the assigned number.

   The benefit from this study is to increase knowledge concerning conception which occurs after the use of oral contraceptives The information obtained through the study is expected to assist nursing personnel in counseling women who desire to become pregnant after taking birth control pills.

Participation in this study is voluntary. If you agree to participate in the study, please read and sign the consent forms for you and your infant. These consent forms will be kept on file by the investigator. You have the right to refuse to participate in the study, and the right to withdraw from the study at any time. If you withdraw, all information obtained from you as a subject will be destroyed. If you have any questions regarding the study, Charlotte Patrick will be glad to answer them.

2. The investigation listed in Paragraph 1 has been explained to me by Charlotte Patrick.

3. a. I understand that the investigation described in Paragraph 1 involves the following possible risks or discomforts:

   Improper release of data
   Embarrassment due to the personal nature of the questions
   Unnecessary concern about the status of the infant

   b. I understand that the investigation described in Paragraph 1 has the following potential benefits to myself and/or others:

   Increase knowledge concerning conception after the use of oral contraceptives
   Assist nursing personnel in counseling women who desire to become pregnant after taking oral contraceptives.

4. An offer to answer all of my questions regarding the study has been made. I understand that I may terminate my participation in the study at any time.

_____ _____

Subject's Signature Date

Consent for Infant to Act as a Subject for Research and Investigation

I (the mother) have received an oral and/or written description of this study, including a fair explanation of the procedures and their purpose, any associated discomforts or risks, and a description of the possible benefits. An offer has been made to me to answer all questions about the study. I understand that my name or my infant's name will not be used in any release of the data and that I am free to withdraw at any time.

Subject is a minor (age _____days).

