A Lifespan Biological Model of Menopause

Paula S. Derry

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Address correspondence to: Paula S. Derry, Ph.D., 4811 Crowson Ave., Baltimore, MD 21212. E-mail address: pderry@bcpl.net.

Thanks are due Elissa Derrickson for recommending that I read *Patterns of Human Growth* (Bogin, 1999).

Abstract

This article continues the author's theoretical reconsideration of the biology of menopause (Derry, 2002). The author's broader-biological theoretical model of menopause, the Lifespan Biological Model, asserts that menopause is best understood by considering the biology of healthy systems. The biological subfield of life history theory combined with the psychological subfield of lifespan development provides a useful starting point to understand the biology of menopause. When compared with other mammals, humans have unusual life stages, one of which is a post-reproductive stage of relatively healthy, competent adulthood. Implications of the model are discussed with regard to conceptualizing: menopause as normal vs. pathological; the arc of development as childhood growth/adult stability/aging senescence vs. lifespan developmental; and the relation of menopause to chronic disease, especially osteoporosis.

Keywords: menopause, women's health, life history theory, adult development

A Lifespan Biological Model of Menopause

The biology of menopause is commonly equated with the biomedical model of menopause. However, the biomedical model, which emphasizes the central importance of estrogen and an overriding focus on disease, is a limited approach to the biology of menopause. It overlooks many known facts about the biology of reproductive hormones, cannot account for what we already know about menopause, and draws heavily on physiology while overlooking other subfields of biology (Derry, 2002). Previously, I (Derry, 2002) began to articulate a broader-biological model. This framework, the Lifespan Biological Model, begins with the assumption that menopause is best understood through the biology of healthy systems rather than through the biology of disease processes. It draws heavily from a broad range of subfields of biology. In this article, I continue to develop the model by examining how the field of biology called life history theory combined with the psychological study of lifespan development provides a useful anchor for understanding the biology of menopause. The basic thesis is this: Female humans have a life stage of post-reproductive, competent, relatively healthy adulthood. It is unusual for a mammal to such have a life stage, but there is nothing unusual about humans having unusual life stages. The human life course (that is, the stages of development throughout childhood and adolescence and adulthood) is unique when compared with other mammals (Bogin, 1999). The Lifespan Biological Model of menopause leads us to ask different questions and consider different dynamics than does the biomedical model.

Basic Assumptions of the Lifespan Biological Model

The Lifespan Biological Model begins with the observation that hormones are team players in complex, multidetermined systems that have a purpose. Hormones help to coordinate bodily functions by altering the rate at which cells do their jobs. However, in normal functioning hormones do not act alone. We can identify powerful cause-and-effect relationships that involve hormones, but these mechanisms are embedded in a larger context. This is illustrated by Pfaff's (1999) review of the biology of reproductive hormones. A female rat must arch her back in a special way ("lordosis") or a male rat cannot copulate with her. A female whose ovaries have been removed, who has no estrogen in her body, will not engage in lordosis. However, powerful as this cause-and-effect relationship is, it is only a small part of the story. For example, if the male does not engage in particular behaviors, for example stroking the female, she also will not engage in lordosis no matter how much estrogen she has. Other hormones, for example progesterone, make it more or less likely that estrogen will affect lordosis, and the brain of a female rat can override the message of her hormones to allow her to reject a particular male. The mechanism is found in rats but not in humans, as ovariectomized women do have sexual intercourse.

Even when physical growth is considered, the effects of hormones are contextual. For example, androgen levels increase during puberty, which results in a growth spurt. But this is only the case in humans; male chimpanzees have a similar increase in androgen without a growth spurt (Bogin, 1999). Female humans have an adolescent growth spurt in most of the skeleton, but the bones of the pelvis are an exception that continues a slow growth rate until adulthood (Bogin, 1999).

