Primate Locomotion: Linking Field and Laboratory Research. *Developments in Primatology: Progress and Prospects.*

Edited by Kristiaan D'Août and Evie E. Vereecke. New York: Springer. $179.00. xvi + 364 p.; ill.; index. ISBN: 978-1-4419-1419-4 (hc); 978-1-4419-1420-0 (eb). 2011.

The locomotor and positional behaviors utilized by primates are arguably the most diverse among mammals. More than a century of research has gone into formally describing primate locomotor diversity and to better understand the underlying biomechanics of different positional and locomotor behaviors in both laboratory and natural settings. This new volume contains 16 research and review articles on nonhuman primate locomotion.

After an introductory chapter by the editors, Chapter 2 reviews both the advantages and pitfalls of locomotion research that takes place in the laboratory and in natural settings (i.e., the field). The laboratory provides a controlled environment to test specific biomechanical hypotheses and the ability to alter experimental conditions, but at the expense of small sample sizes, limited choice of species, and diversity of behaviors that can be studied. Although field studies can remedy some of these problems, three-dimensional motion analysis and accompanying force and energetics data have been untenable. Several chapters in this volume discuss new ways in which animal gait laboratories can be made more naturalistic by altering substrate types, or by incorporating high-tech equipment directly into zoo enclosures, to study complex and irregular locomotor behaviors such as brachiation and leaping in gibbons and siamangs (Chapter 3), bipedalism in baboons (Chapter 5) and sifakas (Chapter 8), or load carrying in great apes (Chapter 7). Other papers describe new attempts to bring advanced laboratory techniques directly to the field to examine gibbon suspension (Chapter 11) and red howler monkey quadrupedalism (Chapter 14). The more interesting papers directly compare field biomechanics data with data acquired from laboratory/captive animals. In general, gait and limb kinematics accord well between wild and captive individuals for habitually quadrupedal primates such as lemurs (Chapter 16) and squirrel monkeys (Chapter 17). In contrast, however, the biomechanics of more acrobatic locomotor behaviors such as forelimb suspension utilized by wild spider and woolly monkeys may not be represented by captive individuals in zoos or animal gait laboratories (Chapter 13).

This collection of papers demonstrates that both laboratory and field research complement each other, and that both are relevant to comprehensively understand primate locomotor biology and its evolution. Future research in this and similar fields will benefit from the continued interdisciplinary approaches demonstrated in this edited volume.

Biren A. Patel, *Anatomical Sciences, Stony Brook University, Stony Brook, New York*

HUMAN BIOLOGY AND HEALTH

The Hygiene Hypothesis and Darwinian Medicine. *Progress in Inflammation Research.*

Edited by Graham A. W. Rook. Basel (Switzerland) and Boston (Massachusetts): Birkhäuser. $189.00. xii + 305 p.; ill.; index. ISBN: 978-3-7643-8902-4. 2009.

This fascinating book is a compilation of chapters that discuss proven and potentially negative effects of a shift from the Paleolithic environment to the modern human niche, constructed by humans in the industrialized world (i.e., disinfected and dewormed Disneyland).

The volume is a welcome compilation of informed perspectives by a wide variety of scientists actively involved in research on the connections between changes in recent human behavior and ecology and the rapidly growing problem of atopic disease (eczema and allergic asthma) and autoimmunity. Several chapters also explore the possible connections between reduced and delayed exposure to infection and parasites and additional important human diseases such as childhood leukemia, type 1 diabetes, depression, atherosclerosis, and Alzheimer's disease. A final chapter discusses the potential roles of additional or alternative changes in modern human lifestyle.

The book provides an up-to-date overview of research into the unintended negative consequences of modern hygiene and other recent changes to the modern human lifestyle on human health. The modern niche of industrialized and opulent societies includes the complete elimination of many helminthic parasites, the massive reduction in foodborne infections with viruses, bacteria, and protozoans, and the reduced exposure to saprophytic microbes from soil and microbes associated with animal dung. The chapters share a common theme of mismatch between a human immune system conditioned by the Pleistocene "environment of evolutionary adaptation" (EEA) and our modern anthropogenic niche. The past environment was microbially and helminthically much richer than our modern environment in the industrialized world with urbanization, sanita-

tion, and antibiotics. In other words, we are facing a "biodiversity crisis in our midst"—with profound consequences for human immune development and function.

