Chapter - 1
Introduction

Menopause: Living it.

“Menopause..... is not simply a biological process. It is a phase of each woman’s life. It may be short or long, complicated or simple, dramatic or subtle, problematical or easy. For each woman, it will be slightly different, with different components, a unique flavor. Just as each of us has her unique scent, her unique set of finger prints, each of us has her way of experiencing menopause and living it. Let us converse, as women all over the world have talked together since the beginning of speech. That is how we learn and grow. Tell me about your menopause”.

---- Van Eyk McCain (1991)

In a woman’s life there are two milestones, both related to menstruation and both to be considered as transition period. The first milestone is the start of menstruation around the 12th year. The event – Menarche, marks the onset of the menstrual cycle. The second milestone is the cessation of menstruation around the 50th year. The event – Menopause, marks the transition from the fertile years to life phase characterized by relative hormonal rest and stability, which shows a certain similarity with the life preceding the first menstruation. Both transitions – which in a way are each other’s mirror image - are to be considered as natural process, which does not mean that their course is always uneventful (Hall, 1997).

Menopause happens to every woman. Unlike other changes that affect a woman’s body, such as pregnancy, menopause is something about which we have no choice, and that is why it is important to understand as much about it as possible. Menopause is defined as ‘the final menstruation’. In reality, it is a
much more gradual ‘stop-start’ series of pauses in ovarian function which are part of the ageing process. In fact, the only universal statement that can be made about menopause is that menstruation stops. All other particulars of the experience vary from woman to woman (Hall, 1997). The term ‘Menopause’ derived from Greek words *meno* (month) and *pauses* (pause), was first used by French physician de Gardanne in 1821 (Wilbush, 1988). At that time western medicine viewed menopause as a medical crisis that contained the potential for causing a variety of diseases, from diarrhoea to diabetes. In the middle of the 20th century the medical profession switched from regarding menopause as the cause of disease and began to think of it as a disease itself. Now menopause is widely considered to be a natural event in a woman’s life, and women living in developed countries can expect to live well into their 70s and 80s. This means that one third of their lives will occur after their childbearing years are over (Clark, 2004).

Menopause is characterized endocrinologically by evidence of decreasing ovarian activity, biologically by decreasing fertility and clinically by alteration in menstrual cycle intervals (WHO, 1981). In fact menopause is the final stage of what may be a gradual process that can take many months or years before the actual cessation of menstruation.

**Terminology**

The relationship between different time periods surrounding menopause is given in Figure 1 (WHO, 1996). The terms and definitions used to describe the various nodal points surrounding menopause as recommended by WHO Scientific Group on Research on Menopause (1981, 1996) are described below:
Figure 1: Relationship between different time periods surrounding menopause.

Natural menopause is defined as the permanent cessation of menstruation resulting from the loss of ovarian follicular activity. Natural menopause is recognized to have occurred after 12 consecutive months of amenorrhea, for which there is no other obvious pathological and physiological cause. Menopause occurs with the final menstrual period (FMP) which is known with certainty only in retrospect a year or more after the event. An adequate independent biological marker for the event does not exist.

Perimenopause should include the period immediately prior to the menopause (when the endocrinological, biological and clinical features of approaching menopause commence) and the first year after menopause. The term “Climacteric” should be abandoned to avoid confusion. (The term climacteric comes from a Greek word meaning “rung of a ladder” and refers to the period of passage out of the reproductive stage of one’s life and into the non-reproductive phase).

Menopausal transition should be reserved for the period of time before the FMP when variability in the menstrual cycle is usually increased.

Premenopause is often used ambiguously either to refer to the one or two years immediately before menopause or to refer to the whole of the reproductive period prior to menopause. The Group recommended that the
term be used consistently in the latter sense to encompass the entire
reproductive period up to the FMP.

**Induced menopause** is defined as the cessation of menstruation which
follows either surgical removal of both ovaries (with or without hysterectomy)
or iatrogenic ablation of ovarian function (e.g., by chemotherapy or radiation).

**Simple hysterectomy**, where at least one ovary is conserved, is used to
define a distinct group of women in whom ovarian function may persist for a
variable period after surgery.

**Postmenopause** is defined as dating from the FMP, although it cannot be
determined until after a period of 12 months of spontaneous amenorrhea has
been observed.

**Premature menopause** should be defined as menopause that occurs at an
age less than two standard deviations below the mean estimated from the
reference population. In practice, in the absence of reliable estimates of the
distribution of age at natural menopause in populations in developing
countries, the age of 40 years is frequently used as an arbitrary cut-off point,
below which menopause is said to be premature.