In sum, the effects of a hormone vary depending upon sex, age, and species, as well as target tissue and a variety of bodily chemicals. Hormones are often intimately interrelated with behavior and appropriate to the social context. Human brains, with their increased complexity, introduce greater complexity and variety into the role of hormones. Chemicals, the brain, and psychological, social, and environmental factors, all influence what effect a reproductive hormone has, how potent it will be, whether a causal mechanism that involves a hormone will be activated, and whether the lack of that hormone will have serious consequences or be barely noticed.

All of this complexity follows from the fact that hormones serve adaptation. Hormones help to maintain homeostasis, that is, physical integrity and sameness in the face of shifting physiological and environmental conditions. They help to orchestrate development across the life span. However, they also serve flexibility—that is, variation in response to varying environmental demands or to the many goals or purposes that a human or animal may have. In order to accomplish all of their functions, hormones are part of larger wholes. We must know the function or purpose or goal of a particular system in order to make sense of the role of hormones within the system. Important as it is to study cause-and-effect mechanisms, the nature of larger wholes guides the search for what mechanisms are important and how they work. However, we know very little about these larger systems of which hormones are only a part, especially in the case of humans. What are these larger wholes or systems? How can we understand their structure, function, or the dynamics by which they work? Life history theory and lifespan developmental psychology provide useful starting points or anchors for asking these questions about the role of reproductive hormones, especially with regard to menopause.

Life History Theory and Lifespan Development

Life history theory and lifespan development provide complementary perspectives on the development of the human life span. Life history theory synthesizes information from many subfields of biology to "unravel the reasons why different species of animals follow different sequences of development" (Bogin, 1999, p. 13). Physical and behavioral attributes of animals and humans are described in terms of whether they are typical of or specific to the species, where in the life cycle they occur, and what apparent function they may serve. Life history theory is "[a] field of biology concerned with the strategy an organism uses to allocate its energy toward growth, maintenance, reproduction, raising offspring to independence, and avoiding death. For a mammal, it is the strategy of when to be born, when to be weaned, how many and what type of pre-reproductive stages of development to pass through, when to reproduce, and when to die" (Bogin, p. 404). Evolutionary theory plays a key role in theoretical explanations.

To understand human experience more fully we must also draw on lifespan developmental psychology, that is, the study of human physical, mental, and social changes over the life span, as they result from the interaction of organism and environment. Developmentalists study physical capabilities, personality, the intrapsychic world, emotions, intellect, social behavior, social structure, culture, and the physical environment. Symbolic thought, the characteristics of the social environment, and human flexibility and purpose are taken into account. Theories tend to explain limited areas within the overall field.

For the rest of this section I will rely on the detailed, thoughtfully considered interpretation provided by the anthropologist Barry Bogin (1999) of life history theory as it pertains to patterns of human growth. Life stages are keys to evolutionary change: new characteristics and new species result from new patterns of development (that is, new life cycles) rather than from changes in genes alone. Life stages are characterized by typical rates of physical growth, as measured by height or weight, particular capacities for feeding (presence of molars, weaning, etc.), other physical and mental competencies, changes in social behavior, and changes in psychological organization. Human development is a combination of life stages common to all mammals, modifications of these life stages, and uniquely human life stages.

The human life course is unique among mammals with regard to the number of life stages, their duration, and the timing of physical changes within life stages. For most mammals, the growth rate (in height or weight) is most rapid following birth and then decelerates. This change in rate is so regular that it can be described with a mathematical formula, and has been found in species of mammals that range from mice to cows. Weaning occurs right around the maximal growth rate; puberty occurs soon after while the growth rate is declining but still high. Many primates and a few other species interrupt the smooth deceleration of the growth curve with a period of especially slow growth added in between infancy and adulthood. During this new life stage, called the "juvenile period," the animal has been weaned and is mature enough to be largely responsible for its own care and feeding, but doesn't reach puberty. Two mathematical formulas rather than one are now required to graph the pattern of physical growth. Only humans require three mathematical formulas to graph their development from infancy to

adulthood. Humans have stages of development—childhood and adolescence—with characteristics not found in other mammals. They begin infancy with the smooth deceleration found in other mammals; infancy is followed by periods of slow growth (childhood), decelerated growth (human juveniles), and growth spurt (adolescence). There are other unusual temporal patterns. For example, most mammals sexually mature soon after weaning, whereas humans delay this type of maturation for many years. Most mammals begin to reproduce soon after puberty, whereas in humans many years intervene between puberty and reproductive maturity (i.e., the ability to reproduce successfully and to raise offspring to adulthood).

