standards, here's how they were regarded by the editors of *Consumer Reports:* "Patent medicine companies which put dollars above human lives are still using the advertising pages of leading magazines to persuade mothers to use this dangerous 'remedy' for their children. Consumers Union believes ... that the heads of the companies responsible for the sale of these products are despicable killers for whom jail sentences would be much too light a punishment. Nor can we find any kind words for the publishers who profit from the advertising for such products ..." (Consumers Union, 1945).

Now, that's telling it like it was ... and is again. We could use a lot more of that feistiness today. Have we all grown too polite? Have we been cowed by the free-market intellectual bullies who castigate critics of American free enterprise? To get out of this hole, we the people will have to decide enough is enough, and unleash the mother of all backlashes. May it happen soon, and may *Overdo$ed America* help catalyze the reaction. If it does, Dr. Abramson would have a patient-treatment story of which he could be very proud.

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Oncogenes, Aneuploidy, and AIDS: A Scientific Life and Times of Peter H. Duesberg by Harvey Bialy. Institute of Biotechnology, Autonomous National University of Mexico, distributed by North Atlantic Books, 2004. 318 pp. $19.95 (paper). ISBN 1-55643-531-2.

Much information is packed into this unusual book, in particular about the present state of cancer research and understanding of cancer and about the present state of affairs regarding HIV and AIDS. These two large topics, cancer and HIV/AIDS, are tied together because the chief contemporary iconoclast in both is Peter Duesberg: in a major review article (Duesberg, 1987), he made the case—never to this day directly challenged, merely ignored—that retroviruses cannot be carcinogens or pathogens.

In relating the course of Duesberg's work in these areas, Bialy describes a number of events of high interest for the sociology of science and scientific unorthodoxy. Though explicitly partisan and exuberantly caustic about some mainstream actors and beliefs, the book is so fully documented that it earns respect even if not complete assent. This reviewer, having read much other material about HIVJAIDS, gives it full assent as to HIVJAIDS. As to cancer I am less well informed, but the case is at least highly plausible, given that the decisive research is still in its early days.

Unfortunately, the book is far from easy reading. References within references are cited without obvious indications of which are the main and which the subsidiary citations. Sarcastic comments on mainstream attitudes and actors are often opaque unless one already knows the story being told here and also accepts the author's viewpoint. But the content is so fascinating, the substance so important, that I could not lay the book down. What follows is chiefly a summary of the book's chief contentions.

The war on cancer, funded sumptuously since the early 1970s, is a necessary historical as well as scientific context for understanding the controversy over HIVJAIDS. Duesberg was a leading figure in the cancer war, fully engaged in the mainstream commitment to find the viral cause(s) of cancer. That commitment stemmed from the fact of the Rous sarcoma virus: in 1911, Peyton Rous was able to induce cancers in chickens by injecting extracts from chicken tumor. The responsible agent turned out to be an RNA virus[1], and Rous received the Nobel Prize in 1966 for discovering "tumor-inducing viruses".

Virologists rushed to find other tumor viruses under the presumption that similar activating viruses responsible for human cancers were waiting to be discovered. Virology, in particular retrovirology, flourished. In 1970, Duesberg collaborated in defining the first retroviral oncogene (a cancer-inducing gene in—carried by—a retrovirus), showing what changes in its RNA converted an avian non-tumor virus into an avian tumor virus (Duesberg & Vogt, 1970). But not many tumor viruses were discovered, and none that caused cancers in humans. Human T-cell lymphotropic virus (HTLV-I), discovered in Robert Gallo's lab[2] in 1980, remains the still controversial claimant for the title of first-discovered human tumor virus; in a major review article, Duesberg (1987) has disputed the validity of this discovery (pp. 63 ff.).

Because tumor viruses turned out to be rare even for animals, the consensus became that precursors of cancer-inducing genes (proto-oncogenes) are present in normal cells and may become activated by various carcinogens or by some viruses. The consequent search for human oncogenes continues apace, and even more so the struggle to find mechanisms by which they actually produce cancers. Lack of useful progress has led to the invention of ever more complicated hypotheses: that oncogenes are prevented from becoming activated by anti-oncogenes, tumor-suppressor genes; mutations may disable those tumor suppressors, whereupon the oncogenes can become activated by other mutations or by viral action.