In the introduction, Rook argues convincingly for the cost of an "evolved dependence." He points out that it is more the lack of "old friends" rather than just relative absence of childhood infections, which causes so many immune complications in modern humans. An extremely simplified rendition of the phenomenon is one of "microbe (and worm) deficit disorder," in which the relative absence of timely exposure to microorganisms and worms is key for tuning the developing immune system away from exaggerated and persistent inflammatory responses. Part of the value of distinguishing between lost "old friends" and hygiene in general is of course that hygiene has had and continues to have many important benefits beyond the benefit of hand washing for surgeons and especially their patients, as Sir Joseph Lister so clearly realized over a century ago.

For nonclinicians, this volume provides an impressive overview of the varied areas of human health, where our mismatches due to the modern human-made niche may well turn out to have disastrous consequences for our health. Insights from studies such as the ones discussed throughout promise to lead to the development of preventive measure and therapeutic interventions and prophylaxis for many of these health problems.

A welcome chapter by George Armelagos puts the phenomena in a context of deep history. The chapter discusses three epidemiological transitions: from Pleistocene foraging to Neolithic farming, from Neolithic farming to industrialized life and, finally, the threat of emerging diseases. Although humans are the only species having undergone these transitions, more discussion of comparative studies, especially those including other primates and our closest living relatives the "great apes," would have been very helpful. Some of the problems plaguing modern humans might not only be related to the three transitions mentioned by Armelagos, but rather further complicated by the vastly different history of even Paleolithic foragers from our closest living relatives the chimpanzees and bonobos. One could argue for a "fourth" and much earlier transition from foraging ape to home base living hominin. Paleolithic humans and their hominin ancestors must have had pathogen regimes drastically differing from those of chimpanzees or bonobos. Key determinants of such differences would have been the use of home bases, the reuse of water sources, and the much larger number of prey animals from which a plethora of microbes would be acquired. A "Darwinian" view of human health should include analyses of such ancient uniquely hominin pathogen regimes and how these might have shaped modern human immune development and disease susceptibility. For example, recent evidence for differences in T-cell regulation and "trigger happiness" of human immunity might have been very relevant. This could help us understand which members of the "pantheon of Paleolithic pathogens" (p. 32)—as George Armelagos so hellenistically put it—actually already represent "modern," i.e., human-adapted pathogens. Humans are the only African primate species that until recently was free of HIV and foamy virus. On the other hand, modern humans have lived with tuberculosis (and many soil mycobacteria as discussed in the book) since long before we migrated out of Africa.

In his chapter on the relationship between delayed infection and childhood leukemia, Mel Greaves takes the convincing view that the "very beneficial impact of depriving our infants and their naïve immune systems of this infectious educational or 'priming' experience" (p. 251) did not come without a price. In other words, like so many things in evolution, the benefits of hygiene form a tradeoff with unintended and very unfortunate negative consequences. The scope of these negative consequences is thoroughly explored throughout the book.

Many of the chapters mention what is part of a long list of key host molecules of the innate immune system, which specifically detect and target potentially dangerous molecules. Such molecules include both those expected from the outside—e.g., pathogen-associated molecular patterns (PAMPs)—and those from the inside—e.g., danger-associated molecular patterns (DAMPs) such as phosphatidylserine associated with cell death or advanced glycoation end products indicating oxidant stress.

A short overview, such as a guided tour through the zoo of innate immune receptors, including a conceptual graphic juxtaposing the host receptors with the defining features of microbial and parasite-associated molecular patterns, would have been very useful. Such a panoramic overview would have to include the ones mentioned in various chapters such as gram-negative bacterial polysaccharide A recognized by TLR2, lipopolysaccharides recognized by TLR4, mycobacterial glycolipids by CD1, bacterial peptidoglycans by Nod2, helminth surface molecules bound by DC-SIGN, and other high mannose binding lectins.