Human infants are unusual in being dependent on others socially and physically for long periods of time, and also in being dependent in ways that allow for care by people other than the mother. For example, the human infant is weaned early relative to other species rather than relying on the mother for food throughout its immature period. Humans, when compared with chimpanzees, are weaned sooner (average age 3 vs. 5 years), when their weight compared to birth weight is relatively lower (2.7 vs. 4.9 times birth weight), even though both species introduce solid food at approximately 2.1 times birth weight. Most mammals wean around the time the first molar appears (so that the young can chew solid food), whereas humans wean before the first molar. Humans begin reproducing relatively late in their lifespan and stop reproducing long before the end of the lifespan, yet the number of young produced while fertile is relatively high because the interbirth interval is relatively low (3 years for humans vs. 5.6 years for chimpanzees), and a larger percentage of young survive in humans than in other animals, even in hunter-gatherer groups.

Menopause

It is unusual for a mammal to have a menopause as humans do. However, there is nothing unusual about humans having unusual life stages. Although disagreement remains, many biologists, physical anthropologists, and others with a life history perspective assert that menopause is a universal life stage unique to humans (Hawkes, O'Connell, Jones, Alvarez, & Charnov, 1998; Pavelka & Fedigan, 1991). Nonhuman primates (i.e., monkeys and apes) sometimes do have a period during old age during which they do not reproduce, which is sometimes cited as evidence for their having a stage analogous to menopause. Pavelka and Fedigan (1991) pointed out, however, that the phenomenon in nonhuman primates differs from that in humans in many crucial ways. First, these nonhuman primates are typically very old, near the end of the known life span of their species and at a time when many body systems are in an advanced state of decline. Only humans stop reproducing approximately halfway through the known life span and prior to the senescence of other body systems. Further, menopause is universal in humans, but not in monkeys and apes. Many species of nonhuman primates have been studied, and within each species some individuals do stop reproducing when they are old, but others remain fertile. Finally, menopause in humans is characterized by the depletion of ovarian follicles. An envelope of cells that manufactures reproductive hormones needed to orchestrate the menstrual cycle surrounds each immature egg in the ovary. In humans, follicles (i.e., eggs with their surrounding cells) are depleted, whereas nonhuman primates typically do not deplete their follicles. Old nonfertile primates continue to have menstrual cycles, and some who live to the end of the known lifespan of their species ovulate within days of their death.

Female humans do not simply use up their follicles. They run out of follicles because they are genetically programmed to do so. Different cell types in the body live for different amounts of time. Red blood cells, for example, live for a matter of months whereas brain cells must last a lifetime. Each cell type responds to different genetic instructions as to its normal life span and when it should die. The vast majority of follicles are not involved in ovulation. A woman who never becomes pregnant might ovulate 300-400 eggs in her lifetime. The rest of the approximately 400,000-500,000 follicles in the body of an average adolescent simply die over time. The rate at which follicles self-destruct is under tight genetic control. Follicles self-destruct throughout the lifespan, including childhood when levels of reproductive hormones are low. The fact that humans run out of follicles, in contrast to other primates who do not, suggests that this could be one of the mechanisms by which menopause evolved. One pathway to evolutionary change is for the rate of a process to change (i.e., regulator gene changes), rather than by a new process or structure developing. Although many biologists assume that human egg cells simply wear out after 50 years, perhaps, alternatively, follicles are genetically programmed to live at most 50 years as part of the programming of the human female body plan. Further, the rate of self-destruction accelerates beginning in the 30s (Richardson, Senikas, & Nelson, 1987); without this acceleration follicle depletion would not occur before a woman's 70s; this change of rate is another possible mechanism for evolutionary change.

Maturational View of Menopause

The Lifespan Biological Model suggests that humans have a life stage preceding old age characterized by post reproductive, competent, relatively healthy adulthood.