Duesberg recognized that the mounting evidence was pointing against rather than for this view and argued his case at length (Duesberg & Schwartz, 1992). By 1997, he had begun to publish evidence that the cause of malignant tumors lies not in mutations of anti-oncogenes and oncogenes but in a much more drastic error when cells divide in order to reproduce, namely, the appearance of aneuploid cells containing an abnormal number of chromosomes. (Normal human cells are diploid—they have paired chromosomes, 46 of them in 23 pairs. Aneuploid cells in human cancers have between 60 and 90 chromosomes. One well-known chromosome-based disorder is Down's syndrome, in which there is an extra copy of chromosome 21.)[3]

That cancer and aneuploidy are intimately related had been actually the mainstream view into the mid-1960s. One obvious reason is that every solid malignant tumor contains a high proportion of aneuploid cells (p. 217). The unresolved question was whether aneuploidy was a consequence of malignancy or its prime cause; Duesberg and others are now beginning to show that it is likely the cause (Chapter 7). That would explain, for example, why such substances as coal tar and asbestos, which are biochemically inactive—they would certainly not be expected to produce mutations in genes—are nevertheless powerful carcinogens (p. 244). Moreover, the aneuploid theory brings focus back onto a basic but often neglected characteristic of cancer: it is not a failure of control of growth, it is a failure of cellular *differentiation*. Malignant cells differ in character from those of the tissue or organ from which they originate; that may be why they metastasize, moving through the body presumably to find a more appropriate home than the parent tissue from which they are changelings.

Why did the war on cancer shift the mainstream focus from aneuploidy to viruses? There is an obvious, plausible explanation: the Crick-Watson recognition of the structure of DNA and the consequent preoccupation of molecular biology with all aspects of the DNA code and its consequences. Viruses are grist for students of DNA and RNA, whereas aneuploidy is not. Historians and sociologists of science will have to dig deep into detail to unravel the story and test the validity of this suggestion, but it is not disputable that molecular biology has been and remains obsessed with DNA. One corollary of this obsession has been the developing of technology for identifying rapidly, easily, and en *masse*, the protein products of normal and of mutated genes. Early results from this seem to support the aneuploid theory: there is no indication that the altered expression of any particular gene characterizes any given type of cancer, rather the metabolic products in malignancies resemble the sort of chaotic mixtures one would expect to find with cells as abnormal as aneuploidy makes them (p. 219). That would also explain why chemotherapy fails once metastasis has set in: the metabolism of the metastasized cells changes ineluctably and continually, and every chemotherapeutic agent soon becomes ineffective (p. 267).

That the metabolic products of malignancies are chaotic mixtures would also explain why presumed oncogenes turn out to be involved in only a small proportion of cancers of a given type (for example, abnormal BRCA1 and BRCA2 genes may account for no more than 10% of all breast cancers[4]). The involvement of a given gene in a given type of malignancy is inferred when its product appears more frequently in the cancerous cells than in normal ones, or when the gene is shown to be present in a mutated form. But it always seems to happen that such a discovered correlation fails to be confirmed by further work on more instances of the same type of cancer. It may well be, then, that these correlations are spurious, random statistical correlations with no causative basis. With grossly disturbed metabolisms, it is likely that some proteins will be present "in excess", but it may be a matter of chance what those are.

Throughout Chapter 1, Bialy illustrates how unthinkingly pursued are certain lines of research[5]—because they are possible rather than because they promise real insight. Although it still remains to be proved that normal cells harbor genes capable of producing cancers (p. 4), claimed discoveries of new oncogenes continue (pp. 10, 47). A far-reaching example of this sort is that results of experiments with cell cultures are taken to show what happens *in vivo* despite the fact that the cultured cells are clearly unlike their *in vivo* ancestors.

