

Science Outsold?

Correcting the falsehoods of
Science Sold Out: Does HIV Really Cause AIDS?
by Dr. Rebecca V. Culshaw

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April, 2007

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Introduction

In *Science Sold Out: Does HIV really cause AIDS?* [1], HIV/AIDS denialist and University of Texas at Tyler Assistant Professor of Mathematics Dr. Rebecca V. Culshaw argues that HIV does not cause AIDS, that HIV may not even exist, and that AIDS itself is just a “sociopolitical construct.” Culshaw chiefly reproduces the earlier arguments of other HIV denialists, often without citing them, crafting a remarkable syncretism of fallacies that she spices with numerous misunderstandings of her own. The result is nothing less than an ironic masterpiece. Rarely does any book—however many times larger than Culshaw’s glorified pamphlet (about 50 total pages of original text)—achieve such a stupendous concentration of easily-demonstrable falsehoods as does *Science Sold Out*. “Falsehoods” because so many of Culshaw’s statements do not reflect differences of opinion, honest misinterpretations or alternative, yet logically consistent, views. They fly in the face of facts as well-established as the path of the Earth around the Sun. I have found several hundred such falsehoods in this book (along with a menagerie of merely controversial statements, contradictions, hyperbole, misuse of terms, and examples of poor writing or editing).

Yet it is not merely the sheer number of falsehoods that sets Culshaw’s writing apart. It is that they seem to be placed on the page without any obvious intent to deceive. Having read Culshaw’s internet comments, listened to her interviews, and perused anything else I could obtain, only with great difficulty can I believe that Culshaw has nefarious goals. She is unlikely to make money spreading her bizarre (and usually second- or third-hand) views on HIV and AIDS. She does not seem to harbor ill-will towards the various groups hardest-hit by AIDS itself, whose members are most likely to suffer and die should they take her words as medical advice. While some reviewers feel otherwise, I do not necessarily view Culshaw as a liar by intent...although I may be a far poorer judge of human character, and she a far better actor, than I imagine.

No, Culshaw’s falsehoods, in my estimation, are born largely of ignorance and naïveté. Culshaw’s ignorance is at times breathtaking. I am challenged to understand how a “mathematical biologist” could not only complete a doctorate program, but attain appointment as an assistant professor at a U.S. university, with large gaps of knowledge regarding elementary biology. Culshaw seems to be confused about the differences between RNA and DNA, the relationship of gene to protein, even, trivially, that yeast are fungi. Nor can I see how one studies HIV—albeit only *in silico*—for over ten years without recognizing the most basic and universally-recognized aspects of HIV reproduction and pathogenesis. There is little in the way of mathematics in her book, but Culshaw invites questions of her competence in her own discipline by erring in the few simple calculations she attempts, taking eyebrow-raising liberties with numerical data, confusing principles of statistics, and “outsourcing” the only mentioned analyses of mathematical models (her purported specialty) to a math teacher in Australia who apparently does not publish on HIV in the peer-reviewed literature. Culshaw also displays a profound ignorance of the standards of proper scholarship that is difficult to reconcile with her academic history and current status. She leaves many of her claims unsupported and unreferenced. Sadly, Culshaw even opens her work to charges of questionable scholarship by failing to attribute ideas properly, even those of other denialists; at least twice, she also apparently copies other authors’ phrases directly without citation. But absent this profound and manifold ignorance, *Science Sold Out* probably could not have been written.

What I view as Culshaw’s naïveté is also maddening. For reasons well beyond my ken, Culshaw has decided to forsake the scientific literature for almost exclusive reliance upon non-peer-reviewed sources of (mis)information. She seems credulously to take any- and everything dispensed by the “experts” of denial as truth, although (or perhaps because?) these pundits have no actual experience with HIV, with

clinical practice, or with science at all. Culshaw puts stock in the distortions of denial-journalist Celia Farber, for example, and apparently does not bother to check Farber's claims against the facts. She follows Peter Duesberg, the most celebrated and influential denialist, seemingly failing to check the primary sources he twisted into knots to make his points. She uncritically reproduces the mathematically- and scientifically-unsound musings of an amateur HIV critic named Mark Craddock instead of verifying them first. And when she occasionally and selectively references the scientific literature, it often appears that she has not read the works she cites; if she has, she certainly has not understood them.

In my opinion, Culshaw is altogether too credulous, a *believer*. She believes, as do many other HIV/AIDS denialists, that she is fighting the good fight, struggling against the powers and principalities of a global conspiracy of genocidal greed. This conspiracy is as powerful and evil in the denialist mind as it is nonsensical and nonexistent in reality. The denialist fable of the "AIDS Establishment" shares much with the perennial tale of the Elders of Zion. Both can frighten the uneducated, both are factually ridiculous, but both also have the power to spread death and destruction if believed. The difference, of course, is that those who suffer from the denialist tale are not the imagined arch-villains, but the very AIDS patients for whom some denialists profess such concern.

A tractate of the *Science Sold Out* sort can be written in little time by an energetic author, a true believer who does not bother to confirm (or perhaps even read) many of her sources. Parts of *Science Sold Out* consist of internet essays that appeared in 2006 on lewrockwell.com, and I see little or no evidence of editing throughout the book, especially not by anyone fluent in the language of biology and medicine. Producing such a work is easy; correcting its mistakes is a more arduous task.

Why, then, have I spent time reviewing this meritless book? Because ignorance and falsehood cannot be ignored when lives hang in the balance. When an AIDS patient stops taking medication because of Culshaw's smooth and comforting falsehoods, or when the government of South Africa justifies anti-science policy decisions based upon the manifestly bad advice of several dilettantish caricatures like Peter Duesberg and fellow denialist Harvey Bialy, falsehoods and ignorance take their toll, and lives are lost. I am of the conviction that science must stand up to denial and expose its dangerous deceptions.

What good can a new antiviral drug perform for a particular patient if that person has already decided, having read Culshaw, that the drug is poisonous, more likely to kill her than AIDS itself? Why should a couple practice safe sex, having heard a radio interview in which Culshaw agrees repeatedly with the show's host: a condom is more likely to kill you than HIV, so don't bother.* In situations like these, *science* has not *sold out*; science has been *outsold*: by ignorance, by sensationalism, by apathy. When such life-threatening ignorance and falsehood are found even at the university faculty level, scientists must take a more active role in spreading the knowledge they help to create. I hope that this review will contribute.

Below, I go into more detail concerning the many falsehoods of *Science Sold Out*. I start with a categorized list of selected false claims and then continue, following the list as a guide, with referenced responses to some of Culshaw's most problematic passages. Many of Culshaw's misstatements are left unaddressed; this review is by no means comprehensive or exhaustive. Similarly, the references I give are but a few of the thousands of publications that could rightfully be cited here. On occasion, my statements are based on general knowledge and are not referenced; their support can be found in book-length reviews of HIV [2] or standard virology and cell biology textbooks, such as [3-6]. Also, for further information on these topics, I encourage the interested reader to peruse the rest of the [AIDSTruth](http://AIDSTruth.com) website.

* "Unauthorized Health Report," September 26, 2006 (downloadable in two parts at podcastpickle.com/media/download/367652 and -367651).

