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Primate Reproductive Aging: From Lemurs to Humans

Sylvia Atsalis · Susan Margulis

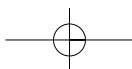
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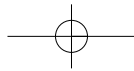
Abstract

The scope of data now available for primates from long-term field and captive studies has opened up exciting possibilities for investigating age-related patterns of reproduction. Valuable information on the aging process can be gleaned through broad cross-taxonomic comparative studies that include lemurs, monkeys, apes and humans. Thus, across all taxa discussed in this volume, female reproduction was found to be complex and dynamic, affected by the interplay of multiple exogenous and endogenous factors. Throughout their lives, females differ in their individual reproductive output. As they age, a period of reproductive instability is common among female primates and perimenopausal-like hormonal changes have been noted in many species. Available data from lemurs and callitrichids indicate that at least in some species, age-related declines in reproduction are manifested as diminished success of females to rear their young to weaning age. Few data are available for New World primates, but the same observation holds true for Old World monkey females, who also are characterized by declines in sexual activity and decreased birth rates. In apes, captive data suggest the presence of an appreciable postreproductive lifespan but this has not been confirmed in the wild. Menopause may be manifested as an evolutionary continuum across primate taxa with the potential for an extended postreproductive lifespan evident in cercopithecines and apes.

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Discussion and analyses on reproductive aging in nonhuman primate females often focus on how reproductive senescence compares to the human menopause. As oft repeated in this volumes contributions, there is a great deal of debate as to how unique the human menopause is, and the degree to which the timing of reproductive termination in other primates results in an appreciable period of postreproductive life, or simply marks the inevitable decline that comes with somatic aging. By comparing observations from a broad range of primate taxa, however, we can evaluate the perceived uniqueness of the human menopause. Therefore, in compiling this volume, we aimed to provide a broad taxonomic overview on the current state of knowledge concerning age-related changes in reproduction in primate females. In so doing, we expected to gain specific taxonomic based insights into commonly posed questions





on the occurrence of menopause, and we anticipated to reach an enhanced appreciation of the length of the putative postreproductive lifespan across primate taxa. We incorporated observations collected from both captive and free-ranging populations, as both types of data can offer different perspectives on the process of reproductive aging in synergistic fashion.

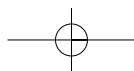
While achieving additional clarity on these issues, we have also been rewarded with a far richer understanding of the factors that influence the ontogeny of the female reproductive life cycle. That female reproduction is a dynamic system, affected by the interplay of multiple and complex exogenous and endogenous factors, has become abundantly clear. This high level of complexity occurs across all taxa. In this chapter, we summarize and spotlight taxonomic differences and unique findings in reproductive aging gleaned from the research described in this volume, while also directing our attention to emerging common patterns that can enhance our understanding of aging in nonhuman primates.

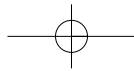
Integrating Multiple Modes of Data Collection

Over time, the scope of data available from long-term field studies on nonhuman primates has opened up exciting possibilities in investigating age-related changes and lifetime patterns of reproduction. Wright, King, Baden and Jernvall's chapter spans over 20 years of data; Borries and Koenig have access to data on langur populations dating 40 years or more in some cases; Shumaker, Wich and Perkins reference data on wild orangutan populations dating 36 years, but wisely indicate that as a result of the longevity of the species, this timeframe is insufficient to truly address aspects of lifetime reproduction.

Data from field sites represent a tremendous opportunity, but also have limitations as the ability to collect physiological data or samples may be limited and the cause of disappearance of individuals from a population often cannot be confirmed. By combining field and captive data, however, there is the possibility of more fully describing patterns within an ecological framework. Wright and co-workers combine field work with laboratory studies on lemur tooth wear patterns. Tardif, Araujo, Arruda, Souza, Yamamoto and French, and Borries and Koenig also augment and strengthen their research using an integrated approach. In the case of the calitrichids, the long-term captive database is complemented by more recently acquired field data, while the long-term langur field work is supplemented and supported by captive data.