Cancer research and HIV/AIDS in the latter decades of the 20th century has involved the same major players: molecular biologists preoccupied with virology. In the early 1980s, molecular biology was awash with war-on-cancer virologists increasingly frustrated by their inability to find human tumor-viruses. Then appeared AIDS: a new illness, clustered in several places just as though the cause were an infectious agent, presumably a virus. Determined efforts to find a virus in serum from people with AIDS brought immediate acceptance when the discovery of what is now known as HIV (human immunodeficiency virus) was announced at a press conference by the Secretary of Health and Human Services. Virologists could now honorably abandon their unproductive search for tumor viruses in order to meet the immediate threat of this new viral epidemic, and they did so in droves: by now, some $50 billion has been spent on the study of HIV and 130,000 research articles have been produced (p. 68).

Duesberg was by no means alone, however, in the early 1980s in asking for proof that the HIV–AIDS connection is one of cause rather than merely a certain degree of correlation. Much of Bialy's book recounts Duesberg's continuing attempts to focus on the issue of causation and to gain attention to the many points he has raised—for two decades—that appear to demonstrate that HIV is *not* a causative factor in AIDS. Bialy has been in a privileged position to follow the story through being Editor of *Bio/Technology* (since 1996, *Nature Technology)* and having known Duesberg since graduate-student days.

It is an ugly story, with many examples of how the mainstream herd (as Thomas Gold called it), stampeding to the feeding troughs of grants and positions and prizes, tramples any individuals who persist in calling for substantive discussion of fundamentals. One unfortunate but understandable, all-too-common, side-effect is that the would-be iconoclasts, frustrated at every turn, slip readily into stridency; in fact, it must be awfully difficult to avoid doing so when, time after time, perfectly reasonable questions are met with evasion, "answers" that beg the question asked, or downright lies. That may well be why Bialy writes in places with such over-the-top sarcasm that uncommitted readers are likely to be turned off rather than persuaded, despite the full documentation provided and the fact that the described events are clear stimuli to righteous anger. For example:

The persistent refusal by Nature—often in the person of its Editor-in-Chief, John Maddox—to allow Duesberg to respond to attacks on his views (and person) published in that journal (pp. 95–124).

- One extraordinary instance: In 1988, Maddox wrote to Duesberg, "It would be a rash person who said that you are wrong, but . . . if we were to publish your paper, we would find ourselves asking people to believe that what has been said so far about the cause of AIDS is a pack of lies" (p. 125).

This is balderdash. No scientific journal "asks people to believe" anything; it offers scientists the opportunity to present their cases, and its duty is to publish conflicting views when they are competently and substantively argued. Maddox reveals here an ambition that can be described only as megalomanic, that everyone should always believe whatever Nature publishes.

- Why was Duesberg not invited to a symposium of leading cancer biologists? "Since Duesberg didn't 'believe in' oncogenes, what was the point in having him speak?" (p. 42)!
- When Duesberg presented experimental results unfavorable to the oncogene hypothesis in a symposium in 1985, he was directly contradicted: "Dr. Weinberg said that a graduate student in his laboratory had made exactly analogous constructions to those described by Dr. Duesberg and had got exactly opposite results". But those contradictory results have never appeared in print, not even in a graduate student's dissertation; by contrast, Duesberg's published results have never been challenged in print (p. 50).

Here are some of the salient points against the view that HIV causes AIDS:

- Despite intense efforts, by 1995 all that could be said was, "HIV causes AIDS, in some manner not understood" (p. 116, citing John Maddox). A decade later, the mechanism remains just as mysterious: "the reason why HIV-1 infection is pathogenic is still debated" (Stevenson, 2003); "We still do not understand the origin of the AIDS epidemic; the slow destruction of the immune system by factors in addition to HIV infection of CD4+ T cells; the importance of cofactors in AIDS progression and virus transmission; and the nature of the HIV reservoir that resists triple drug therapy" (Montagnier, 2000).

At first, it had been thought that HIV invaded quietly and lay dormant before beginning its nefarious activity, that it was a lentivirus, a "slow virus". The type specimen of lentivirus was the agent that causes kuru. Since then, however, that disease and its kin (scrapie, BSE or mad-cow disease, Creutzfeld-Jakob disease) have been ascribed to the action of prions, not of any virus, neither regular nor "slow". Later, HIV was thought to be active at once and so vigorously that it soon exhausted the immune system's capacity to replenish itself; that notion led to highly active anti-retroviral treatment (HAART)—which soon had to be abandoned, after doing less than no good to a number of people with AIDS.