Acknowledgments

I would like to thank Robert C. Gallo and John P. Moore for their insightful comments on the manuscript. My gratitude also goes to Nicholas J. Bennett, Jeanne Bergman, Brian T. Foley, Robert K. Funkhouser, Nicoli Nattrass, and Ruy M. Ribeiro for reviewing the manuscript and for their suggestions and aid. I thank S.A. Smith for valuable information on endogenous retroviruses. Thank you, as well, to all members of AIDSTruth.org and others who have taken a conscientious stand against the lies and distortions of HIV/AIDS denial.

Selected Falsehoods from *Science Sold Out: Does HIV Really Cause AIDS?*

The following are paraphrased from “facts” presented by Dr. Rebecca Culshaw in *Science Sold Out*; almost all are given explicitly, not merely by implication. Although “fact” is one of the most frequently-used words in Culshaw’s tractate—three times in one paragraph alone—real facts are in short supply. Without exception, the “facts” listed below are falsehoods. There is no credible evidence that any assertion on this list is true as formulated by Culshaw. Available evidence indicates they are all wrong. Many of these statements are made by Culshaw more than once, indicating that they are not the result of a one-time mistake or sloppy writing. Following the list, I examine each statement in order, giving page numbers, explanations of why each statement is wrong, and references to accurate literature when warranted.

Mathematics, Statistics, and Epidemiology of HIV

1. The number of HIV infections in the United States has remained constant since 1985
2. The latest CDC report estimates one million HIV infections in the United States
3. HIV never spread exponentially
4. HIV does not spread like an infectious agent
5. HIV does not follow “Farr’s law”
6. If HIV does not follow Farr’s law, it is not infectious
7. HIV prevalence and AIDS incidence never match, so HIV cannot cause AIDS
8. Only half of early AIDS patients had HIV
9. Transmission rates are not high enough to support an epidemic, as proven by the “mainstream literature”
10. There is no “solid evidence” that HIV is transmitted sexually
11. There is no “solid evidence” that HIV can be transmitted by blood
12. Perinatal transmission is the most efficient means of HIV transmission

On HIV/AIDS in Africa

1. AIDS in Africa is the fraudulent diagnosis of “normal” diseases as a new syndrome
2. African AIDS looks nothing like American or European AIDS; there is little symptomatic overlap
3. AIDS in Africa is a “fabrication,” invented so that scientists could get more money
4. AIDS in Africa is evidence of the inherent racism of scientists
5. HIV statistics in Africa are contrived, with “no basis in reality”
6. HIV statistics in Africa are derived solely from testing at maternity clinics
7. AIDS diagnosis in Africa does not require an antibody test
8. HIV transmission rates in Africa are identical to those in the US, so there cannot be an epidemic in Africa
9. AIDS did not exist in Africa before 1983
10. HIV did not come from non-human primates; if it had, the zoonotic jump must logically have occurred “long ago”
11. This is because, in recent memory, nothing has changed the interactions of people and primates in Africa

On the definition of AIDS

1. The CDC expanded the AIDS definition in 1993 to ensure fewer absolute numbers of AIDS deaths
2. Some AIDS-defining conditions have “absolutely nothing” to do with immune deficiency
3. Kaposi’s Sarcoma has nothing to do with immune deficiency
4. Kaposi’s Sarcoma is only seen in homosexual men
5. Kaposi’s Sarcoma is “mysteriously absent” in pediatric AIDS
6. AIDS today does not resemble the first cases of AIDS
7. The inclusion of invasive cervical cancer as an AIDS-defining condition was politically motivated
8. Invasive cervical cancer is common among women with no immune suppression
9. Including recurrent bacterial infections as pediatric AIDS-defining makes no sense since many children have them; also, if this condition applies to children, it should logically apply to adults, but it does not
10. A high total lymphocyte count means that a child does not have AIDS
11. AIDS patients have “very few, if any, bacterial infections”
12. AIDS is actually just a “sociopolitical construct”
13. AIDS is simply an expression of racism and homophobia
14. If the fear of AIDS would end, the epidemic would end

On Antiretroviral Drugs

1. 6.7-8.8% of North American HIV-positive people die every year if they take antiretrovirals
2. Antiretroviral drugs do not exist; they just kill or change cells, not viruses
3. Any true antiretroviral drug would necessarily eradicate its targeted virus from the body
4. Antiretrovirals are not specific for viruses, because if they were, smaller doses would suffice
5. If antiretrovirals were specific for HIV, one would be enough; combination therapy would be unnecessary
6. Antiretrovirals likely cause birth defects, stillbirth, and cancer and should not be used by pregnant women
7. The most toxic antiretrovirals are reserved for babies
8. AZT’s side effects are symptoms of AIDS, so many AIDS cases are caused by antiretroviral drugs
9. The stories of antiretrovirals giving patients a new lease on life are fiction
10. Protease inhibitors can have temporary benefits, but only because they kill the agents of opportunistic infection
11. More AIDS patients are killed by HIV protease inhibitors than by AIDS itself
12. Recent reductions in AIDS deaths are the result of lower doses of “toxic drugs”
13. Immune Reconstitution Disease (IRD) happens when the immune system is “confused” by antiretrovirals
14. There is no evidence that any anti-HIV drugs prevent AIDS
15. The efficacy of antiretrovirals was established by “pure faith,” not by science

Concerning HIV Tests

1. The positive predictive value of HIV tests is less than 2% in the general population
2. Half of all adults have been tested for HIV
3. At least one million people in the United States have tested false-positive for HIV at least once
4. Pregnancy commonly causes false-positive HIV test results
5. HIV-seropositive babies are presumed positive for HIV even though “more than half” of them will eventually “revert.”

6. HIV tests have abnormally high rates of false-positive results
7. HIV tests are worse in specificity, sensitivity, and reproducibility than tests for other diseases
8. HIV PCR probably does not work and is not reliable
9. Unless RT-PCR is perfect, it is worthless as a quantitative tool
10. Scientists are well-aware that RT-PCR has never been “validated”
11. HIV viral load RT-PCR overestimates infectious virions by 60,000 times or more
12. If HIV ELISA gives false positive for undiluted serum, the test is worthless
13. Using “positive” and “negative” to describe an ELISA result is ridiculous; using “reactive” and “non-reactive” would be better
14. A truly HIV-positive sample should show antibody reaction with all bands on HIV Western Blot
15. Antibodies to human endogenous retroviruses (HERVs) cross-react with HIV
16. *“(A)ll laboratory tests used to assess the severity of HIV infection are virtually worthless”*
(original italicized)
17. Reliable risk factors for AIDS do not include HIV infection

HIV Virology, or Whether the Virus Exists

1. Retroviruses are just RNA with a protein shell
2. Because of this protein shell, which “disappears” in the infected cell, they are called “enveloped viruses”
3. 3% of the human genome is retroviral in nature
4. These retroviral sequences (humans are “full of” them) are activated whenever cells are growing, dying, or under stress
5. HIV PCR tests amplify these cellular sequences
6. A positive HIV PCR test probably means that the body is under stress and releasing endogenous sequences
7. HIV PCR never looks for a whole genome, just small fragments of a retrovirus
8. HIV PCR amplifies cellular DNA and RNA from “decaying cells”
9. Transposable elements, made of RNA, compose 40% of the human genome
10. Transposable elements cleave to form endogenous retroviruses
11. Endogenous retroviral sequences are transmitted perinatally
12. Perinatal transmission is the most efficient means of transmission for HIV (also found above)
13. The evidence indicates that HIV is not an exogenous retrovirus
14. HIV may not exist as a unique virus
15. No one knows what “HIV” really is
16. The existence of HIV has not been demonstrated by electron microscopy
17. The similarity of endogenous and exogenous retroviruses by EM distinguishes retroviruses from “ordinary” viruses
18. The mutation rate of HIV is “unprecedented in the history of viruses”
19. No virus could mutate as much as HIV is said to do and still survive
20. HIV could not possibly develop drug resistances and yet survive
21. Influenza has a “segmented chromosome,” necessary for recombination
22. HIV, lacking the segmented chromosome, cannot recombine, leaving RT error as its only mutation strategy