Semi-free-ranging primate populations, such as the rhesus population studied by Johnson and Kapsalis, lend themselves to long-term investigation and to careful scrutiny of data for conducting analyses within an evolutionary theoretical framework. Shumaker and co-workers take a comparative approach. Drawing from captive and field work, they discover surprising contrasts between observed patterns of

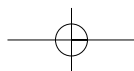


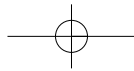


age-related reproduction in captive and wild populations of orangutans. The results of their investigation suggest that captive data should be approached with some caution as management decisions can significantly influence a female's reproductive history. Conversely, the advantage to captive studies is that records of past husbandry decisions (including social grouping and contraception history) coupled with available information on health, can help to explain a specific female's reproductive history as it relates to birthing events. To reach relevant and accurate conclusions on reproductive history of each female these records must be closely investigated. On the other hand, small sample sizes, particularly from wild populations, may be at the root of the difference noted in the orangutan study, i.e. that captive orangutans have a shorter reproductive lifespan while females in the wild reproduce throughout their lives. Emerging studies from wild and captive gorilla and chimpanzee populations may help to clarify the reasons for this dissimilarity.

Finally, Erwin and Hof call attention to the ways that animal models can generate valuable information for comparative studies in primate biology. This observation was clearly highlighted by results from experimental protocols on macaques and squirrel monkeys described by Kaplan and by Williams, respectively. These and other experimental studies offer an opportunity to recognize physiological processes that are homologous between humans and nonhuman primates. Although experimental animal studies usually are conducted for the benefit of human health, we agree with Erwin and Hof that they have the potential of offering useful insights for veterinary clinicians that can apply the newfound understanding of homologous processes to improving animal health. Increasingly, zoo veterinarians are recognizing the importance of diagnosing and addressing age-related changes in zoo animals by using to the symptoms identified in aging humans as a guide, and by taking advantage of the diagnostic techniques available from physicians [1].

Historically, interpretations of age-related reproductive patterns have been based on circumstantial evidence: interbirth intervals late in life that exceed the species norm, declining sexual activity (as remarked by Borries and Koenig), lack of observed breeding behavior, and changes in social relationships. In the absence of hormonal data, these observations can be used as conservative indicators of reproductive function. With the many recent advances in enzyme immunoassay (EIA) and radioimmunoassay (RIA) techniques for noninvasive measurement of steroid hormones from opportunistically collected urine and fecal samples, we now have the opportunity to validate bioassays for reproductive state by providing quantitative measures of reproductive hormones. Videan, Fritz, Heward and Murphy, and Atsalis and Margulis, provide hormonal data in support of age-related reproductive declines in chimpanzees and complete reproductive termination in gorillas. In particular, Videan and co-workers were able to decouple the presumed association between sexual swelling and ovulatory cycling in common chimpanzees, thus uncovering the potential for an appreciable postreproductive lifespan in this taxon. Hormonal and behavioral evaluation of gorillas demonstrates the occurrence of reproductive termination





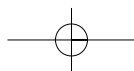
(menopause), as well as hormonal irregularity (perimenopausal-like patterns) beginning well in advance of complete acyclicity. Other chapters, too, hint at the potential value of incorporating hormonal evidence in support of demographic and behavioral observations. Borries and Koenig, Tardif and co-workers, Shumaker and co-workers, and Williams, all provide hormonal support of conclusions gleaned from other types of data. Synthesis of these different data modalities – behavioral, demographic, and physiological – represents a key contribution that facilitates broad discussion about the evolutionary implications that socioecological influences on reproductive aging patterns.

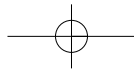
Of pivotal importance to assessing age-specific reproductive schedules is knowing female age. Birthdates are common knowledge in captive populations, but rarely is this information available for subjects in natural populations. Borries and Koenig estimated the age of langur females by combining physical signs of aging with data on sexual activity and last parturition. Tardif and co-workers used their knowledge of dental condition to establish age estimates in callitrichids.

In addition to individual and demographic information, the availability of longitudinal hormonal profiles is of particular importance, because in their absence age-related cessation of reproductive function cannot be confirmed. Fecal hormonal analyses have been applied with success both in captive and in wild primate populations and they are becoming increasingly popular as a way to gauge ovarian function in a noninvasive manner. When animals can be accessed regularly – such as in captivity – fecal analysis permits longitudinal hormonal profiling of specific individuals whose ages are known. As our own research on captive gorillas illustrates, an appreciable sample size can lead to successfully establishing population norms for hormonal concentrations. Females can be evaluated in light of the available information. Attention can be brought to irregularities in their hormonal profiles, leading to a better understanding of reproductive potential and alerting to possible health problems.