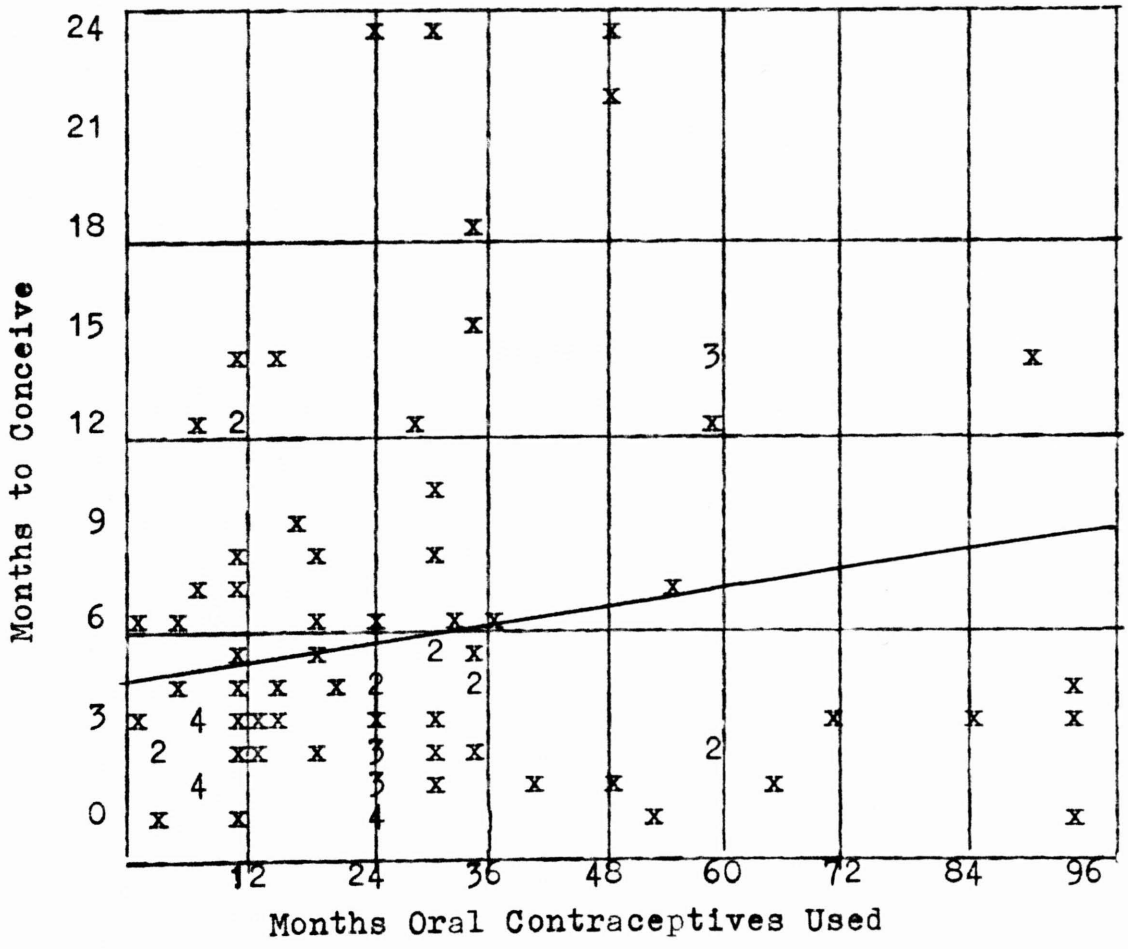
_____ _____

Mother's Signature Date

APPENDIX G

SCATTER DIAGRAM 1

CORRELATION OF LENGTH OF TIME ORAL CONTRACEPTIVES WERE USED AND TIME TO CONCEIVE

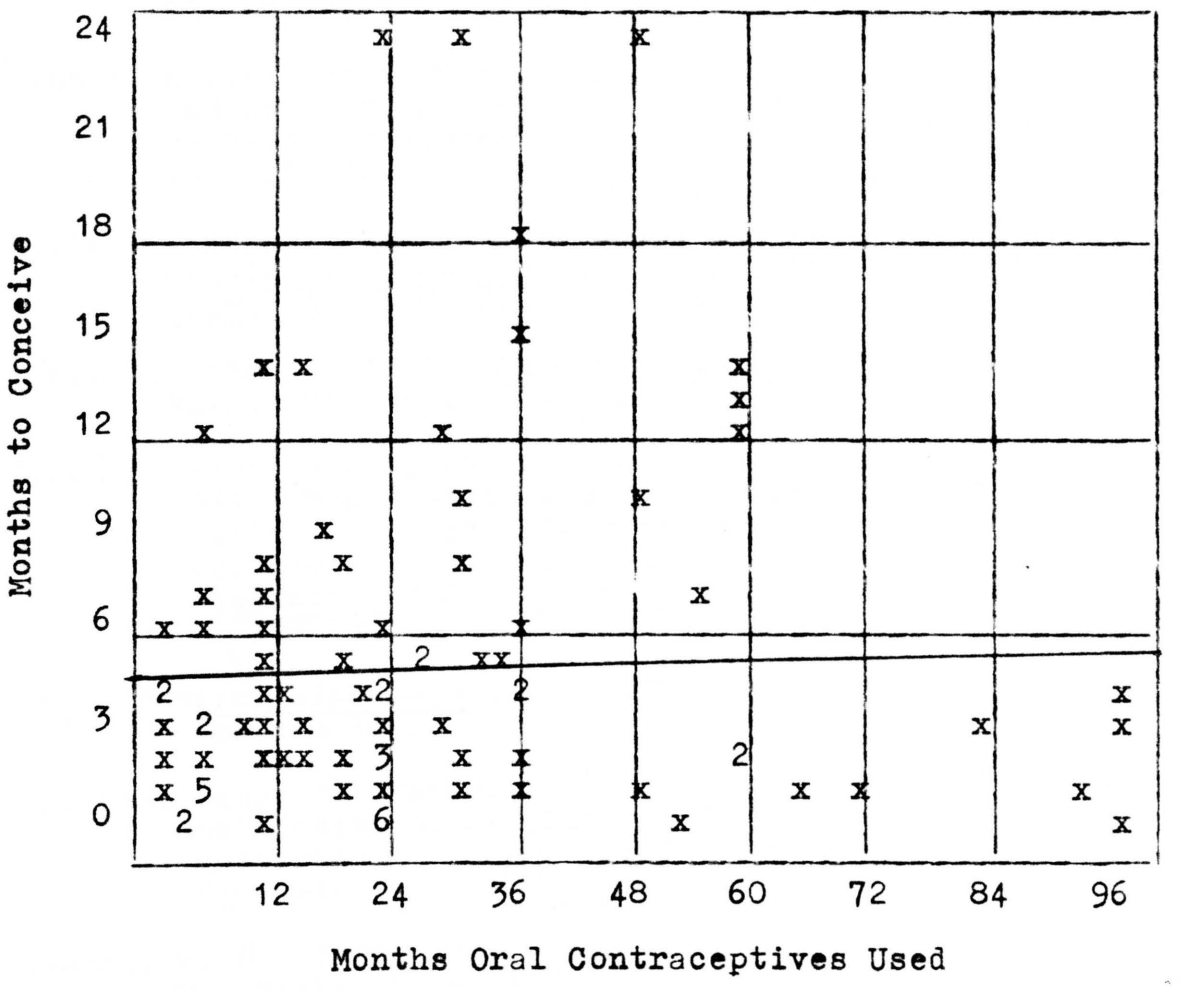


Regression Line Slope = .0377

APPENDIX H

SCATTER DIAGRAM 2

CORRELATION OF LENGTH OF TIME ORAL CONTRACEPTIVES WERE USED AND ADJUSTED TIME TO CONCEIVE



Regression Line Slope = .0135

REFERENCES CITED

Alberman, Eva; Creasy, M.; Elliott, Maureen; and Spicer, C. 1976. Maternal factors associated with fetal chromsomal anomalies in spontaneous abortions. British Journal of Obstetrics and Gynecology 83: 621-627.