On HIV Proteomics

1. Many “HIV proteins” are not actually HIV proteins at all, including p24, p13, p32, and gp41
2. HIV gp160 and gp120 are simply oligomers of gp41
3. The “oligomer” gp41 is a “component of cellular actin”
4. Luc Montagnier proved that gp41 is actin

5. Many HIV-negative people have p24 in their blood
6. p24 cannot be found in numerous AIDS patients
7. gp120, tat, and nef are not “specific” to HIV, but are found in endogenous retroviruses
8. These proteins supposedly induce apoptosis; but since HERVS do not cause apoptosis, HIV should not, either

On HIV and Pathogenicity

1. HIV is not active during the final stages of disease
2. HIV antibodies are not protective
3. HIV antibodies are supposedly a sign of “imminent doom”
4. No one know how HIV works
5. There is no mechanism for HIV-mediated T-cell death
6. HIV does not kill T-cells directly
7. Low CD4 counts are found in healthy individuals as a result of normal fluctuations, so CD4 count is invalid as a diagnostic tool
8. No retrovirus kills cells outside of the laboratory
9. Cultured cells die in the presence of HIV only if toxic chemicals are added
10. But the same cells die in the absence of HIV when these chemicals are added, so HIV does not induce apoptosis
11. HIV virions are not present in sufficient numbers to cause disease
12. Very little HIV is found in the blood of AIDS patients
13. Only one in 10,000 CD4+ T-cells is infected with HIV
14. Lymph node infection is also low

On the Adaptive Immune System

1. CD4+ cells consist of two groups: Th1 and Th2
2. Th1 cells exclusively fight intracellular pathogens; Th2 cells exclusively fight bacteria
3. Th2 cells are found in the lymph nodes and bone marrow, Th1 cells exclusively in the circulating blood
4. A Th1-Th2 shift occurs during the course of HIV infection
5. Th2 cells can be infected, but Th1 cells cannot
6. Th1 cells would not die unless HIV infected them

On the Early History of HIV/AIDS Research

1. The first five AIDS patients were patients of Dr. Michael Gottlieb
2. Dr. Gottlieb first concocted a “syndrome,” then searched far and wide for patients to fill the bill
3. The syndrome was a “clever idea” since it could include anything
4. T-cell counting was included by Gottlieb because it had recently been invented, not because it was relevant
5. Sexual transmission of the AIDS agent was favored from the beginning even though the initial patients did not know each other
6. Alternative hypotheses for AIDS were ignored
7. Sexual transmission of HIV was “simply assumed”
8. “Contact tracing” and other epidemiological procedures were not followed for AIDS
9. The discovery of HIV was announced by press conference before any supporting papers were published
10. After the press conference announcing HIV as the causative agent of AIDS, all debate was suppressed

On Legal Issues Involving HIV

1. All U.S. states keep lists of HIV-infected individuals within their borders; these lists are used to discriminate and violate human rights
2. HIV-positive pregnant women are in general encouraged to terminate their pregnancies
3. HIV-positive pregnant women are forced to take antiretroviral drugs
4. HIV-positive pregnant women are forced to undergo Cesarean section delivery
5. Breastfeeding by HIV-positive mothers is banned in “many states”
6. Babies of HIV-positive mothers are forced to take antiretrovirals against their mothers’ wishes
7. HIV-positive children are forced to take antiretrovirals against their and their parents’ wishes

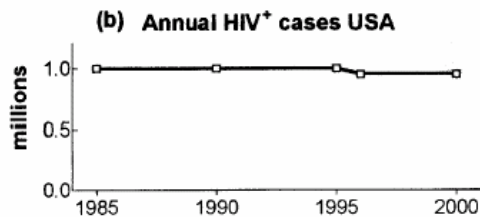
Miscellaneous Interesting Statements and Implications

1. Most people who deny that HIV causes AIDS are “credentialed doctors and scientists”
2. The CDC speaks through Oprah Winfrey
3. Yeast are not fungi
4. Cytomegalovirus (CMV) is not a herpes virus, and there is apparently only one herpes virus

Mathematics, Statistics, and Epidemiology of HIV

1. The number of HIV infections in the United States has remained constant since 1985 (pp.1-3)
2. The latest CDC report estimates one million HIV infections in the United States (p.2)

The former statement relies uncritically on blatant data misrepresentation by another author; for the second statement, Dr. Culshaw performs this manipulation herself. On page 2, Culshaw presents “Figure 1,” the first and only figure in her book. This graph purports to show the prevalence of HIV in the United States from 1985 to 2000. In the figure, prevalence remains constant at 1 million from 1985 until 1995 (three data points), then declines slightly to about 900,000 (last two data points).



From [7], Figure 1b.

Although Culshaw does not, as is customary, explicitly attribute her graph in the legend or the accompanying text, it was downloaded from the website www.rethinkaids.info (“Rethinking AIDS, the group for the scientific reappraisal of the HIV/AIDS hypothesis” or “RA,” has recently redesigned and modified this website, moving it to rethinkingaids.com). Much-reproduced on the internet, this graph originates from Figure 1b of a twice-rejected publication [7] by Peter Duesberg—the most prominent HIV/AIDS denialist and one of very few active scientists in the movement; Claus Koehnlein—a German “alternative treatment” doctor; and David Rasnick, who has falsely claimed to be a professor at the University of California, Berkeley and the “Creator of Protease Inhibitors” ([8], accessed 3-26-2007).

Duesberg et al derive their first data point from Curran JW et al, [9]. Curran and colleagues estimated the HIV prevalence in the United States in 1985 in the range of 500,000 to 1 million, cautioning that this is a “very rough” estimate due to the small number of tested individuals and the difficulty of extrapolating from risk groups to the general population. Duesberg et al take this estimated range, drop all reference to estimates, and graph the upper bound of the range as a single data point. They do the same for the remaining time points, deriving their numbers, they claim, from CDC reports. In each case, Duesberg et al choose and graph numbers that maintain a flat prevalence curve. (It is not clear why only five data points are shown, since an earlier version of the graph, appearing in a 1998 paper [10] by Duesberg and Rasnick (Figure 1A), shows a value for each year, beginning in 1984, as does a still earlier graph from Duesberg’s 1996 *Inventing the AIDS Virus*, p.194 [11].)

Nor is Culshaw likely to be unaware of the dishonest scholarship by the graph’s creators; Culshaw employs the same tactic herself. “Please note also that although the graph terminates in the year 2000, official estimates remain similar, and the latest CDC estimates for HIV prevalence state that approximately one million Americans currently test positive for HIV..., a fact that would change the graph little” (p.2). Culshaw selects the lower bound of the CDC’s estimated range of 1,039,000 to 1,185,000 HIV infected persons in the United States in 2003 [12], rounds it down, and calls it one

million...the better to continue the artificially flat line in Figure 1. While some estimation methods *do* present figures around one million, Culshaw does not mention these, nor does she refer to the substantially wider estimated ranges from the World Health Organization ([13]—1.2 million estimated infected, with a range of 720,000 to 2 million).