Reproduction across the Lifespan

The ontogenetic progression of a female primate's lifetime reproductive schedule is not a smooth trajectory from high fertility in the peak reproductive years to incrementally diminishing fertility as the female ages. Kaplan, in particular, revealed that primate female reproduction is not experienced as a regularly cycling wheel of hormonal increases and decreases followed by gradual decline. Perimenopause is a notable period of transition and it can start relatively early in a female's reproductive life. And, while the symptoms of perimenopause have gained wide recognition in recent years, Kaplan provides abundant evidence of the importance of premenopausal health, not confined to the perimenopausal period, in the development of postmenopausal coronary heart disease and osteoporosis in human females. Indeed, both the physical and psychological health





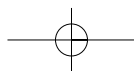
of the premenopausal female foreshadows her health status in the postmenopausal years. This observation makes clear the important connections that develop throughout a female's reproductive lifespan.

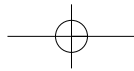
Both human and nonhuman primate females can be affected in this way. Other contributions in this volume further highlight the commonalities between humans and other primates. For instance, evidence for perimenopause has been discovered in many primate species [see Atsalis and Margulis, this vol., pp. 119–146]. It is also clear from Kaplan and other contributions in this volume, including our own on gorillas, that a great deal of disparity exists in individual reproductive output among females. Johnson and Kapsalis amplified this point well with their singular approach to the study of reproductive aging in rhesus macaques. These researchers discovered that poor reproductive outcome was manifested at all ages, and was not confined solely to the oldest age cohorts. Both nonproducing and producing females were found in larger than expected numbers each year of the study indicating a great deal of heterogeneity in female fertility. Thus, sudden catastrophic loss of fertility occurs in a minority of females *each chronological year*, an observation that is consistent with evolutionary theory on aging, i.e. that alleles with negative age-specific effects begin operating at reproductive onset. In short, the data attest that in primate populations there are always females who terminate reproduction well before the potential menopausal age for the species.

In proposing the 'premature acceleration hypothesis,' Kaplan seeks to explain the ways that premenopausal (not just peri and post menopausal) women experience disruptions in hormonal function as a result of physical and social stresses. Thus, individual variability in the manner that reproductive termination is manifested – with some females experiencing abrupt reproductive cessation, whereas others show a more gradual decline (with longer interbirth intervals and interrupted cycles) – may also be the result of differential individual response to the complex interplay between exogenous and endogenous factors. As Kaplan notes, these factors also impinge on the health and reproductive function of nonhuman females as evidenced by studies on various macaque species. The differential effect of these factors may explain the variability in reproductive output noticed for other species described in this volume such as for rhesus macaques (Johnson and Kapsalis) and orangutans (Shumaker, Wich and Perkins).

Menopause: Conserved or Derived?

In the first chapter of this volume, Erwin and Hof expand at length on the importance to comparative and evolutionary biologists of identifying traits as conserved or derived within specific taxonomic parameters. We concur that those of us schooled in the evolutionary and comparative approach tend to view with 'suspicion any claims to human uniqueness'. As a result, we are more inclined to hone in on the similarities between humans and the other primates, rather than on the differences. Undoubtedly, the question of complete reproductive termination in nonhuman primates and its





association with a postreproductive lifespan will continue to spawn future discussions and debate, but the breadth of the discussions in this volume has brought to focus certain undeniable commonalities and patterns among primate taxa.

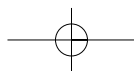
To begin with, female primates commonly undergo a period of reproductive instability as they age. This observation was demonstrated by the collective of studies in this volume. As surmised by Tardif and co-workers, this period of 'age sensitivity to reproductive investment' is associated with alterations in the hormonal environment and declines in fertility. It is often followed by complete sterility. Noticeably, the contributions in this volume reveal not only the regular presence of the variable period across taxa, but also that this period can be lengthy compared to the potential lifespan of the species.