Ambani, LaLit; Joshi, Narendra, J.; Vaidya, Roma A.; and Davi, P. K. 1977. Are hormonal contraceptives teratogenic? Fertility and Sterility 28: 791-796.

Beland, Irene L., and Passos, Joyce Y. 1975. Clinical nursing pathophysiological and psychosocial approach. 3rd ed. New York: MacMillan.

Bennett, John P. 1974. Chemical contraception. New York: Columbia University Press.

Berger, Gary; Taylor, Robert N., Jr.; and Treloar, Alan E. 1977. The risk of post-pill amenorrhea: a preliminary report from the menstrual and reproduction history research program. International Journal of Gynaecology Obstetrics 15: 128-132.

Birth Control with Lo/Ovral. 1978. Philadelphia: Wyeth Laboratories.

Buttram, Veasy C.; Vanderheyden, Jozef D.; Besch, Paige K.; and Acosta, A. Arnaldo. 1974. Post "pill" amenorrhea. International Journal of Fertility 19: 37-44.

Cannon, W. B. 1939. The wisdom of the body. Rev. ed. New York: W. W. Norton.

Chez, Ronald A. 1976. Perspectives on pharmacology of oral contraceptives. In Current concepts in oral contraceptive treatment; part I, normal healthy woman. New Jersey: Health Learning Systems.

David, T. J., and O'Callaghan, S. E. 1974. Birth defects and oral hormone preparations. Lancet 7868: 1236.

Dickey, Richard P. 1977. Treatment of post-pill amenorrhea. International Journal of Gynaecology Obstetrics 15: 128-132.

Family planning with the pill, a manual for nurses. 1967. New York: G. D. Searle & Co.

Ford, Kathleen. 1978. Contraceptive use in the United States, 1973-1976. Family Planning Perspectives 10: 264-268.

Friedman, Stanley, and Goldfien, Alan. 1969. Amenorrhea and galactorrhea following oral contraceptive therapy. Journal of American Medical Association 210: 1888-1891.

Golditch, Ira M. 1972. Postcontraception amenorrhea. Obstetric and Gynecology 39: 903-908.

Good, Andrew E., and Kempers, Roger D. 1974. Prolonged over-suppression syndrome. Medical Clinics of North America 58: 861-867.

Guyton, Arthur C. 1976. Textbook of medical physiology. 5th ed. Philadelphia: W. B. Saunders Co.

Halbert, David R., and Christian, C. D. 1969. Amenorrhea following oral contraceptives. Obstetrics and Gynecology 34: 161-167.

Hatcher, Robert A.; Stewart, Gary K.; Stewart, Felicia; Guest, Felicia; Stratton, Pamela; and Wright, Angela H. 1978. Contraceptive technology 1978-1979. 9th rev. ed. New York: Irvington.

Heinonen, Olli; Slone, Dennis; Monson, Richard R.; Hook, Ernest B.; and Shapiro, Samuel. 1977. Cardiovascular birth defects and antenatal exposure to female sex hormones. New England Journal of Medicine 296: 67-70.

Hubbard, Charles W. 1977. Family planning education. 2nd ed. St. Louis: The C. V. Mosby Co.

Huxall, Linda K. 1977. Today's pill and the individual woman. Maternal Child Nursing 2: 359-363.

Janerich, Dwight T. 1975. The pill and subsequent pregnancies. Lancet 7907: 681-682.

Janerich, D. T.; Flink, E. M.; and Keogh, M. D. 1976. Down's syndrome and oral contraceptive usage. British Journal of Obstetrics and Gynecology 617-620.

Janerich, Dwight T.; Lawrence, Charles E.; and Jacobson, Herbert I. 1976. Fertility patterns after discontinuation of use of oral contraceptives. Lancet 7068: 1051-1053.

Janerich, Dwight T.; Piper, Joyce M.; and Glebatis, D. M. 1974. Oral contraceptives and congenital limb reduction of defects. The New England Journal of Medicine 291: 697-700.