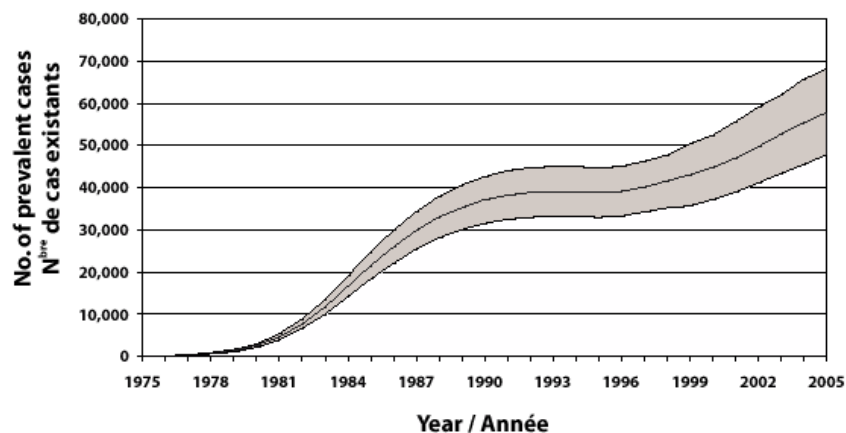
To summarize, Duesberg et al, via Culshaw, graph prevalence estimates derived with different methodologies and at different times together on the same graph without noting that the estimates are not necessarily truly comparable. They reduce estimated ranges to single data points without explaining their reasons or method. They pick numbers that best match what they are trying to prove and discard the rest. Similarly, Culshaw presents a recent prevalence figure that is not even within the estimated range from the source she gives. These tactics are evidence of professional incompetence if not scholarly malfeasance, and are particularly disturbing when lives are at stake.

3-6. “...if HIV is a new pathogen, then its prevalence should not have remained constant—it should have clearly increased, according to Farr’s Law, which asserts that a new contagion spreads exponentially throughout the population” (p.3)

As we have seen, claims of constant prevalence for HIV, even in the United States, depend upon a willingness to misrepresent or even manipulate the surveillance data. Taking into account that the estimates are ranges, and keeping in mind the difficulty in obtaining these estimates, it is apparent that HIV prevalence has risen steadily since the discovery of the virus.

Furthermore, medical surveillance never had the chance to observe the early spread of HIV in the U.S.: AIDS was described, and HIV tests developed, only after the virus had established itself in the population. Pre-1985 estimates are especially difficult to derive.

In other countries, where HIV most likely asserted itself later than in the United States, data show a sharp initial increase in prevalence. This is the case in Culshaw’s country of citizenship, Canada. (See [THIS SITE](#) for estimates of Canada’s HIV prevalence from 1975-2005.) Estimated infections rise from zero in the late 1970s to ~35,000 by 1990, level off slightly, then increase gradually to about 65,000 by 2005.



From: [14], Figure 1, “Estimated number of prevalent HIV infections in Canada, including range of uncertainty, by year”

The appeal to “Farr’s Law,” like Culshaw’s Figure 1, is taken (unattributed) from Peter Duesberg, who popularized the denialist abuse of this postulate at least as early as 1992 [15]. Duesberg may have based his argument on a *Lancet* publication from 1990 [16]. Farr’s Law states that easily-transmitted (e.g. airborne), seasonal pathogens like flu will spread exponentially, then fade just as quickly, while other pathogens or parasites—for example, those that depend on more restricted routes of transmission—remain at a relatively constant level in the population. Both Duesberg and Culshaw fail to recognize that some microbes, in some populations, fall somewhere between these two categories. For example, a sexually-transmitted microbe may not spread exponentially when introduced into a new population. The rate of spread, the eventual equilibrium prevalence, and the time it takes to reach this “set point” depend on many factors. As early as the mid-1980s, epidemiologists predicted (see [17]) that HIV prevalence in the United States would eventually “plateau” in high-risk groups (“saturation effect”) due to the interplay of deaths and relatively low transmission rates. A similar leveling-off could be expected to occur, albeit later, in the general, low-risk population. Culshaw’s willingness to reduce the complexity of HIV epidemiology to the issue of “young” or “old” pathogen—as determined by nothing but Duesberg’s simplistic version of the nearly two-century-old Farr’s Law—is curious and unscientific.

Culshaw draws another erroneous conclusion from Farr’s Law: that HIV is not infectious. As noted, a leveling-off of HIV prevalence has not yet occurred in the United States; instead, it continues to rise steadily according to all available evidence. Yet even a true flat-lining of the prevalence curve would not justify Culshaw’s conclusion that HIV does not spread like an infectious agent. A steady prevalence level would signify not that infection does not occur, but simply that the number of deaths of infected persons approximately balances the number of new infections.

Culshaw repeatedly demonstrates unfamiliarity with basic concepts of disease epidemiology that should be well-known to any mathematician, let alone one with her background in infectious disease modeling.

7. “...the fact is that in no case does HIV prevalence ever fit with AIDS incidence” (p.1).

HIV-positive patients may present with AIDS only after a latency period of months, years, or even decades, depending upon the individual. As noted, the first authoritative estimate of HIV prevalence in the US dates from 1985 [9]. Prior to that, we can model and guess, but reliable numbers are hard to come by. HIV was likely present, if rare, in the United States since at least the 1960s. Presumably, the virus spread rapidly during the 1970s. If we had a reliable graph of this prevalence curve, it would likely fit very nicely with AIDS incidence in the early 1980s.

8. In early AIDS patients, “fewer than half” were HIV-positive (p.19).

We know now that every AIDS patient is infected with HIV, regardless of whether the very earliest studies performed by scientists working under difficult circumstances and without the benefit of today’s advanced assays, could measure the virus in every single patient. Culshaw misrepresents the results of one paper from 1984, applies them to the entire epidemic, and argues on this basis that HIV cannot cause AIDS. As is the case with every known disease, human knowledge of HIV and AIDS is not encapsulated in any solitary scientific article, no matter how important that early, pioneering article is.

9. “(A)ll mainstream evidence reveals the infectivity of HIV...to be so negligible as to be incapable of sustaining any sort of epidemic” (p.63)

Culshaw gives no references for this statement, a classic non sequitur. She does not provide transmission rates, explain why they are “negligible,” or tell her readers what level of infectivity would be required, in her view, to sustain an epidemic.

10. There is no “solid evidence” that HIV is transmitted sexually

11. There is no “solid evidence” that HIV can be transmitted by blood

12. Perinatal transmission is the most efficient means of HIV transmission (all, p.45)

The perinatal transmission rate of HIV is estimated at around 25% if no intervention occurs (an early study [18] estimated 13-32% and 25-48% in industrialized and developing states, respectively). This rate is lowered substantially by antiretroviral therapy (see, e.g. [19]), even single-dose therapy. Delivery by Caesarian section can reduce transmission to around 1%. In contrast, transfusion with blood containing HIV will produce infection in as many as 9 out of 10 cases [20, 21], and transmission via organ transplant may also be efficient. This underscores the importance of blood and organ supply screening.