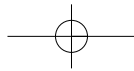
Kaplan's observations on human aging highlight the complex relationship between somatic and reproductive senescence. As a result of this interaction, the challenge that often arises when investigating changes in the hormonal environment as the nonhuman primate female ages is to distinguish between elements of somatic decline and the possibility of early reproductive termination leading to a measurable postreproductive lifespan. In short, if the female's body shows multiple signs of decrepitude in other somatic functions then attempting to place differential emphasis on an aging reproductive system is likely misguided. The span of observations presented in this volume provides us with an opportunity to assess the conserved or derived nature of menopause and to see its evolution as part of a continuum.

Wright, King, Baden and Jernvall, as well as Tardif, Araujo, Arruda, Souza, Yamamoto and French report on the age-related declines in reproduction in *Propithecus edwardsi* and *Saguinus* spp, respectively. In both cases, reproduction does not appear to decline dramatically with age; females continue to be sexually active, bearing infants till death. Age-related declines are manifested largely as the diminished success of females who are approaching the end of their lives at rearing their infants to weaning age. Overall, this outcome appears to be a natural occurrence of somatic aging.

In other cases presented in this volume, loss of reproductive function occurs relatively early in the lifespan of a species, perhaps too early to be characterized as part of somatic aging. The Cebidae represent the most poorly studied primate group even with their historically widespread use as subjects in laboratory studies. The data on squirrel monkeys presented by Williams suggest that despite a lifespan of up to 20 years, reproductive decline is apparent after age 12, most likely as a result of older squirrel monkey females experiencing less frequent ovulations and poor implantation rates. Whether this observation represents a pattern common among the Cebidae, or unique to squirrel monkeys, remains to be examined. As a group, the Cebidae include a number of extremely long-lived species, including capuchins, documented to live into their 40s. Clearly, further investigation on age-related reproductive changes among the Cebidae is called for.

The chapters on Old World primates and Great Apes underscore the much greater attention that has been paid to these taxonomic groups, in some cases as a result of



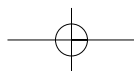


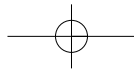
their use in biomedical research, in others because of a growing body of information coming from long-term field studies and from aging zoo populations. The gradual accumulation of data from these sources as well as from provisioned free-ranging populations has facilitated the use of a longitudinal and population-level approach to assess reproductive aging. For example, Johnson and Kapsalis report that birth rates decline with age in rhesus macaques as early as the second half of the first decade of female life. In addition, Borries and Koenig inform us that Hanuman langur females can live to at least 32 years of age. In Hanuman langurs, evidence for decline of reproductive function was apparent through declines in sexual activity, decreased birth rates, and an inability of aging females to raise their last offspring. Following last birth, both *Semnopithecus* and *Trachypithecus* females commonly lived 2–3 times longer than the expected interbirth intervals of their populations, and a postreproductive lifespan of up to 9 years has been reported for Hanuman langurs [2].

Exceptionally long-lived as they are, average and maximum species-specific lifespans remain undetermined for ape species. Consequently, monitoring geriatric female reproductive life is of particular interest as the postreproductive lifespan could potentially be of appreciable length. Results presented by Videan and co-workers support the presence of a long period of perimenopausal variability in female chimpanzees. Moreover, with some captive female chimpanzees living to and even past 60, and with menopause sometimes occurring at around 40, the potential for postreproductive period up to 20 years is possible. Similarly, among cycling female gorillas, Atsalis and Margulis provide evidence that the geriatric group exhibited a great deal of variability in their cycles, both in length and in the fluctuations of specific hormonal patterns. A postreproductive period of approximately 25% of currently known maximum lifespan was estimated. Shumaker and co-workers observed that in captive orangutans, reproduction cessation occurred at the age of 41. Given a maximum lifespan of 58 in captivity, the postreproductive period can be as much as 29% maximum lifespan. Data from the wild, however, do not support these observations as a decrease in birth rates was not associated with age. As sample sizes of observations on aging animals from long-term studies in the wild increase, continued comparisons between natural and captive populations will help us to understand the underlying cause of these apparent differences.