Klinger, Harold P.; Glasser, Marvin; and Kava, H. Wallace. 1976. Contraceptives and the concepters. Obstetrics and Gynecology 48: 40+.

Korba, Vladimir, and Heil, Charles G. 1975. Eight years of fertilicy control with Norgestrel-ethinyl estradiol (Ovral): an updated clinical review. Fertility and Sterility 26: 973-981.

Langley, L. L. 1965. Homeostasis. New York: Von Nostrand Reinhold.

Lefebvre, Yves. 1970. Anatomical and functional changes induced by oral contraception. Canadian Medical Association Journal 102: 621-624.

Manisoff, Miriam. 1969. Family planning, a teaching guide for nurses. New York: Planned Parenthood World Population.

Mears, Eleanor. 1968. Pregnancy following antifertility agents. International Journal of Fertility 13: 310-315.

Mears, E., and Grant, E. 1962. Anovlar as an oral contraceptive. British Medical Journal 11: 75-79.

Mishell, Daniel R. 1976a. Current status of oral contraceptive steroids. Clinical Obstetrics and Gynecology 19: 743-764.

Mishell, Daniel R. 1976b. The postpartum postabortion woman. In Current concepts in oral contraceptive treatment; part II: Woman at risk. New Jersey: Health Learning Systems.

Moghissi, Kamran S. 1973. Cervical mucus: what we know and why it's important. In Reproduction endorcinology. Edited by Medcom Learning Systems. Philadelphia: Wyeth Laboratories.

Murray, Juanita F. 1971. Theoretical issues in professional nursing. New York: Appleton-Century-Crofts.

Nora, James J., and Nora, Audrey H. 1973. Birth defects and oral contraceptives. Lancet 7808: 941.

Nora, James J., and Nora Audrey H. 1974. Can the pill cause birth defects? New England Journal of Medicine 291: 14.

Nora, James J.; Nora, Audrey; Blu, Janet; Ingram, Joy; Fountain, Agnes; Peterson, Marilyn; Lortscher, Randall H.; and Kimberling, William J. 1978. Exogenous, progestogen and estrogen implicated in birth defects. Journal of American Medical Association 240: 837-843.

Peterson, Clare Gray. 1972. Perspectives in surgery. Philadelphia: Lea & Febiger.

Peterson, William F. 1969. Pregnancy following oral contraceptive therapy. Obstetrics and Gynecology 34: 363-367.

Pill taken during or just before pregnancy not linked to various birth defects; need more study of heart ills. 1977. Family Planning Perspectives 9: 132-134.

Polit, Denise, and Hungler, Bernadette. 1978. Nursing research principles and methods. Philadelphia: J. B. Lippincott.

Robinson, S. C. 1971. Pregnancy outcome following oral contraceptives. American Journal of Obstetrics-Gynecology 109: 354-358.

Rothman, Kenneth J. 1977. Fetal loss, twinning and birth weight after oral contraceptives use. New England Journal of Medicine 297: 468-471.

Taber, Ben Z. 1968. Oral contraception and future fertility. International Journal of Fertility 13: 427-430.

Thorn, George W. 1977. Disturbances of menstruation. In Harrison's principles of internal medicine. 8th ed. Edited by G. W. Thorn, R. Adams, E. Braunwald, K. Isselbacher, and R. G. Petersdorf. New York: McGraw-Hill.

Tietze, Christopher. 1968. Fertility after discontinuation of intrauterine and oral contraception. International Journal of Fertility 13: 385-389.

Tyler, Edward T. 1973. Conception control: the pill is best for most. In Reproduction endocrinology. Edited by Medcom Learning Systems. Philadelphia: Wyeth Laboratories.

Tyson, John E.; Andreasson, Barbara; Huth, Janice; Smith, Beverly; and Zacur, Howard. 1975. Neuroendrocrine dysfunction in galactorrhea-amenorrhea after oral contraceptive use. Journal of Obstetrics and Gynecology 46: 1-11.

Westoff, Charles F.; Bumpass, Larry; and Ryder, Norman R. 1969. Oral contraception, coital frequency, and the time required to conceive. Social Biology 16: 1-10.

Wolfers, D. 1970. The probability of conception after discontinuance of oral contraception: a note on "oral contraception, coital frequency, and the time required to conceive," by Westoff, Bumpass, and Ryder. Social Biology 17: 57-59.

Yen, Samuel S. 1973. Hypothalmic-pituitary discharge. In Reproduction endocrinology. Edited by Medcom Learning Systems. Philadelphia: Wyeth Laboratories.

Zatuchini, Gerald I. 1978. Contraception: current methods. The Female Patient (May): 48-50.