Defending the Cavewoman

AND OTHER TALES OF EVOLUTIONARY NEUROLOGY

by Harold L. Klawans

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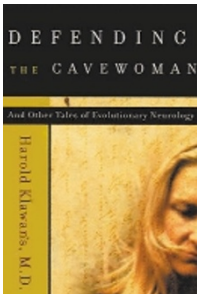
The use of neurological case histories to explore aspects of mind–brain function has a long tradition, with the most well-known contemporary exponent being the neurologist and author Oliver Sacks. It was a pleasure, therefore, to review a book in this genre written by the late Harold Klawans, who was a working clinical neurologist. Klawans' stated aim is to give a neurologist's account of human evolution through the recounting and interpretation of a number of clinical vignettes. Many of the tales and their interpretation make interesting reading for a clinical neurologist, although whether they can be really used to say much about human evolution is debatable.

The book consists of a preface and 13 chapters, and is divided broadly into two parts: the first, the 'ascent of cognitive function'; and the second, 'the brain's soft spots'. Readers may find the style of the book a little folksy, yet it is always easy to read. Most chapters begin with an introduction to the patient and his or her neurological problem. In the first section, there are interesting accounts of patients with disorders of language and movement. Although it was not stated, one assumes that the names of Klawans' patients and those of at least some his medical colleagues have been changed to avoid embarrassment or worse. The importance of these cases for the cerebral localization of function, human development and evolution is discussed.

Among other patients discussed, Klawans describes a patient with epileptic aphasia (Landau-Klefner syndrome) treated successfully with neuro-surgery (Morrell's procedure); a conductor who retained his musical gifts despite a severe stroke causing hemiplegia and global aphasia; the effects of acquired dyslexia in a professor of English; as well as the effects of psychosocial deprivation on language development. The second section of the book departs from classical neurology and neuropsychology and encompasses some diseases that are of interest now to geneticists and molecular biologists as well as neurologists. In particular, there are interesting yet tragic descriptions of a family with Huntingdon chorea and a patient with Creutzfeldt-Jakob disease.



The strongest aspects of the book are the humane and vivid descriptions of Klawans' patients, their conditions, and the ways in which their lives were affected. There are many references to art, music and literature; famous names of the arts and science crop up regularly throughout the text. For example, did the great science fiction writer Kurt Vonnegut in his 1963 description of "ice-nine," as a substance that converts all that it touches into its own ice-like crystalline structure, anticipate Stanley Prusiner's prion?

The uniting theme of evolutionary neurology is somewhat harder to follow, and at times the concept is rather stretched. Klawans has several main points. First, aspects of our brain function have been selected for and certain anomalies may be best understood by appeal to Darwinian principals. One might reasonably ask whether there are any aspects of the human condition that cannot be 'understood' retrospectively in this way. A further point is that learning and the brain plasticity it requires underpin cultural and social changes that, in turn, affect the processes of natural selection.

Some of the examples given provide rather tenuous support for the involvement of natural selection in shaping human disease. For example, it is argued that wildebeests don't get Parkinson disease because the slower baby wildebeests with 'less robust' (that is, vulnerable) basal ganglia are eaten by lions before reaching reproductive maturity, and the parkinsonian tendency is therefore selected out. I am not a veterinary surgeon, but is it not possible that wildebeest do slow as they age beyond their reproductive prime, and that their 'Parkinson disease' is 'diagnosed' at this point by the lions? Are there remnants of our ancestors in our nervous system? Klawans explains to a patient with a syndrome of painful foot and moving toe that it has occurred because of an abnormality of circuits in her vestigal (or 'dinosaur') 'spinal brain'. Maybe clinical governance has taken its toll, but I suspect most clinicians—even those with a paelentological bent—would shy away from using examples from *Jurassic Park* to enlighten patients about their condition.

What of the cavewoman in the title? Klawans credits her first with bringing language into the lives of our ancestors through her prolonged nurturing of the child. And around 200,000 years ago, by surviving a bottleneck in human evolution, she has managed to pass on to us small yet vital amounts of her mitochondrial DNA and, finally, her slim hips and the resulting cephalo–pelvic disproportion prevented successful interbreeding with the bigger, tougher, larger-headed, and therefore larger-brained,

Cancer goes prime time

On 30 March, the US cable television channel HBO debuted Cancer: Evolution to Revolution, a documentary designed to inform the public about cancer treatment, research and politics. The 2.5-hour special describes the pathogenic mechanisms and treatment strategies for various types of cancer, including colon, prostate, lung, breast, ovarian, cervical and cancers. Placing particular emphasis on the role of the patient in seeking out the best possible care, it advocates participation in clinical trials, and explains to viewers the importance of these trials in the development of new therapies. Through interviews with patients, clinicians, researchers (Richard Klausner, Bert Vogelstein and Harold Varmus) and politicians (Florida senator Connie Mack), the program provides a broad overview of the factors that affect basic and clinical cancer research, and insight into the lives of cancer victims and their families. The special will also air 5, 8, 11 and 17 April.

Neanderthal. We have much to thank her for—well maybe.

Are these tales of evolutionary neurology? That I think depends on one's understanding of evolution. Using 'evolution' to link together the clinical themes, however, does work and the framework it provides leads to stimulating writing. Mostly these are tales of neurology patients and very interesting and well told they are. Neurologists, neuroscientists, students and interested general physicians will find this a book that entertains and stimulates their enthusiasm for wider aspects of the subject.