**Biology of menopause**

Menopause is natural biological experience, which is an inevitable event in
the lives of all women. The transition from regular menstrual cycle
(characteristic of reproductive phase) to amenorrhea following menopause
may be marked by a period of menstrual cycle irregularity (Treolar, 1967 and
Vollman, 1969). The duration of the transition and the nature of the irregularity
vary widely among women. The process of oogenesis does not occur in the
postnatal female (Potter, 1963; Wynn and Doar, 1969). It occurs after the first
great wave of atresia between 5th month in utero. According to Dewitt (1989),
the human female is born with a fixed number of potential ova, and unlike the
situation in males, no germ cells are produced after birth. The fixed numbers of primary oocytes (approximately 1 million) are maintained in a state of meiotic arrest until ovulation and fertilization. The vast majority of these primary oocytes degenerate between birth and menopause, with only about 400 being ovulated during the reproductive years. The cyclic changes in the ovary and the uterus, collectively termed the menstrual cycle, are regulated and controlled by endocrine events of the hypothalamus, pituitary and the ovaries themselves. In humans, female reproductive aging involves two major features: the loss of regular cycling with menstruation, and cessation of ovulation.

The reproductive aging of all female mammals is complicated by the fact that the ovaries not only store the gametes, they also secrete female sex hormones and therefore play a critical role in hormonal regulation of reproductive function (Harmon and Talbert, 1985). The changes that occur in the ovaries influence the hypothalamus-pituitary axis and their hormone production in a feedback loop (Figure 2), which in turn influences the hormone production and functions of ovaries themselves (Van Keep et al., 1978).

The number of potential egg cells available is fixed at birth and this number steadily decline thereafter. The vast majority of egg cells are lost by the process of artesia (degeneration) with at least 50% of potential oocytes being depleted before puberty (Block, 1952). A relatively small number of potential oocytes are actually spent by way of ovulation. In spite of a report of small numbers of apparently normal oocytes in the ovaries of some post menopausal women (Costoff and Mahesh, 1975), oocytes depletion does appear to be the starting point for a series of changes that underlie the climacteric period of woman’s life (Gosden, 1985).
In humans, a certain critical mass of oocytes may be necessary for the ovaries to respond to the action of FSH (Follicle-stimulating hormone), as even in pre- and peri-menopausal women the remaining oocytes become increasingly unresponsive to the hormones of the pituitary (Anderson, 1983). In the perimenopausal period, with the ovarian follicle population approaching depletion follicular growth and menstrual bleeding become more irregular. During the periods of relative ovarian inactivity, estrogen levels are lower and FSH and LH (Luteinizing hormone) levels are higher, but they return to normal when follicles start growing. Anovulatory cycles may be common at this time (Van Keep et al., 1978). The end of reproductive ability is thus a fairly straightforward result of the depletion of potential ova for fertilization. The menstrual cycle, including monthly periods of menstrual bleeding, ceases secondarily as a result of the great reduction in estrogen and progesterone. Estrogen is necessary for the regular building up of the lining of the uterus in preparation for implantation, and progesterone for the subsequent shedding of...
this lining if implantation does not occur. Although the uterus, like most organs, does experience some intrinsic ageing changes (Naeye, 1983; Gosden 1985), inadequate estrogen stimulation in postmenopausal women is largely responsible for the marked atrophy of this structure (Gibbons et al., 1979).

With increasing age, various morphological and physiological changes are accompanied in women’s life. The reproductive life of women ends with varying degree of suddenness with menopause and is considered as the most critical biological event in the body, and from this stage, the reproductive function of women is completely ceased by consequently arresting the menstruation flow of blood and ovulation (Sengupta and Rajkhowa, 1996; Kalita and Sengupta, 1997).

**Stages of normal reproductive ageing in women**

The new classification system for reproductive aging created by stages of reproductive ageing workshop (STRAW) includes seven stages, based on menstrual cycle pattern and follicle stimulating hormone (FSH) (Figure 3). The reproductive stage has three components (early, peak, and late) and begins with menarche. The menopausal transition is divided into early and late stages and is defined by both menstrual cycle variability and an increase in FSH levels. Menstrual cycle variability in the early menopausal transition is characterized by a change in cycle-to-cycle length of seven days or more; the late menopausal transition is characterized by two or more skipped cycles and one episode of absent menses for 60 days or longer. The menopausal transition ends with the final menstrual period (FMP). The postmenopause stage is also divided into early and late phases. The early postmenopause phase is defined as the first five years after the FMP and late postmenopause phase ends at the time of death. STRAW (2001) pointed out, however, that not all healthy women will follow this pattern; some will “seesaw” back and forth between stages or skip a stage altogether.
Figure 3: Stages of normal reproductive aging in women

Evolution of menopause

Why do women cease fertility rather abruptly through menopause at an age well before generalized senescence renders child rearing biologically impossible? The two main evolutionary hypotheses are that menopause serves either, to protect mothers from rising age-specific maternal mortality risks, thereby protecting their highly dependent younger children from death if mother dies, or, to provide post reproductive grandmothers who enhance their inclusive fitness by helping to care and provide for their daughters’ children.