Although menopause marks the absolute end of reproduction, fertility has typically been declining for many years, and most women are infertile before menopause. The evolution of this life stage may have involved regulator gene changes, perhaps those that control the rate of follicle death. A slowing down of the overall rate of change in the body, as is typical of earlier human life stages, may also be involved: Many body systems are beginning to decline, as suggested by increasing vulnerability to chronic illness, but this occurs slowly compared to the acceleration in rates of illness found later.

Biologically oriented professionals disagree about the evolutionary origins of menopause (see, for example, Hawkes, et al., 1998, for a review of theories). Some assert that menopause is adaptive, and therefore became part of the human genome through natural selection. For example, the "grandmother hypothesis" (Hawkes, O'Connell, & Jones, 1997) suggests that women who had stopped having their own children helped to care for the children of their relatives. This increased the numbers of their relatives who survived and helped human groups to settle in a broader range of environments. The "grandmother hypothesis" often narrowly focuses on feeding the young, but older women serve a variety of useful functions in their groups. Others argue that menopause was a byproduct of some other change. For example, perhaps genes that created a longer lifespan or that were needed earlier in life inadvertently resulted in menopause; menopause, once it existed, then may have taken on new functions, some of them adaptive (Bogin, 1999).

Evolutionary biologists, anthropologists, and psychologists have linked the meaning of menopause, especially whether or not it is due simply to senescence, to whether evidence could be found of an advantage with regard to natural selection.

However, these scientists do not argue that childhood or other stages of life do not exist because the competing theories about possible adaptive advantages have not been reconciled or fully evaluated. The first question to answer is whether the data suggest that a coherent life stage exists. If it does, then an evolutionary explanation can be sought. Further, theories that narrowly focus on food-gathering or other such behaviors that directly foster the survival of one's own descendants are unlikely to account for survival in human groups. It is useful to add a perspective based on lifespan developmental psychology in order to understand the dynamics of gene/development interactions, and therefore the life course.

The evidence suggests that menopause is a universal, even unique, human attribute. However, life stages are characterized by sociocultural and psychological as well as physical changes. What we observe when we look at humans is that they live in groups that are characterized by a high degree of interdependence. Humans cooperate in practical tasks that range from childcare to hunting. The normal development of the human brain is itself dependent on social experiences. As described above, human babies are unusual among mammals in having adapted to being cared for by people other than the mother. Humans also live in a world of symbolic meaning with regard to their personal and social experiences. Humans form relationships based on symbolic and cultural meanings. Even defining who is related to whom, or what one's responsibilities to different kin are, is only in part a matter of genetics and varies from one group to another. Someone must make and enforce decisions that maintain social meaning and cohesion. Sex, age, and family position (e.g., being head of a multigenerational household) are among the categories by which social power is allotted.

We cannot know what life was like for prehistoric humans. However, we do know that among modern hunter/gatherers, women in their 50s and 60s and older are commonly found. They are not regarded as anomalies or oddities. They are physically healthy and typically have recognized social roles in which they serve important functions for their social groups. In some groups they gather crucial food for young children (e.g., Hawkes, et al., 1997). They are repositories of cultural memory (Diamond, 1996). In addition, the post reproductive period is often portrayed as one in which social power is high (Brown & Kerns, 1985). Women play a variety of leadership roles, such as deciding who will marry whom or defining kinship relationships as well as assigning practical tasks (e.g., Lee, 1985). (Very old, often fragile, people can be in a different social category; a discussion of their roles is outside the purview of this paper.) Consistent with the speculation that the post-reproductive period may be associated with high social power, many psychological theorists assert that personality development during the 40s and 50s involves a shift toward increased psychological autonomy, concern for the common good, and differentiation between personal and social realities (e.g., Helson & Wink, 1992; Notman, 1990).

