A PIECE OF MY MIND

A Wild Rotation

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The patient was rushed into the room, listless, intermittently trying to lift his head only to fall back down. Soon, he became unresponsive and cold. I placed the ultrasound probe on his chest and saw a barely contracting heart—heart failure. A massive clot filled the left atrium. The team became silent, then quickly regained its composure, and the supervising doctor began disbursing orders in rapid fire. We stabilized the patient, though he remained in serious condition, and then we shifted to research mode. We emailed doctors across the country: "Have you seen acute dilated cardiomyopathy before in similar patients? He is a 3-year-old meerkat."

I would never have predicted that I would spend my final month of medical school performing fetal ultrasounds on a pregnant gorilla, phlebotomizing a 500-pound tapir with hemochromatosis, caring for a meerkat in heart failure, and investigating medical mysteries across the animal kingdom. Yet spending the final month of my MD-PhD program working at the veterinary hospital of a zoo was one of the more remarkable and humbling experiences I had during medical school— a unique capstone to my education as a physician-scientist.

Early during medical school, I became fascinated by the diversity of anatomy and physiology across the animal kingdom. After lectures on cardiology, I read the scant literature on whale heart physiology, in near disbelief that the aorta of a sperm whale has a 2-foot circumference and a staggering cardiac output of 450 liters per minute.[1] It was breathtaking trying to imagine the dynamics of blood flow in such a massive cardiovascular system. During neurology courses, I was amazed to learn that marsupials do not have a corpus callosum connecting the hemispheres of their brain (they are connected via a different tract). The differences between "us" and "them" across the myriad dimensions of function seemed to probe basic assumptions about human pathophysiology. What mechanisms protect giraffes from hypertensive organ damage when their systolic blood pressures are twice that of humans?[2] How do hibernating bears avoid uremia despite months of minimal urine output?[3] The human animal, I came to appreciate, is but a single point among a cloud of points revealing otherwise invisible physiologic trends and questioning principles often taken for granted. This perspective also seemed an inexhaustible source of research ideas with potential to affect both human and animal health.

Later in medical school, I read about the remarkable ways in which diseases can be prevalent in specific species but not others. I helped diagnose my family's cocker spaniel with Evans syndrome—the co-occurrence of autoimmune hemolytic anemia and thrombocytopenia—and was intrigued to learn that Evans syndrome and immune thrombocytopenia more commonly afflict cocker spaniels, suggesting a genetic susceptibility for this breed and an opportunity to reveal some of the mystery of its cause. One of the first patients I saw on the wards in medical school had Evans syndrome. The look on the clinical team's faces when I blurted out, "My dog has that!" was priceless. Yet it spurred me to share with my colleagues the bridges I was finding between human and animal medicine.

These experiences led me to reach out to the Franklin Park Zoo's veterinary hospital in Boston, whose veterinarians bravely agreed to host a medical student for an admittedly unorthodox, perhaps unprecedented rotation. And for both the veterinarians and myself, this experiment changed how we view and understand medicine.

For nearly every disease I saw at the zoo, the simple question of why certain species, human or nonhuman, are susceptible to it, while others are not, raised immediate possibilities for research into their etiology. Chimpanzees have an ostensibly more atherogenic lipid profile than humans, yet they do not appear to get atherosclerosis; instead, they and other great apes (gorillas, orangutans, and bonobos) are susceptible to a different disease—fibrosing cardiomyopathy—that is uncommon in humans.[4] At the zoo, I helped perform cardiac ultrasounds of the gorillas as part of the Great Ape Heart Project to understand how heart disease manifests in our closest cousins. When I cared for a cotton-top tamarin with colitis and a bowel obstruction secondary to colon cancer, I learned that tamarins (a small New World monkey) have high rates of chronic colitis and subsequent colon cancer. Remarkably, this appears to preferentially occur to tamarins in captivity,[5] suggesting an environmental etiology and an opportunity to study the underlying causes of inflammatory bowel disease. At the zoo, I realized that natural veterinary disease models present unique opportunities for elucidating disease etiology beyond induced disease models often used in research, since they manifest spontaneously and in more natural contexts. They may also provide an animal model where one does not otherwise exist. For example, hepatitis B virus research was greatly advanced when a related virus was discovered in woodchucks at the Philadelphia Zoo,[6] and in 1909, a tumor in a chicken from a Long Island farm led to the seminal discovery of the Rous sarcoma virus, which was later pivotal to revealing the first oncogene and the genetic origins of cancer.[7] Efforts to understand susceptibilities to specific cancers among dog breeds,[8] as well as possible lower rates of cancer relative to body mass in large animals such as elephants,[9] may also provide insight into genetic factors mediating protection from and susceptibility to cancer.