Recent theoretical work indicates that both factors are necessary if menopause is to provide an evolutionary advantage (Shanely et al., 2007). If menopause does have an advantage, it offsets the obvious disadvantage of curtailed childbearing. The age of menopause is at least partly genetically determined (Peccei, 1995; Sneider et al., 1998; Kirk et al., 2001; Peltary et al., 2005) which supports the idea that selection may have acted to optimize the
length of the fertile portion of the life cycle. If menopause is unique to human females and universal to females of our species, then an evolutionary approach to understanding it is in order. The “grandmother hypothesis” suggests that menopause is an adaptive response to selection pressure favoring women who cease to reproduce and invest their energy on the survival and reproduction of existing offspring and their children. Non adaptive explanations for the evolution of menopause treat this reproductive cessation as a by-product of increased life span or as pleiotropic effect, or both.

Genetics of menopause

Twin and family studies have provided evidence that genetic factor contribute to the determination of menopause (Cramer et al., 1995; Togerson et al., 1997 and Snieder et al., 1998). Krauss et al. (1987) reported premature ovarian failure and premature menopause at the age 24-37 years due to an interstitial deletion of the long arm of the X chromosome. The importance of chromosome X in the onset of natural menopause was recently confirmed by the results of a genome wide linkage scan in Dutch sister pairs (Van Asselt et al., 2004). However, only few genes were directly tested for the effects on age at menopause. The first report was that phosphate deficiency of the blood enzymes galactose-1-phosphate uridyl transferase (reduced activity) might be associated with infertility and early menopause (Cramer et al., 1989). Recently, factor V Leiden mutation was reported to accelerate the onset of natural menopause (Van Asselt et al., 2004). The estrogen receptor a (ER-a) gene may be one of the potential candidate gene underlying the onset of menopause. ER-a is a member of the family of steroid transcription factors and regulates expression of many genes and proteins (Evans, 1988). It plays an important physiological role in mediating the specific effects of the estrogen on the growth, differentiation, and function of reproductive tissues, such as ovary, uterus and vagina (Pelletier and Alfy, 2000). The Pvu II polymorphism of this gene was reported to be associated with age at menopause.
**Demography of menopause**

Numbers of menopausal women are projected to increase rapidly from the world total of 467 million in 1990 to 1.2 billion by 2030. The great majority of this growth will occur in the developing world, where the number of postmenopausal women will triple between 1990 and 2030. Postmenopausal women will also be increasing as a proportion of the total population, from 9% in 1990 to 14% in 2030. Ultimately this figure will go much higher since the proportions in developed world would be over 20% by 2030. In the decade of the 1990s, nearly 25 million women passed through menopause each year worldwide, this figure is projected to increase to 47 million by the decade of the 2020s (Hill, 1996).

The average age at which menopause occurs is approximately 50 years; it is possible that some variability exists between developed and developing countries. Projections of the world population to the year 2030, available from the World Bank’s 1993 World development report, have been used to describe the size and distribution of the population of postmenopausal women. These population projections divide the world into eight geographical regions designed to be homogenous with respect to their economies, social structure and epidemiology. Figure 4 shows the projected population of postmenopausal women by region for each decade from 1990 to 2030. In 1990, 40% of postmenopausal women lived in industrialized regions and 60% lived in developing countries. These population projections indicate that in 1990, there were approximately 467 million women in the world aged 50 years and over. This number is expected to increase to 1200 million by the year 2030 (Hill, 1996). By 2030, the proportion of postmenopausal women in the total population will have increased everywhere, most dramatic increase being from 8% to 17% in China and from 15% to 23% in the industrialized world. A total of 130 million Indian women are expected to live beyond the menopause into old age by 2015 (Sengupta, 2003). The average median age of postmenopausal women is around 62 years, varying from 60 years in sub-Saharan Africa to 65 years in the industrialized world. By 2030 it is predicted
that these median ages will have increased to 64 years globally, and to 68 years in the industrialized world.

Figure 4: Population of postmenopausal women by region, 1990-2030.