Implications of Maturational View

Development is often viewed as occurring only until adulthood. Positive changes toward increasing growth and complexity (i.e., childhood and adolescence) are followed by periods of stability (i.e., adulthood) and then decline (i.e., midlife and old age). Aging is sometimes defined as degenerative changes (Gosden, 1996). This view of the arc of development tends to focus attention on assuming that changes that occur in midlife and beyond are best understood by the dynamics of senescence, that is, an understanding of

how a system is wearing out, becoming less efficient, or otherwise declining in function. In the biomedical model, menopause occurs when an aging reproductive system has stopped doing its job. Some professionals believe that this is normal whereas others believe that menopause is an endocrinopathy, but even those who assert that menopause is "perfectly natural" may also assert that it has negative health consequences. The preconception that animals should reproduce throughout their lives makes it appear natural that the cessation of menstruation (and therefore reproductive uselessness) would be a key event either initiating or even hastening the aging process. Disease-oriented explanations tend to seem inherently plausible, and the risk is that the biology of healthy systems will be overlooked. For example, irregular menstrual periods during perimenopause are often described as "symptoms" (North American Menopause Society, 2000) whereas irregular periods after menarche are assumed to be normal. Menopause has been linked to degenerative chronic illnesses, such as heart or bone disease, based on weak or ambiguous evidence.

If menopause is viewed as the senescence of the reproductive system, then it also appears inherently plausible that if estrogen levels sharply decline, this must be a deficiency. This viewpoint precludes the necessity for asking what function estrogen serves in post reproductive women, and whether lower levels suffice for normal functioning once estrogen is not needed to support reproduction. The idea that hormones facilitate specific functions that must be identified tends to be overlooked. The presence of receptors does not automatically mean that a hormone is needed for health. Receptor sensitivity (i.e., the likelihood that a receptor will respond to a hormone) can vary throughout the life course. For example, the presence of estrogen receptors in body

tissues such as the brain or urinary tract is assumed to mean in and of itself that these tissues must have estrogen in order to be healthy. Yet prepubescent girls have low estrogen levels but not poor bone health or other problems attributed to menopause. Further, the idea that menopause initiates senescence has led to a telescoping of midlife and old age. High rates of bone fracture and heart disease are typical 20 to 30 years after menopause, yet are conceptualized as being "postmenopausal," that is, dating from this time. A small increase in risk is conflated with the initial stages of disease.

The idea that menopause is maturational rather than degenerative leads us to ask different questions and to see different dynamics as inherently plausible. If the assumption is made that a life stage exists in which humans are post reproductive but relatively healthy because senescence is slow or slowed down, then we are more likely to think in terms of the dynamics of healthy systems and also to look for compensatory mechanisms (that help to slow down senescence) in addition to degenerative processes. This keeps us focused on the idea that concepts used to understand earlier stages of life continue to be relevant, especially concepts that changes may have developmental meaning, may be positive or functional, and that compensatory mechanisms may be at work. Assumptions that menopause fosters pathologies, such as chronic illnesses, may appear less a matter of common sense, and therefore more in need of proof, if post reproductive adulthood is a time of relative health and slow, rather than accelerated, senescence. If a post reproductive woman is thought of as a competent group member who often serves a leadership role, the stereotype that at menopause women naturally become fuzzy-headed, have poor memories, or in other ways have deteriorating brains would seem less plausible in the absence of strong evidence. It is also more likely that

compensatory mechanisms that preserve function would be considered. For example, as discussed below, bone becomes wider (and therefore stronger) at the same time bone density is thinning. Estradiol levels sharply decline, but estrone becomes the dominant estrogen after menopause; often dismissed as a weak estrogen, estrone is far easier for the body to use, and in that sense more effective, than is estradiol. Compensatory processes may have general importance throughout the life course. For example, positron emission tomography (PET) scans show less left hemisphere firing during cognitive tasks by elderly than by younger adults. However, older adults with good cognitive functioning develop a pattern of right-hemisphere firing not found earlier.