Such a comparative medicine approach in fact has a long history. Rudolf Virchow, the father of pathology, was a proponent, famously stating in the 19th century, "Between animal and human medicine, there is no dividing line—nor should there be. The object is different but the experience obtained constitutes the basis of all medicine." Yet physicians today rarely think in these terms. Recently, Natterson-Horowitz's book *Zoobiquity*

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and ensuing conferences on the topic have helped generate renewed interest. More broadly, an approach called One Health is also growing in prominence, which considers not just human and veterinary medicine, but also the environmental factors (biodiversity, ecology, socioeconomics) affecting and affected by both.

At the zoo, the boundary between human and animal medicine seemed an artificial construct. Nature does not hold human disease on a pedestal, nor does it preferentially target diseases to humans. Yet talking to many physicians, veterinarians, and students reveals an asymmetry—the veterinary world routinely looks to human medicine for insight, while the opposite is not true. Human doctors are often surprised to hear that diseases affecting humans are also found in other animals. The oft-heard response of "Animals get that too?" when speaking to my colleagues belies the prevalent human-centric view of medicine. As a result, insights from veterinary medicine that may have major impact in understanding human disease are missed.

However, there are few concerted efforts in the biomedical research community to systematically explore the vast opportunities for comparative medicine research. Grants for physicians, veterinarians, and researchers working together in collaborative projects may help. Notably, the revolution in genomics technologies now provides a key to unlock many previously inaccessible comparative medicine questions. Now would be a uniquely productive time to invest in this approach. Both human and animal medicine stand to benefit immensely.

Education can also play an important role. Medical education may be reinforcing the boundaries between human and animal medicine by not instilling in medical students an appreciation that nearly every disease manifests in other species in both interestingly similar and different ways. Veterinary medicine is not similar to pediatrics, as some physicians may quip, and its potential to inform human medicine is not limited to just zoonoses. Veterinary medicine is also geriatrics, oncology, cardiology, dermatology, rheumatology, behavior—all the disciplines seen in human medicine. Incorporating even modest comparative medicine and evolutionary medicine teaching in medical school curricula would help ensure that the countless variations in natural disease that may inform human medicine are not overlooked. Certainly, the goal would not be to teach veterinary medicine to medical students, but rather to raise awareness among students that they are seeing only a small slice of physiology and disease and that the many idiopathic unknowns of human disease often have illuminating counterparts in other animals. Human medicine is the tip of the iceberg, and briefly introducing comparative medicine would at least teach students that there *is* an iceberg. Medical students would be enriched by this broad way of thinking, stimulating research ideas early in their careers, especially among aspiring physician-scientists, and facilitating closer ties between human and animal doctors over the long term.

Nearly every day at the zoo, the veterinarians and I would make fascinating, unexpected connections between human and veterinary medicine. One memorable experience occurred while I helped treat a bird with a dilated esophagus. One of the veterinarians mentioned as a matter of course that pathologic dilation of the foregut in some birds (parrots), called proventricular dilatation disease (PDD), is caused by a neurotropic virus. My thoughts immediately raced to achalasia, a similar disease in humans whose cause has long eluded research. Searching the literature, I learned that a viral etiology for achalasia had indeed been proposed for decades and that the laboratories of Ganem and DeRisi who discovered the viral cause of PDD had been investigating achalasia tissues for a similar virus. Though this search has not yet borne fruit, these frequent interspecies disease connections were exhilarating.

Helping with the routine animal care at the zoo was also humbling. My first morning was spent trying to coax a 150-pound African desert tortoise to stay still just long enough to slide an x-ray film under him while also balancing a portable x-ray machine on a tripod above. He would not stay still, but we gently persisted to confirm he did not have bladder stones, a dangerous condition to which the species is prone. Checking the glucose levels of a ferret with an insulinoma (pancreatic tumors prevalent in the species), vaccinating a headstrong reindeer for West Nile virus, and helping resuscitate a premature newborn goat were just some of the many meaningful moments I shared.

Sadly, Jeffrey our meerkat died one week after being admitted to the hospital. As we cared for him during his stay, we watched fondly as he stretched, despite his weakness, to the tall lookout posture for which meerkats are famous. We learned that another group of veterinarians (A.M. and M.G., personal communication) had recently reviewed a large number of cases and found that nearly a quarter of meerkats die of cardiomyopathy, most often of the dilated type we had seen—a possible new species-specific disease with potential for research. I thought of Asclepius who learned secrets of healing from the animal kingdom, the snake of his serpent-entwined rod that is the symbol of medicine. As Oscar Wilde and George Bernard Shaw said of Americans and British, human and veterinary doctors sometimes seem like colleagues divided by a common language. But together, we can cure our patients' shared ills.

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