Even sexual transmission can at times occur at an efficiency comparable with that of perinatal transmission. Sexual transmission is erroneously presumed by Culshaw to be extremely and uniformly inefficient. (For Culshaw’s likely—and unreferenced—source for this falsehood, see [11], p.179.) While transmission is often inefficient during chronic infection, viral loads are high during acute and late-stage disease, greatly increasing the chance of transmission. During the acute phase of HIV infection (characterized by high viral loads), infected men may pass HIV to their heterosexual partners at rates up to 20% or more (depending on frequency of coitus) in the absence of other STDs, and up to 50% or more when other STDs are present [22, 23]. Another study suggests that nearly half of sexually-transmitted HIV infections occur during the acute phase of disease in the infecting partner [24]. Thus, while perinatal transmission is sometimes more efficient than sexual transmission, it is by no means “the most efficient mode” of viral spread—direct blood-borne transmission holds that dubious “honor.”

HIV and AIDS in Africa

1. AIDS in Africa is the fraudulent diagnosis of “normal” diseases as a new syndrome
2. African AIDS looks nothing like American or European AIDS; there is little symptomatic overlap (p.4)

Culshaw repeats these old denialist chestnuts without explanation or reference. I have seen nothing factual to support these claims, neither from Culshaw nor from her sources. AIDS in Africa, like AIDS in every other part of the world, occurs when HIV degrades the immune system, affording opportunistic infections and other diseases a favorable setting. Which disease or diseases, specifically, predominate in a particular HIV-positive, immunocompromised population depends on many factors, including environmental factors. Put more succinctly, “an opportunistic infection...will obviously respond to the terrain” [25]. This is why it is useful to look at AIDS as many different epidemics in Africa, not just one as Culshaw implies. The spectrum of AIDS-related diseases varies not just between Africa and the United States, but by geographical area in Africa and by risk group throughout the world.

There is nothing “normal” about how AIDS-defining diseases strike Africans infected with HIV. Tuberculosis (TB), as one illustrative example, has always been a problem; but with the spread of HIV, it is now affecting those who would otherwise be at very low risk.

Mary Mbaziira, a veteran nurse at Masaka Hospital just north of Rakai [Uganda], remembers that before the advent of AIDS, TB was largely confined to "very poor people or those herding cattle," who contract the germ from raw milk. As AIDS spread, who came down with TB? "People around," she says, gesturing expansively.[26]

This observation by a local health worker is confirmed by statistics. In the AIDS era, death rates among the young and usually less-affected have risen [27, 28]. Tuberculosis rates have increased dramatically overall [29]. Most of this increase is due to HIV-mediated immune system compromise, and restoring CD4+ counts through antiretroviral therapy can reduce co-infection with tuberculosis [30]. The case fatality rate (CFR) of TB has also increased because of HIV, and local TB CFR is correlated with local HIV prevalence [31] In addition, HIV-associated tuberculosis can have unique aspects, including “extrapulmonary disease, disseminated disease, rapid progression, visceral lymphadenopathy, tissue abscesses, and negative tuberculin skin test” [32], that are seen in Africa and in the rest of the world.

Clearly, HIV-associated tuberculosis is not “normal;” and neither are the other diseases associated with AIDS, whether or not they are officially listed as “AIDS-defining.” Nor is AIDS a new name for poverty or malnutrition ([33] and [34] or [on-line](#) article). Conditions such as poverty and malnutrition may create a “fertile terrain” for the spread of HIV and the progression to AIDS ([35], [pdf](#)), but they do not cause or constitute AIDS. Anyone who claims that they do has ignored or fundamentally misunderstood the literature.

As for the symptomatic overlap between HIV/AIDS symptomology between Africa and the US (point 2, above), one wonders if Culshaw would characterize malaria as a “pure fabrication” because its prevalence is different in Africa and Europe. Does she deny problems with malnutrition or clean water availability in some locales? Does she believe access to health care is not a problem anywhere in Africa? To prop up her arguments, Culshaw conveniently ignores the very real differences between many aspects of public health in Africa and Europe or North America, and, as we have seen, opportunistic infections and other diseases are not uniformly distributed around the world—for reasons apparent to anyone who bothers to look.

It is certainly true, for example, that tuberculosis rates are higher among African HIV patients than in their US counterparts. This should not be a surprise: tuberculosis is more common in Africa in general. Importantly, though, HIV is responsible for a similar percentage increase in tuberculosis cases in Africa and the United States. In some countries in Africa (e.g., South Africa), HIV is thought to be responsible for 50% or more of new tuberculosis cases, but continent-wide, for just under one third. In the United States, HIV is blamed for over a quarter of new TB cases [36]. Thus, in terms of percentage, HIV has a comparable influence on TB in Africa and the United States.

As a second example, *Pneumocystis carinii* pneumonia (PCP), seems to be more prevalent in the US than in Africa. However, since PCP can be difficult to diagnose, and the necessary equipment for accurate testing is relatively rare in many resource-poor areas, including large parts of Africa, PCP is likely to be underdiagnosed in Africa. Consistent with this hypothesis, studies that report the highest rates of PCP in Africa are those that use the most advanced diagnostic methods [37].

In addition to the influence of diagnostic practices on apparent rates of AIDS-related conditions such as PCP, many other factors could be mentioned [38, 39]. For one, antibiotic treatments for diseases not immediately associated with HIV may also act against some AIDS-related conditions. Trimethoprim-sulfamethoxazole (TMP-SMZ) is widely available and used against many common pathogens, including *Salmonella* and *Vibrio* species; it also appears to act against malaria. Since TMP-SMZ is one of the most effective anti-PCP therapies, individuals who are taking this combination drug for other reasons will also be less likely to develop PCP in the context of HIV. The lack of available treatments for some AIDS-defining conditions results in higher death tolls due to these conditions in Africa than in the US (*Cryptococcus*, for example). It is also important to consider the impact of a wide range of health issues, e.g., the potential mutual influence of HIV and malaria.

In conclusion, there is substantial overlap between “symptomatic presentations” in the US/Europe and Africa, and any differences in epidemiology and symptomology are often due to local influences. The biomedical research community continues to explore and explain these differences in the medical literature to enhance our understanding of the various epidemics and the factors that contribute to them. Differences between the AIDS epidemics do not prove in any way that African AIDS is a lie.

3. AIDS in Africa is a “fabrication” (p.3), invented so that scientists could get more money

4. AIDS in Africa is evidence of the inherent racism of scientists

Consistently, Culshaw presents no evidence of fabrication or that scientists are motivated by greed or hatred. One wonders to what Culshaw attributes the actions of thousands of African scientists and doctors: avarice or racism? (See [this article](#) on African HIV/AIDS science and medicine [26].)

5. “(M)ost of the reports we hear about HIV rates in places like Asia and Africa are simply statistical contrivances with no basis in reality” (p.1)

Just as in the United States, it is true that not every HIV-positive individual is catalogued anywhere else. Faced with the implausibility of counting everyone, statistical models are used to extrapolate population-level numbers from smaller sample sizes [40]. There are more and less accurate ways to do this, but all methodologies have a firm “basis in reality.”

6. HIV statistics in Africa are derived solely from testing at maternity clinics (pp.85-86)

Antenatal testing data have certainly been instrumental in monitoring HIV infection levels, but if Culshaw has read any primary sources about AIDS in Africa, she should know that many countries also use population-based (“second-generation”) methods of surveillance. (16 countries that use this approach are discussed in [41]; 19 are listed in [42], along with several more that used population-based methods as early as the 1980s.) Some countries also survey high-risk populations. In her simplistic description of medical surveillance in Africa, Culshaw manages at least to contradict her assertion from page 1 (AIDS statistics have “no basis in reality”). Even if all HIV prevalence estimates in “places like Asia and Africa” were based solely on single tests of blood “left behind” at clinics (they most assuredly are not), this would still constitute the “basis in reality” that Culshaw denies exists.