Virus

THE CO-DISCOVERER OF HIV TRACKS ITS RAMPAGE AND CHARTS THE FUTURE

by Luc Montagnier; Stephen Sartarelli (Translator)

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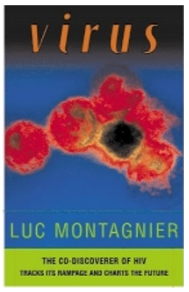
Medical and scientific research is often competitive, sometimes even confrontational, and occasionally bitter and vengeful. A book recently written by Pasteur Institute virologist Luc Montagnier, entitled *Virus: The Co-Discoverer of HIV Tracks Its Rampage and Charts the Future*, is a personal account of such bitterness. The virus in question is HIV (or HTLV-III, LAV, IDAV or ARV as it was sometimes called). The result is Montagnier's autobiography of the acrimony experienced in the early days of AIDS research.

The AIDS era began in 1980 or 1981 as a few clusters of unexplainable Kaposi sarcoma, *Pneumocystis carinii* pneumonia or *Mycobacterium avium* tuberculosis that were unprecedented in previously healthy young adults. For those involved in the research at the beginning, the first controversy was whether AIDS, then called GRID (gay-related immunodeficiency), was an infectious disease at all. Popular hypothetical causes were autoimmunity due to rectal exposure to semen, or drugs such as amyl or butyl nitrate 'poppers' used to enhance sexual performance. In retrospect, such explanations seem irrational, but they did not seem so at the time.

At the same time, those with a background in infectious diseases or microbiology pushed for research to find an infectious etiology. Some concentrated on Epstein-Barr virus or cytomegalovirus (before the era of human herpes virus 8), because of their association with chronic lymphoid infections and/or, however loosely, Kaposi sarcoma. Hepatitis B was also considered because it was known to be highly prevalent in homosexual men. The Centers for Disease Control conducted dozens of seroepidemiological surveys using various viruses, bacteria, fungi and protozoa as antigens, yet they did not include the human lymphotropic retrovirus found a few years earlier by Robert Gallo and his associates at the National Institutes of Health (NIH).



To some researchers working with retroviruses, such as Montagnier, it seemed logical to consider a potential retroviral etiology for AIDS. Montagnier was not alone. At the same time or perhaps even earlier, other scientists, such as Robert Gallo's group at the NIH and the Essex group at Harvard University, were looking for potential links between AIDS and new human retroviruses. In Gallo's case, the rationale was fairly obvious: He had recently discovered the first true human retrovirus and it preferentially infected $CD4^+$ T lymphocytes—the exact cell type that was depleted in AIDS patients. The rationale of the Essex group was somewhat complementary as they were working with a lymphotropic retrovirus of cats that caused T-cell immunosuppression and fatality. It thus seemed logical to hypothesize that a new human T-lymphotropic retrovirus could be the cause of AIDS.

According to Montagnier, a retrovirus would be a logical cause of AIDS, but it wouldn't be related to the HTLV described earlier by Gallo, as Montagnier believed the latter caused only cell proliferation. At the same time the Harvard group and others sought evidence of a serologically related variant of HTLV in AIDS patients, Gallo looked for virus-like particles and reverse transcriptase activity. In Montagnier's portrayal, he was the only one who searched for and found the 'right' virus, initially called lymphadenopathy-associated virus (LAV). However, retrospective interpretations are always easy. Both patients described in Montagnier's initial *Science* paper were described as having antibodies that were capable of cross-reacting with HTLV-infected cells. The last sentence of the first paragraph of his now-historic paper states, "The virus appears to be a member of the human T cell leukemia virus (HTLV) family." This observation, which was presumably important to Montagnier at the time, has been conveniently overlooked or minimized in *Virus*.

In the book, Montagnier also reviews early life experiences that led him to a career in medical research: a serious auto accident that left him with an "attractive dimple," the chemistry lab in his basement, and the pride he felt in his first experiments with freshwater algae. He is critical of the "French nationalistic narrow-mindedness" that apparently drove him to pursue much of his research training in London or Glasgow. He vividly describes his personal frustrations while trying to pursue AIDS research in Paris in the early 1980s. However, he does not seem to recognize that others had the same problems. Throughout the US and Europe, AIDS research would receive little or no targeted funding until several years later.

Montagnier also criticizes the scientific community's lack of support for his hypothesis that *Mycoplasma penetrans* was an important cofactor that allowed HIV to cause AIDS. He even proposes that mycoplasma alone might be responsible for the rare cases of HIV-negative 'AIDS-like diseases', a topic that had a brief flash of notoriety in the early 1990s but soon fell by the wayside as many of the HIV-negative 'AIDS cases' showed spontaneous improvement. As we learned more about the pathogenesis of AIDS, "essential cofactors" or other non-HIV causes became less and less interesting to almost everyone except perhaps Peter Duesberg.

For those who continue to wonder about the culture of AIDS research during the early days, *Virus* may be appealing. To neutralize some of the bias, *Virus Hunting*, by Gallo, might be read at the same time. While reviewing the latter for *The New York Times*, Natalie Angier stated, "Maybe we have heard quite enough about who discovered the cause of AIDS." Her comment seems even more appropriate for *Virus*.