Once it had been imagined that HIV kills T-cells. But it was found to infect only about 1 in 1000 of those, so clearly it could not kill them directly. Thereupon it was suggested that HIV somehow sets off an auto-immune rampage; but that too turned out not to be the case.

There is no explanation for how HIV can destroy the immune system. There is no treatment for AIDS and no vaccine, whereas other viral and retroviral diseases (e.g. polio, influenza) are effectively defeated by vaccines.

On the other hand, the overwhelming majority of AIDS patients are known to have been at risk for damaged immune systems through heavy use of drugs, recurring infections with the common sexually transmitted diseases, or infusion of blood or blood products. HIV/AIDS dissidents point to some combination of those risk factors as producing AIDS.

- The mainstream evades, it does not answer the points raised in questioning that HIV causes AIDS. Duesberg (1989) published his argument in company with an extraordinary editorial comment that promised a rebuttal by Robert Gallo. That rebuttal has never been made (p. 147).
  When not evasive, the mainstream may mislead.

For example, "more than fifty chimpanzees have been successfully infected [with HIV] for more than seventeen years", yet none has developed AIDS (pp. 136–137). In response, leading lights of the mainstream (Blattner et al., 1988) could do no better than offer a red herring about how viruses affect humans as opposed to *monkeys;* but chimps are physiologically close to humans whereas monkeys are not.

For another example, it is insinuated that HIV can always be isolated from people with AIDS, whereas that has been possible only in "most" of them (there are thousands of HIV-free AIDS cases, p. 207), and only "by culture or polymerase chain reaction" (pp. 144, 206). Culturing uses immortalized T-cells (whose non-immortalized parents HIV is supposed to kill!, p. 207), and it is a large and uncertain inferential step to assume that anything that later appears in the culture was present in the original extract from the patient. As for polymerase chain reaction, the man who received a Nobel Prize for inventing the technique (Kary Mullis) has persistently called these claims invalid.

HIV replicates rapidly in culture and yet is supposed to lie "latent" for decades *in vivo* (pp. 147–149).

- The mainstream even makes some demonstrably false claims, for example, that AIDS was recognized as early as 1981 "among sexually active heterosexuals in some parts of equatorial Africa" (p. 141, citing Blattner et al., (1988)). The "discovery" of heterosexual AIDS in Africa actually came only years later with reports that AIDS might be as common in Africa among women as among men (Altman, 1985).

  Although HIV infection is about equally distributed among young American men and women applying to enlist in the Armed Forces (p. 184), AIDS is not equally distributed: more than 80% of cases in the two decades up to 2003 have been men[6].
- The mainstream ascribes the decreased incidence of AIDS—in the United States since the early 1990s—to the success of "safe sex" campaigning. Obviously, the same campaign should have brought decreased incidence of all sexually transmitted diseases; yet the incidence of chlamydia, for example, went from 7000 in 1984 to 380,000 in 1991 and 500,000 in 1998 (p. 165).
- AIDS in Africa is not the same disease as in Europe and America. In 1982, it was *speculated* that "slim disease"—prolonged diarrhea, fever, and profound wasting—might be AIDS (Kamradt et al., 1985); but those symptoms have been endemic in Africa for a long time.

Almost immediately, diagnosis of AIDS in Africa came to be based officially on the Bangui definition *which does not require a test for HIV* (Quinn et al., 1986; WHO, 1986); nor, strangely enough, does it include the opportunistic diseases that *characterized* AIDS when it was first recognized in the United States—Kaposi's sarcoma and *Pneumocystis* pneumonia (p. 184).