7. AIDS diagnosis in Africa does not require an antibody test

This statement may have been partially accurate twenty years ago; today it is completely false. The so-called “Bangui Definition” of the World Health Organization (WHO) from 1985 did not require HIV-specific tests for diagnosis (and for good reason, since tests were not generally available). This does not mean that tests were never used. Uganda began testing for HIV as soon as antibody tests became available, for example. Results from some of this work were published in the medical literature and showed that Slim patients who were tested were positive for antibodies to HIV [43].

The WHO issued an amended definition in Abidjan in 1994. Among the changes, testing was explicitly urged unless local conditions precluded it. Many African countries immediately moved to the Abidjan definition; others continued to use the Bangui definition but added a requirement for HIV serology. Still other African states have adopted the US CDC diagnostic requirements. By the year 2000, only a handful of countries still adhered solely to Bangui (see Table 3, p.158 of [42]). In countries with HIV prevalence under 10%, multiple tests are recommended [44, 45]. Yet Culshaw, either unaware of these developments or ignoring them, maintains that AIDS diagnosis does not require HIV-specific tests anywhere in Africa. (Among the potential sources for this falsehood—and Culshaw does not identify her source—is inaccurate information in [46], p.184.)

Note, as well, that “antibody tests” are not the only HIV-specific tests in use, although ELISAs are fairly simple procedures that require only minimal training and technical skill to perform properly. (See, however, the testimony of molecular biologist Harvey Bialy, who was apparently unable to perform ELISA correctly in South Africa despite his supposedly high level of experience, at [47]).

8. HIV transmission rates in Africa are identical to those in the US, so there cannot be an epidemic in Africa (p.85).

Uncharacteristically, Culshaw gives three references for this claim (but no supporting explanations): Gray et al, 2001 [48], Hugonnet et al, 2002 [49], and Padian et al, 1997 [50]. This (for Culshaw) unusual practice is, however, somewhat diminished in effectiveness, since she uses the same sources elsewhere (p.45) to argue that HIV *cannot* be sexually transmitted, but here, to “prove” that HIV has limited sexual transmissibility. It is unlikely that Culshaw carefully read any of these references, since (in accordance with medical ethics) the studies described therein include safe-sex education and promotion of sexual practices not necessarily typical of the general population, and/or increased access to STD clinics and treatment. Hence, the results may not be representative of transmission rates in the population.

Culshaw seems to have chosen these studies based upon their low determined transmission rates; indeed, these articles (and especially Padian et al) are among the most-cited—if not well-read—by HIV/AIDS denialist authors. While it is possible that Culshaw read these publications, she seems to be ignorant of their methods.

In any case, Culshaw’s direct comparison of these studies is questionable. To validate her claim that transmission rates are identical globally, Culshaw would first need to show that the African and U.S. transmission studies were comparable (did the studies use similar methods, examine similar populations, work within similar time scales?). She would need to demonstrate that the African and US study groups were representative of the African continent and the United States as a whole, respectively. Culshaw would also do well to give an account of the spread of HIV in both Africa and the US. Finally, she would have to show how and why this evidence proves that a “heterosexually transmitted epidemic” is impossible anywhere in the world. Culshaw takes none of these steps; instead, she selectively pulls one piece of data from each paper’s abstract (actually, it is unclear to me *what* she is looking at in Hugonnet et al [49]), without apparently considering the rest of each study.

Examining her sources more closely, we find the following quote from Gray et al, who examine per-act transmission probabilities among HIV-1 discordant monogamous couples in a Rakai-district cohort in Uganda:

Transmission probability per act varies greatly with the HIV-1 viral load of the HIV-1-infected partner, which suggests that interventions to reduce viral load could reduce transmission... Younger age and genital ulceration also increased the probability of transmission per act [48].

Thus, even if we were to assume that the per-act transmission probabilities suggested in this study are representative not only of all of Africa, but of the entire world, we would expect to find higher prevalence of HIV infection among populations with larger proportions of younger people, higher incidence of STDs that include genital ulceration, and lower proportions of HIV-positive individuals with access to viral-load controlling therapies. Each of these conditions is fulfilled in many populations on the African continent, as contrasted with, for example, the North American population.

Importantly, Culshaw ignores the many publications suggesting a relatively higher rate of transmission in Africa than in higher-income areas (see [51] and references therein), including even a later publication from the Gray et al group (Wawer et al, 2005) that shows much higher rates of transmission during the acute and late phases of infection [23]. Such selective quoting of the literature is scholastically unacceptable.

9. AIDS did not exist in Africa before 1983 (p.61).

AIDS not only *existed* in Africa before 1983, it was also *diagnosed* before 1983: “The first AIDS case in Uganda was diagnosed in 1981(...)a cumulative total of 43,875 clinical AIDS cases had been reported” by June, 1984 [52]. See [this article](#) for a description of a Ugandan Slim victim who died in 1980 [26]; he was not the first. The oldest known sample of HIV was found in plasma drawn in Kinshasa in 1959 ([53], see also [54, 55]). Many retrospective diagnoses may be found in the literature, including [56]. Or is Culshaw taking the point of view that nothing exists until it is named?

10. HIV did not come from non-human primates; if it had, the zoonotic jump must logically have occurred “long ago”

11. This is because, in recent memory, nothing has changed the interactions of humans and primates in Africa. On HIV-1 and -2 arising from SIV: “logically, such a zoonotic jump, if it were possible, should have happened long ago” (p.61).

HIV-1 is related most closely to a simian immunodeficiency virus (SIV) that infects chimpanzees, called SIVcpz, and HIV-2 to SIVagm of the African Green Monkey. These close evolutionary relationships suggest that HIV-1 and HIV-2 arose from SIVcpz and SIVagm, respectively (see, among many others, [57, 58]). Zoonotic transmission occurred at some time in the past through close contact between humans and non-human primates, for example during the hunting of chimpanzees or their butchering as “bush meat.” It is not known precisely when this species jump occurred. Most phylogenetics-based estimates place it at slightly less than a century ago (ca. 1930).

Culshaw objects to the entire hypothesis of zoonosis for HIV, claiming that the interactions between humans and non-human primates have not changed substantially in recent years. While refuting this point goes well beyond the scope of this review, African population changes alone, during the colonial and postcolonial eras, have substantially changed the interactions between humans and animals. Transport networks are considered particularly critical, not only within Africa but between Africa and the rest of the world. HIV/AIDS is an African disease first diagnosed in the USA. How many earlier infection bursts failed to perpetuate beyond small, isolated geographical areas not visited by travelers? How many African AIDS cases went unnoticed and unrecorded? We do not know. Also, while Culshaw speaks of logic, she does not define “long ago.” Should the jump have occurred a thousand years ago, or ten thousand? At what point is it logical, in Culshaw’s view, to assume that a jump would have occurred?