It should likely also have mentioned the peptidoglycan recognizing bacterially induced C-type lectin REG3G, the chitin and beta-glucan-specific dectin and galectins, such as galectin-1, which inhibits certain enveloped viruses. Equally important

would be the mention of I-type lectins (Siglecs), many of which can recognize PAMPs as well as host self-molecules (also called self-associated molecular patterns or SAMPs). Incidentally, many of these Siglecs are expressed mostly on immune cells and have undergone uniquely human changes in the last five million years since our lineage diverged from that of the two species of chimpanzees (our closest living relatives that show very little atopic or autoimmune disease even in captivity).

The book covers a very wide scope of phenomena and human pathogens, parasites, commensals, and symbionts. One group of omnipresent organisms that was notably absent from any discussion are fungi. Given the existence of innate detectors of fungi-specific PAMP, what is the role of the altered fungal environment in modern industrialized life? For example, opportunities for fungal contamination such as sick building syndrome, which is thought to involve fungal spores and the exposure is via dissemination in a building's ventilation system.

It is worth pointing out that many of the relevant molecular patterns in PAMPs, DAMPs, and SAMPs are either entirely or at least in part defined by glycans, the oligo- or polysaccharide chains decorating glycolipids and glycoproteins. These include: the peptidoglycans and zwitterionic polysaccharides of bacterial cell walls, glycolipids of mycobacteria, the lipopolysaccharides of bacteria, the protozoan glycan antigens (Glycophosphoinositol-anchored glycoproteins), beta-glucans of fungi, and worm surface glycans, including divergent glycans (terminal xylose, high mannose N-glycans) and immune modulatory helminthic glycans (e.g., the lacto-N-fucopentaose III (LNFPIII) shown to drive Th2 responses). So at the obvious risk of appearing too glycocentric, I think that colleagues working on phenomena related to the hygiene hypothesis could benefit from paying more attention to the "glycome" of the human host and its many inhabitants, including long-term residents (symbionts), casual visitors (commensals), and shameless usurpers (pathogens), bear different patterns of glycosylation. Some of the most common plant allergens include glycan motifs shared between plants and helminths (terminal xylose) but absent from humans. Interactions are often influenced by host glycosylation and also by dietary glycans. An illustration of the latter is the realization of the unique glycan composition of human breast milk. Apart from a radically different protein levels and protein and fat composition, human milk contains hundreds of secreted oligosaccharides, many of which with unknown effects. Human milk also lacks the antigenic, xenoglycan N-glycolylneuraminic acid present in bovine milk from which most infant formula is derived. It follows that among the most striking "lifestyle" changes must be the low levels and the much reduced duration of breastfeeding, a very recent phenomenon in human evolution with drastic consequences for the molecular environment of the infant gut and its associated immune system. This change is addressed and its potential consequences for immune development are cogently highlighted in the last chapter, but surprisingly barely mentioned in the earlier chapters, including the ones discussing the development of the immune systems. The well-documented impact of breastfeeding on immune development would have warranted more discussion of the potential negative impact of low breastfeeding practice. Incidentally, chimpanzees are the mammalian species with the longest known lactation (up to four years) and comparative analyses of primate species combined with ethnographic data indicate a weaning age for ancestral humans of over two years.

With regard to food consumed by mature modern humans, one wonders about the potential effect of industrialized processed food that exposes people to large quantities of "neo foodstuffs" from industrialized processing, including large quantities of glycans such as carrageenans (sulfated galactans with demonstrated immune modulatory effects), guar gum (galactomannan), and of course free fructose from high fructose corn syrup, all glycans that have never been part of the human diet in such quantities.

The Hygiene Hypothesis and Darwinian Medicine is precious addition to this emerging field, and the large collection of ideas presented by the authors will benefit and motivate many researchers who are puzzled by the way that "modern life" with all its improvements is biting back and causing much suffering, especially among the younger members of our species. Underexposure to "Old Friend-Associated Molecular Patterns" or OFAMPs such as those encountered on many helminthes and symbiotic microbiota is essentially wreaking havoc with several aspects of modern human immune regulation and function. An obvious approach would be to develop a better understanding of the beneficial effects of old friends, possibly allowing controlled exposure to well-"domesticated" old friends and the engineering of robust mimics of the OFAMPs as preventative agents.

Pascal Gagneux, *Cell & Molecular Medicine, University of California, San Diego, La Jolla, California*