Menopause marks the end of reproductive life, with unfulfilled dreams for childbearing for some, and the beginning of increased risk for the health estrogen deprivation. On the other hand, it signifies a time when women no longer need to experience the inconvenience associated with menses, when they are free from dysmenorrhea, and when they need not fear unwanted pregnancies (MacDonald, 1985). Menopause occurs in midlife at a time when many women are experiencing changes in roles, responsibilities, and relationships that accompany ageing generally and the maturation of children and their departure from home in particular. These changes may create considerable stress for some women, affecting their identity, self-esteem, and social and family relationships. For others, these might mark the beginning of more fulfilling relationships and new challenges for positive psychological growth. Thus, menopause is a critical transition in women's lives not only because of biological changes they are experiencing, but also because of the
co-occurring physical, social and psychological changes (Matthews, 1992). It is widely acknowledged that the end of menstruation is a complex biosocial process. Anthropological researches suggests (Flint, 1974; Walfish et al., 1984; Yeh, 1989; Flint & Suprapti, 1990; Lock, 1998) that menopause should not be conceptualized as an invariant biological transformation, and that it is more appropriate to think biology and culture as continuous feedback relationship of ongoing exchange, in which both are subject to variation. The biology and evolution of menopause among women continues to present a fascinating challenge to biologists, anthropologists, and primatologists (Peccei, 1995; Thomas & Fretts, 2001). Among primates, rhesus macaques experience menopause when approximately two-third of their life cycle is completed and the profile of which is similar to that of human females. While in chimpanzees normal cycling is observed till death (Hodgen et al., 1977; Graham, 1979). The transition from premenopause to post menopause status has been associated with changes in body composition. Mostly, there is an increase in central adiposity, particularly in visceral fat, but the findings are not consistent for weight gain (Ley et al., 1992; Tremolliers et al., 1996). It is still unclear whether the central deposition of fat and weight gain are continuous processes from premenopause to post menopause period, or if they occur at menopause transition or in early post menopause (Bjorkelund et al., 1996; Toth et al., 2000). There are relatively few data on changes in adiposity and fat distribution associated with menopause in women. This is an important issue because of the relationships that have been noted between obesity and cardiovascular diseases (Manson et al., 1995), and obesity and certain cancers (Austin et al., 1991; Colditz, 1993) in postmenopausal women.

Present study

The International Conference on Population and Development (1994), recommended a life cycle approach in women's health, i.e., women of all ages needed due attention, right from conception to old age rather than only in the reproductive ages. India, being a signatory to this conference changed the then existing Maternal and Child Health (MCH) programme to Reproductive
and Child Health (RCH) programme for providing health care to all sub-sections of the population. But not much effort has been made to study the needs of women in the late reproductive years who are nearing menopausal age or have moved into the postmenopausal stage although there has been growing attention on ageing, which mainly focuses on women aged 60 and above. The recent health policy adopted by India also does not lay emphasis on the issues of older women especially during their menopausal period. Therefore, any attempt to study the issue of menopause assumes significance in the current Indian context (Syamala and Sivakami, 2005).

At present, India has a population greater than 1 billion, i.e., 16% of the global population, occupying 2.4% of the land area, and life expectancy has risen from 37 years (1947) to 63 years (1998). With increasing life expectancy, it is expected that female menopausal population in India beyond 50 years age will more than double during 1991-2016, from 53 million to 130 million. 30% of menopausal population is presently living in urban areas, as compared to 23% in 1981. Menopause is emerging as an issue owing to rapid globalization, urbanization, awareness and increased longevity in urban middle age Indian women. Thus, menopause is a critical transition in women’s lives not only because of the biological and physical changes they are experiencing, but also because of the co-occurring social changes. There is a need to study the whole phase of midlife in women from premenopause to postmenopause with associated biological, social and health related changes that occur during this phase of life. It is evident that numerous studies on menopause are available on this vital aspect in a woman’s life in developed countries. However, studies from developing countries including India are few, and most of these have confined to reporting only average age at menopause. Therefore, it is proposed to undertake the present study on “Menopause among Punjabi Brahmin and Khatri women of Chandigarh: A biosocial study” with following objectives:

- to report socio-economic and life style characteristics of the subjects,
- to find mean and median age at menopause among women of two groups,
to assess the association between age at menopause and different variables (anthropometric, physiological, socio-economic, and life-style characteristics),

- to evaluate anthropometric measures among menopausal women of two groups,
- to evaluate measures of blood pressure among menopausal women of two groups,
- to report menopausal symptoms and related health problems among Punjabi women, and,
- to attempt an inter-community comparison of the foregoing objectives.