A student recently asked me what field I would go into now if starting all over, and I instantly replied, “Anthropology.” How we humans arose is among the most beguiling questions one can ponder, but until recently, this was an endeavor limited essentially by two tools: radiocarbon dating and morphometric analysis of bones and skulls. However, despite the rare and so often frustratingly incomplete material at hand, this science has been a glorious success, as exemplified by the epochal hominin fossil discoveries of Louis and Mary Leakey and later ones made by others, including notably, their son Richard and daughter-in-law Meave. Indeed, one might view anthropology to be as exciting as any scientific endeavor—at the lab bench or out in the field—in the entire recorded history of science.

Few, if any, anthropologists working back then in what might be deemed the first zenith of this science could have imagined that there would someday be a complete transformation. Pasteur could never have dreamed of today’s microbiomes, although he might well have been delighted to know of our diverse but benign inhabitants, having spent his life dealing with pathogenic ones. Nor could the ancient Persian astronomers or even later, Tycho Brae, have dreamed of the Hubble telescope. Svante Pääbo has seen his dream come true.

In his riveting account of the advent of this new era, the author shares the intrepid adventure that he and others undertook to get from ancient hominids pieces of DNA sufficiently intact and long enough for sequence determination. Along the way, he delves into the entire landscape of prehuman and human anthropology, as well as the essentials of handling archeological DNA, with possible contamination lurking everywhere. He reveals himself to be an uncommonly good writer for a general audience, and yet, he fulfills the “Lewis Thomas standard” in that no peer reader will feel the subject has been unduly simplified or (worse) distorted. Although I had known of Pääbo’s work and had always thought that his research publications were finely crafted, I would not have predicted that he was so skilled a writer in this broader audience mode.

The quality of DNA needed for sequence determination rests not just on the phosphodiester bonds that connect adjacent deoxyribose-base conjugates along each of the two chains but more importantly, the bond between the deoxyribose and the base, called a N-glycosidic linkage. This bond is vulnerable to low pH and heat, especially where the base is a purine (1), and absent the base, that position in the DNA is null as an analytical sequence entity. Even more vexing in dealing with archeological DNA specimens is its notorious propensity to have undergone deamination at the C-4 position of cytidine’s pyrimidine ring, as the author emphasizes. Moreover, the sheer age of these recovered, ancient DNAs, having sat for thousands of years amid the hydroxyapatite bone matrix, now fossilized, adds the factor of not chemical but purely physical damage, steadily accumulating from cosmic radiation bombardment over such long times. Many anthropologists who were keen in the 1970s and thereafter to start working with archeological DNA gave up hope when they consulted nucleic acid biochemists and learned all this well-established lore of damage.

At a skillfully designed place in the story’s timeline, which incidentally is not a strict linear temporal narr-
tive, making the book all the more engaging in my view, Pääbo introduces the reader to a true hero, Allan C. Wilson. Having been a precocious student with the biochemists Arthur Pardee and later Nathan Kaplan, Wilson arrived as a faculty member at the University of California, Berkeley, and soon became a leader in genomics (before the field went by that name). He saw that the sequence arrangements in extant DNA told an ancient tale of horizontal exchange, amplification, deletion, and intragenome mobility before almost any of his contemporaries had this idea (2). Pääbo vividly describes his time in Wilson’s lab and the prevailing view there, catalyzed by Wilson, that a record of human evolution resides within the DNA sequence per se. However, although the author clearly drank the Wilson lab Kool-Aid, there was an even bigger idea afloat. The sequence of us extant humans can only reveal so much, but if ancient hominin DNA could also be recovered and analyzed, well...

The story then moves on to recite many field expeditions to archeological sites by intrepid seekers and the fitful attempts to get ancient hominid DNA. The author cites scientists’ generosity and transparency in their zeal to advance knowledge; e.g., a bone fragment is sent by a DNA-nonconversant digger to a DNA sequencing expert. Along the way, the author is evocative about the sense of community that he witnessed and indeed was partly responsible for, but also on the personal complexities that arose. In a particularly riveting vignette, the author describes his romantic relationship with the partner of a key collaborator and how this affected the work and yet miraculously, somehow did not bring it down. Throughout the book, Pääbo writes with intimacy and sensitivity and warmly credits all who played key roles.

What then is the author’s story? It has three parts. The first is that he and others spent many years and had many failures trying to get DNA from ancient hominin bones, and when they finally did, it was almost always not in decent shape. The second is that the author and colleagues finally succeeded in sequencing the nuclear DNA from a Neanderthal. These people were a dead-end in hominid evolution, and yet, we have inherited a small amount of DNA (ca. 1.2% of our genome) from them. There surely have been many instances in evolution when the demise of one partner in an interbreeding subspecies became extinct, leaving only a footprint in the line going forward, now propagated solely by the other subspecies. However, the comparison of the human genome with Neanderthal (a nonhuman or at least a human subspecies) provides a vivid case and one that takes on added meaning beyond evolutionary biology per se, as in some very distant way, it is about us.

The second part of the story is that the extraordinary accomplishment of getting the Neanderthal genome now casts these people as what is known as a “type specimen.” For more than one century, biologists had assembled phylogenies based on morphological characteristics and also threw down the gauntlet of the nonfertility of the progeny of a cross as the test of species distinction. We can now begin to imagine that if sequence-ready DNA could be recovered from the transitional ape-human species (the so-called protohominid genera, such as Australopithecus, and the several other related tribes, clades, or subspecies of protohominids that have now been added to the list), then the Neanderthal genome would give us a powerful lens to reach back beyond any anthropologist’s dreams.

The third part of the story in this book is the most spellbinding of all and runs as a strong current throughout. It is the story of the author himself. This is not done in any narcissistic sweep of the pen; indeed, the author is quite restrained as to himself. Over the course of the work, at every turn, defeat and disaster were at hand. The tumbling edifice of the idea and the improbability, perhaps impossibility, of its empirical reduction seemed all about, and if Cassandra had been on the scene, she would have wailed her prophecies of doom. However, as in the legend, she had been nullified by her father Apollo who was miffed at her and declared all her prophecies inaccurate, and so, they were for the Neanderthal genome project. Cassandra’s wails were never heard, and somehow, in all the angst and dust, a single, extraordinary mind and man persisted. He is the third part of this story.
Unbroken: The Intrepid Pursuit of Archeological DNA

Thoru Pederson

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