We note here that our estimates of nonhuman primate postreproductive lifespans and those of others [3] are based on maximum reported lifespan for a species. Although in the context of human reproductive aging, an average lifespan measure is more commonly used, at present, we do not have ample sample sizes for nonhuman primates to adequately determine their postreproductive periods in any other way. Over time, and with the continued application of longitudinal analyses, we will be able to more clearly define appropriate average and maximum lifespans for nonhuman primates.

As Wright, King, Baden and Jernvall comment 'since lifetime reproductive success is the currency of evolutionary success, the long postreproductive lifespan of human females requires explanation'. An evolutionary explanation for early reproductive ter-

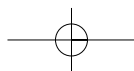


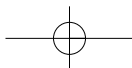


mination can best be provided through comparative studies within the taxonomic context of other primates, and other mammals. If a single conclusion can be gleaned from the anthology of this volume it is that overreachingly menopause, defined as the complete cessation of ovarian follicular function followed by a lengthy postreproductive lifespan, appears to be broadly manifested in primate taxa as an evolutionary continuum. One might view the evolution of reproductive senescence – the manner that it is manifested – as a continuum across primate and likely other mammalian taxa with humans at one end of the spectrum. We borrow from and enhance the evolutionary scenario offered by Wright and co-workers: Lemurs, reflecting the basal primate mode of senescence, do not seem to exhibit diminishing reproductive output with age (although offspring survival of aged females is not ensured especially under dire climatic conditions). Similarly, in callitrichids, old females continue to reproduce but exhibit a lengthy period of hormonal instability. Reproductive cessation occurs in the last quarter of a monkey's life (Cebidae and Old World), while apes may spend about a 1/3 of life postreproductively. Menopause in humans punctuates the first half of maximum lifespan. Decreased offspring survival and the slowing down of reproduction in older females of all these taxa may be a way to conserve energy resources as the body declines. In this vein and based on their observations in lemurs, Wright and co-workers propose that the evolution of menopause may have its origin in a long lifespan that compromises female ability to buffer reproductive success against environmental fluctuations. This is an attractive scenario that can be further validated and refined by bridging some of the gaps in our knowledge on reproductive aging in the more poorly studied primate subtaxa and in other long lived mammals. Thus, from a phylogenetic perspective, we may tentatively conclude that menopause associated with a postreproductive lifespan has its antecedents dating to the divergence of Old and New World primate groups, in that the potential for an extended postreproductive lifespan is evident in cercopithecine primates and apes, but appears to be lacking in prosimians and callitrichid primates. The cebids remain somewhat equivocal, due largely to the dearth of information on patterns of reproductive aging and longevity in this group. Although we may not often see females attaining advanced age in wild populations, the genetic potential is there thus establishing an evolutionary continuum that culminates in the extremely lengthy postreproductive lifespan characteristic of our own species.

Conclusion

Until recently, the occurrence of reproductive termination in nonhuman primates was questioned. With more studies confirming the presence of menopausal non-human primate females in wild and captive populations, the direction of research efforts has been somewhat redefined; from seeking to establish the fact of reproductive termination in nonhuman primate taxa, to the need for measuring the length of





postreproductive lifespan. In this new quest, evidence from all lines of research fields will prove of utmost utility.

Conventional wisdom maintains that predation, disease and other external factors of mortality preclude observation of high rates of senescence in the wild. It follows then that in natural populations not many female primates will reach an age at which menopause and postreproductive life would manifest themselves. Borries and Koenig call attention to the fact that the presence of old individuals is only occasionally acknowledged in the scientific literature with quantitative compilations confined only to a handful of populations. Yet, observations in this volume make clear that nonreproductive females of old age have been documented in many different species under captive and natural conditions. The available data are critical in their importance because they indicate that the proportion of aging females may be higher than expected in some populations, possibly dependent on local ecological and social conditions. In the future, we look forward to seeing more analyses that include data on aged females. These will lead to increased understanding of the biology and behavior of geriatric females and to additional insights into the processes of reproductive aging. For now, we anticipate that the findings from this volume will serve to expedite continued investigation across taxa, across the lifespan, and across disciplines to fully elucidate the diversity of patterns exemplified among primates. Only then can we evaluate the evolutionary and ecological significance of reproductive patterns in light of taxonomic and temporal trajectories.

Acknowledgements

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