Zoonotic transmission is a well-known phenomenon. **Rabies** is transmitted between mammals and causes tens of thousands of human deaths every year. **Ebola** and **Marburg virus** are well-known zoonoses affecting humans and non-human primates [59, 60]. **Influenza** virus sources (birds and pigs) have been covered extensively in the news media, and as such are familiar even to those who do not have extensive familiarity with the scientific literature. Strangely, Culshaw does not ask why new strains of influenza continue to emerge, even though relations between humans and birds or pigs have hardly changed in thousands of years. Crossover of smallpox relative “**monkeypox**,” (the etiological agent is an orthopoxvirus) has caused outbreaks in many locations, including in the Democratic Republic of Congo in 1996 [61]. In 2003, prairie dogs infected by pouched rats brought illegally from Africa spread the disease in the United States [62]. **Tularemia** is another disease that has crossed from prairie dogs to humans, with the first known case in 2002 [63]. Bats are also a source of “new” diseases, including the **Hendra and Nipah viruses** and some **coronaviruses** [64]. Zoonotic transmission of disease agents occurs often, is well-characterized, and is by far the most plausible explanation for the origin of HIV.

On the definition of AIDS

1. The CDC expanded the AIDS definition in 1993 to ensure fewer absolute numbers of AIDS deaths (pp.26-27)

On pages 26-27, referring to the CDC's 1993 inclusion of CD4+ T-cell count below 200 cells per microliter as an AIDS-defining condition, Culshaw writes that the CDC wished to "create the illusion" that anti-HIV strategies were working. Thus, "(t)he effect of introducing an entire class of 'healthy AIDS patients' (sic) was, first of all, to more than double the actual number of AIDS cases and, secondly, to drastically decrease the number (sic) of those patients who actually died."

In these sentences, Culshaw makes several errors. First, she omits any mention of the well-documented reasons for the CDC's expanded AIDS definition (see [65] and references therein). For example, extensive study has shown that HIV-positive patients with CD4+ helper T-cell counts below 200 per microliter are statistically more likely to contract certain infections than those with higher CD4+ counts. These patients are thus only superficially "healthy" and stand to benefit from prophylactic treatment against, e.g., the causative agent of *Pneumocystis pneumonia* (PCP). Second, Culshaw implies—without any supporting documentation, as none exists—that the CDC change was deliberately designed to doctor HIV/AIDS mortality statistics and thereby provide support for what she calls the pharmaceutical industry's "toxic drugs" (pp.27, 28, 31, etc.).

The third error is particularly puzzling, coming as it does from an academic mathematician: a confusion of absolute numbers with percentages, coupled with a logical impossibility. Culshaw uses the word "number" twice where only "proportion" would make sense in context. If officials at the CDC had wished, via sleight of hand, "to drastically decrease the number" of AIDS deaths, they should have made the AIDS definition more *exclusive*, not more *inclusive*. It would be logically impossible for the absolute number of deaths to decline as a direct "effect of introducing an entire class" of potential fatalities, a class that is just as large again as the previous total of AIDS patients.

Yet, had Culshaw correctly written "proportion" (as she does later, p.27), this point would still remain invalid. After AIDS deaths in the U.S. peaked at over 51,000 in 1995, a decline occurred not only in the *proportion* of AIDS cases resulting in death, but, in fact, also in the *absolute numbers* (as summarized in [66]). If the latter drop had not been observed, Culshaw might have had an opening to build a case...albeit weakened from lack of supporting citation. The dramatic decrease in absolute numbers of AIDS deaths in the late 1990s—from 51,000 in 1995 to around 18,500 in 1999—cannot logically be ascribed to an increase in the total number of AIDS patients. It is instead a tribute to the efficacy of combination therapy.

2. Some AIDS-defining conditions have "absolutely nothing" to do with immune deficiency (pp.23, 25, 34)

This is another fallacy popularized by Peter Duesberg, whom Culshaw does not cite here. Various conditions that are disproportionately diagnosed in HIV positive individuals, especially when plausibly and mechanistically tied to HIV and/or resultant immunodeficiency, have been added to the list of AIDS-defining conditions. Every condition on the list has something "to do" with immune deficiency.

3. Kaposi's sarcoma has nothing to do with immune deficiency (p.23)

Life-threatening cases of Kaposi's sarcoma (KS) are associated with immune suppression. While HIV does not directly *cause* KS—Kaposi's Sarcoma Herpes Virus (KSHV, also known as HHV-8) is the sexually-transmitted culprit—HIV and the immunodeficiency pursuant to infection create an environment favorable to KSHV replication and growth of the cancer [67]. The sudden appearance of many cases of life-threatening KS, normally a rare and relatively benign cancer seen most often in certain ethnic groups, helped alert clinicians to the existence of AIDS.

4. Kaposi's sarcoma is seen only in homosexual men (p.32)

Culshaw states rather unambiguously that KS is absent “in all non-homosexual risk groups.” This is categorically false (Culshaw seems to have taken this falsehood from Peter Duesberg—“only homosexual males have Kaposi's sarcoma” [10]—or Heinrich Kremer, who doubts the existence of heterosexual KS, as seen in this highly inaccurate [piece](#) [68]). In truth, KS is found at higher rates in the HIV-positive homosexual male population, but also disproportionately affects HIV-positive males in general; HIV-positive women also develop KS. Some studies have found that injecting drug use (IDU) associates with higher risk of KS, although others dispute this [69]. In any case, KS is by no means unique to homosexual men.

5. Kaposi's Sarcoma is “mysteriously absent” in pediatric AIDS (p.32)

Since the causative agent of KS is another sexually-transmitted virus (KSHV or HHV-8), this virus is found predominantly in several high-risk groups that do not usually contain children (see, however, [70]). Thus, its absence is not at all “mysterious.” Nor is it actually absent, only extremely rare, in pediatric AIDS patients (see [71] for an early case report).

6. AIDS today does not resemble the first recognized cases of AIDS (p.23)

The opportunistic infections and other conditions that were recognized as AIDS-defining in early cases remain associated with AIDS today. Since the early 1980s, new AIDS-defining conditions have been added to diagnostic guidelines. To say that AIDS today does not resemble AIDS in 1981 is, however, quite a stretch, particularly to those who may die of it.

7. The inclusion of invasive cervical cancer as an AIDS-defining condition was politically motivated **8. Invasive cervical cancer is common among women with no immune suppression (p.25)**

Without any evidence (and Culshaw gives none), there is no reason to assume that political motivations played any role—much less an exclusive role—in expanding the definition of AIDS to include any condition, including invasive cervical cancer. This charge is taken from Peter Duesberg (specifically from *Inventing the AIDS Virus*, p.209 [11]) without reference.

Invasive cervical cancer is not “common.” Rather, it is classified as a “rare disease” by the NIH. The prevalence of the cancer is enhanced by immune suppression, as recognized long before the connection with HIV was established [72]. HIV-infected women are reportedly ten times more likely to suffer from the disease than matched HIV-negative women (see [65] and references therein; some studies find a

somewhat lower increased risk), and survival rates are found to be lower in HIV-infected women [73], hence the inclusion of invasive cervical cancer in AIDS diagnostic criteria.

9. Including recurrent bacterial infections as pediatric AIDS-defining makes no sense since many children have them; also, if this condition applies to children, it should logically apply to adults, but it does not (p.32)

10. A high total lymphocyte count means that a child does not have AIDS (p.65)

Culshaw wrongly assumes that no recurrent bacterial infections are included in the AIDS diagnostic criteria for adults. Recurrent pneumonia was added to the list in 1993 [65].