Sub-Saharan Africa is supposedly being devastated by AIDS—between 1980 and 2000, an *estimated* 1,000,000 died therefrom. But during that period the total population grew at 2.6% per annum, an increase of 274 million. The gathering of death certificates and official reports in that region is not accurate enough to verify that *estimate,* which amounts to about 1/3 of 1% of the change in population (p. 194). That these estimates of AIDS deaths are grossly unreliable has been documented by South African journalist Rian Malan: he found that the UNAIDS estimate of 250,000 AIDS deaths in South Africa was *at least* 4 times greater than the actual number of 65,000 or fewer (Malan 2001, 2003).

- At last count, some 98,000 harmless retroviruses had been found to be incorporated in the human genome (p. 174). Like other harmless retroviruses, HIV is found in only a tiny proportion of cells. It is found in about the same proportion in the T-cells that it supposedly somehow kills as in other cells that are not affected in AIDS (pp. 149–152). Like other harmless retroviruses, HIV is efficiently (25–50%) transmitted from mother to child (p. 183). All latent parasites, whether disease-producing or not, are activated when there is an immune deficiency: the appearance of HIV may be a *consequence* of AIDS rather than its cause (p. 159).

No matter these and other counter-arguments: The belief that HIV causes AIDS is firmly entrenched in the conventional wisdom. One reason is this: "Most scientists have neither time nor inclination to follow specialist literature in fields outside their own. They depend, consequently, on journals like *Science* and *Nature* to tell them what is considered important" (pp. 144–145). Not only scientists, but journalists and science writers likewise take their cue from those periodicals, or from the many scientists who simply parrot what they have read in them. The general public then gets the same "confirming" information from all directions. If by (mis)chance someone like Duesberg is slated to appear on television, the authorities often manage to substitute one of their own (p. 164). This is indeed the age of knowledge monopolies (Bauer, 2004); and the degree to which this knowledge monopoly has captured public belief is illustrated by the fact that the US government has declared that AIDS *in Africa* represents a security threat *to the United States* (p. 189).

The power of the HIV/AIDS knowledge monopoly can be verified very readily: just tell someone that HIV does not cause AIDS, and observe the reaction. For decades I have experienced kindly incredulity when I claim that the Loch Ness Monster exists; but when I claim that HIV does not cause AIDS, I encounter serious disturbance or horror.

Harvey Bialy has performed a great public service by bringing together meticulously documented information of vital importance about two of the most troubling sources of human suffering. I hope this summary will bring this book to many readers who are willing to overlook the weaknesses of presentation I noted near the outset. A number of important points in it were quite new to me, despite having read quite a lot on these subjects. For instance, I had not known that HIV infection among young Americans showed no bias as to sex whereas AIDS very much does. I had also not previously pondered the evolutionary significance of the fact that mammalian species all have about the same number of genes (35,000 or so) whereas they differ greatly in their chromosome numbers (p. 270), and so I was led to further fascinating reading. One can hardly ask more from a book than that.

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Notes

[1] DNA and RNA, virus and retrovirus: The genetic code is written in DNA. DNA's commands to make proteins are transcribed and sent via "messenger"

RNA. DNA viruses commandeer the cell's protein-making machinery to replicate virus DNA instead of normal cell DNA. RNA viruses, also called retroviruses, require an enzyme, reverse transcriptase, to manufacture the DNA corresponding to its RNA, and this DNA is then incorporated into the cell's DNA. "Reverse transcriptase" was so named because it engineers the opposite of what was thought to be the normal transcription of DNA into messenger RNA.

2 Connoisseurs will appreciate Gunther Stent's comment: "If Crick publishes it, you read it thinking it right. With Gallo, it's the opposite" (p. 61). Luc Montagnier (2000: 37) has also called Gallo incompetent. Most observers discount Gallo's claim to be co-discoverer of HIV: later analysis showed his "HTLV-III" to be identical to the "LAV" that Montagnier had sent him.

3 For a concise summary of the aneuploid theory of cancer, by a co-worker of Duesberg, see www.annieappleseedproject.org/antheorofcan.html (accessed 20 January 2005).

4 http://www.breastcancer.org/genetics_breast_cancer.html (accessed 26 January 2005).

5 For a similar comment, see Brenner, S. (1999). Sillycon valley fever. Current Biology, 9, R671.

6 http://www.cdc.gov/hiv/stats.htm#aidscases (accessed 25 January 2005).

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