Bone Health

Osteoporosis, a pathology in which bone is fragile and vulnerable to fracture, provides an example of how a maturational view of menopause lends itself to different data interpretations and different theoretical questions. Bone mineral density (BMD) has been considered of central importance to diagnosis and treatment. Low BMD was originally considered a risk factor for osteoporosis. However, in 1994 the World Health Organization defined the disease as present if BMD is low, even in the absence of fracture. As evidence has accumulated more recently, definitions are shifting again. A National Institutes of Health consensus caucus (National Institutes of Health, 2000), for example, defined the disease in terms of compromised bone strength, and emphasized that bone strength and the likelihood of fracture depend on many factors in addition to BMD.

For many women, BMD decreases at an accelerated rate for approximately 5 years around the time of menopause. Within a biomedical framework, BMD loss at

menopause was therefore assumed to be crucial to the development of osteoporosis, and treatment with a prescription estrogen beginning at menopause was asserted to be the treatment of choice. This connection appeared to be so natural that other important facts were overlooked. For example, the average age of fracture (approximately age 80 for hip fracture) is long after menopause. Age is a stronger predictor of fracture risk than is menopause status; the likelihood of fracture increases with age in both men and women (e.g., De Laet, van Hout, Burger, Hofman, & Pols, 1997; Kanis, 1993). Country of residence and secular trends are more strongly related to fracture risk than is sex, which suggests that lifestyle factors may be crucial (Kanis, 1993).

The heuristic that changes might be normative or compensatory rather than pathological can lead to a different interpretation of experimental data than is found within the biomedical model. For example, research that documents that low BMD is widespread among postmenopausal-aged women (e.g., close to 50 percent in Siris et al., 2001) is interpreted within a biomedical model as indicating the serious, almost epidemic, nature of a problem. However, it is also possible that a common change may be a normative change. Developmental change is suggested by evidence that an internal set point may be at work. As mentioned above, bone on average is lost at a higher rate for approximately 5 years after menopause and then slows down. Within a biomedical model, this suggests accelerated senescence. However, bone loss appears to reach a certain point and then slow down regardless of when menopause begins. In one study, for example, women who reached menopause later had a higher rate of bone loss than did women who reached menopause at a younger age; the result was that by age 64 there was no correlation between age at menopause and BMD (Ahlborg et al. 2001). This

adjustment of rate suggests that it could be the case that a developmental change guided by an internal set point is at work. As an analogy, if the adolescent growth spurt began at a later age for some adolescents, there would be a sharper spurt than for those adolescents who begin the spurt earlier. Further, BMD declines not simply because older osteoblasts (i.e., cells that build bone) stop doing their job. For example, some preliminary results suggest that older osteoblasts trigger greater production of osteoclasts (which break bone down) than do younger osteoblasts, thereby actively influencing the lowering of BMD (Cao, Venton, Sakata, & Halloran, 2003). Compensatory processes may also be at work. For example, bone is not simply being lost, it is also changing shape. As adults age their bone density lessens, but the overall bone becomes wider in circumference; wider bone maintains bone strength even when bone is thinner (Ahlborg, Johnell, Turner, Rannevik, & Karlsson, 2003).

The development of osteoporosis clearly is multifactorial. BMD correlates with fracture when large groups of people are compared, but it is a poor predictor of fracture for individuals. For example, BMD accounted for four percent of the risk reduction in fracture enjoyed by raloxifene-users, which left 96% unexplained (Sarker et al., 2002). Perhaps low BMD increases vulnerability to fracture when compensatory changes don't occur or when low BMD is found in combination with disease-promoting factors, such as smoking cigarettes or additional age-related changes in the structure of bone. Perhaps effective treatments might be found by identifying and ameliorating these additional factors rather than by focusing narrowly on maintaining BMD. For example, exercise programs that improve balance reduce the number of falls and the frequency of fracture even when they do not affect BMD (e.g., Day et al., 2002).

Conclusion

Basic assumptions and theoretical models are crucially important in the study of menopause. The biomedical model directs attention towards disease processes and away from normal functioning. This overemphasis must be balanced with a consideration of the biology of healthy systems. In healthy systems, the effects of hormones vary with their physical and psychosociocultural contexts. Life history theory augmented with lifespan developmental psychology provides a starting point from which to consider how to conceptualize this normal context.

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