Nevertheless, diagnostic differences do separate adult and pediatric criteria, and for good reason. Quantitatively and qualitatively—and including the response to HIV [74, 75]—the immune systems of infants and toddlers are different from those of older children and adults. It is thus not a particular surprise that an immunodeficient child might fall prey to diseases seen relatively rarely in the immunocompromised adult (and vice versa; see earlier discussion of KS). A pediatrician must be on the lookout for symptoms that might not appear in adults, hence several unique conditions are CDC criteria for a pediatric AIDS diagnosis [76]. Treatment recommendations are also different for young (i.e. <6 year old) children. For example, whereas prophylactic treatment for fungal pneumonia is recommended for adults with CD4+ counts under 200/ul, it is encouraged even at higher CD4+ counts for children up to six years of age and for *all* HIV+ infants in the first year, regardless of CD4+ count. This is because the average young child has a much higher total number of CD4+ lymphocytes than the average adult. In contrast to adult disease, the “risk of developing PCP in this age group is only weakly dependent on the T-helper cell count” [77]. In other words, even children with “high” CD4+ T-cell counts can develop AIDS-defining conditions. One study of perinatally-infected infants found *Pneumocystis carinii* pneumonia (PCP) in a child with a total lymphocyte count of about 10,000 [78]; several other children with PCP also displayed higher-than-average counts.

Culshaw follows denialist Celia Farber ([79] and in various online fora) in erroneously assuming that AIDS cannot be diagnosed if the CD4+ T-cell count is above 200/ul, but Culshaw further confuses the issue by equating high total lymphocyte count with high CD4+ T-cell count. This is not necessarily true. Importantly, AIDS diagnosis can occur in the presence of high total lymphocyte counts, even high CD4+ counts, although this is much more likely to be seen in pediatric cases than in adults. CD4+ deficiency is not absolutely necessary for AIDS diagnosis. Furthermore, AIDS diagnosis may rely on low *ratios* of CD4+ cells to total lymphocytes, not just low absolute numbers. The quantity and quality of T-cells in children and adults, quite simply, differ, reflecting real immunological differences. Equating the immune systems of children and adults is unjustified and could be disastrous in the clinical setting.

11. AIDS patients have “very few, if any, bacterial infections” (p.33)

This claim is absurd, yet Culshaw gives no evidence to support it. AIDS patients actually have many more bacterial infections than healthy persons. HIV-positive individuals are at elevated risk of (e.g.) bacterial pneumonia compared with HIV-negative individuals [80]. Several other AIDS-defining conditions are caused by bacterial agents [65]. Additional opportunistic infections, while not on the CDC list, are commonly found in AIDS patients. A few examples include the various bacterial causative agents of esophagitis (see [this medscape page](#)) and of GI infections (see [HERE](#)). Infections by *Haemophilus*, *Pseudomonas*, *Rhodococcus*, and *Salmonella* species are described [HERE](#). This last piece also notes that a 1992 study found bacterial infections to be the leading cause of death in HIV-positive patients in Rhode Island between 1988 and 1990 [81].

12. AIDS is actually just a “sociopolitical construct” (p.7)

13. AIDS is simply an expression of racism and homophobia (p.61)

14. If the fear of AIDS would end, the epidemic would end (p.61)

AIDS is a clinically-defined syndrome, not a sociopolitical construct. AIDS occurs in the presence or the absence of any number of reprehensible attitudes, although HIV/AIDS researchers have long fought the tendency (notably espoused by denialists such as Peter Duesberg and the “natural hygiene” movement) to “blame the victim” rather than the virus. Practitioners of science and medicine have sought to overcome barriers erected by misunderstanding, prejudice and politics to treat the syndrome effectively. HIV—not fear—causes AIDS.

On Antiretroviral Drugs

1. **“...the annual mortality rate of North American HIV-positives who are treated with anti-HIV drugs—between 6.7 and 8.8 percent—is much higher than the estimated 1 to 2 percent global mortality rate of HIV-positives if all AIDS cases were fatal in a given year” (pp.28-29).**

Here, Culshaw represents two discrete values as a range (the opposite of what was done in her first few pages with HIV prevalence data), quotes selectively, and misrepresents the primary literature. As such, this quote represents an egregious example of questionable scholarship...or worse. First, no solid mortality numbers are available for all North Americans who are HIV-positive and take antiretrovirals. Second, the numbers given here are not in fact a range, but two distinct estimates for two distinct cohorts. Third, the reference Culshaw gives contains brazen scholarly misconduct that Culshaw should have noticed had she read her source material carefully.

In the absence of universal, compulsory HIV testing and mandatory HIV reporting, only estimates of the prevalence of HIV in North America are possible. As noted above, the most recent CDC estimate of HIV prevalence in the United States suggests that between ~1.05 and 1.2 million individuals are HIV-positive; the WHO estimates 1.2 million. The number of deaths in individuals with AIDS can be estimated more precisely (since AIDS diagnoses are reportable throughout the United States). Using the CDC estimates to calculate crudely a very *rough* overall rate of death with AIDS in the HIV+ population in the United States results in a current annual range from about 1.4 to about 1.6 percent.

Antiretroviral drug treatment is not included in the CDC’s annual surveillance reports, so estimates are not available for annual mortality rates of all persons in the United States (much less all of North America) who are treated for HIV. The best that can be done is to examine the evidence from the many cohort studies of HIV+ individuals...but it is fallacious to extrapolate directly the results of such studies to the entire continent.

The two values given as the bounds of a range in Culshaw’s quote—6.7 and 8.8 percent—are two discrete mortality rates (in fact, the 6.7% rate is not even an *annual* mortality rate) from studies conducted at different times and locations and involving different cohorts of HIV+ patients with different characteristics, not all of whom were treated with antiretrovirals (Hogg et al and Palella et al, [82, 83]). The differences in the two studies do not allow the direct comparison of these rates, much less an assumption that they represent an annual mortality rate range for the entire North American continent. The Palella et al study examined only HIV+ individuals whose CD4+ T-cell counts were under 100/microliter (many under 50/ul), and were thus already AIDS patients; some had other AIDS-defining conditions. Some patients were treatment-naive (and had by far the highest mortality rate in the final reported study period); some had taken only monotherapy (one drug). The patients in this study were very sick and do not represent the wider HIV+ population. In the FJ Hogg et al paper, 6.7% is the mortality rate for a median of 28 months; the authors give 2.9% as the annual rate. Again, the patients studied were not all initially asymptomatic, and those who died were disproportionately those with low T-cell counts. Had Culshaw read the published papers from these two studies, (and cited them, as is customary when primary data are used), she could not honestly have represented these rates as she does...unless she lacks the elementary mathematical skills to understand what she read.

Yet even the review article that Culshaw cites as her source [7]—an inaccurate and demonstrably mendacious piece from three denialist authors, published only after extensive “shopping” around to

journals—does not present the rates of 6.7 and 8.8 percent as a range. This error is Culshaw’s alone, an inexplicable mistake for a university scholar.

As an aside, the Duesberg review from 2003 [7] is representative of the denialist literature in its willful manipulation and misrepresentation of more scrupulous scientists’ data. In this 30-page review, the authors complain that earlier versions of their manuscript had previously been rejected (or not accepted) by two journals with wider circulation than the eventual publisher, the Indian *Journal of Biosciences*. Reading the paper closely raises the question of why this third journal did not also reject it. Take the following sentence fragment as one example.

...the Palella-study found that the mortality of initially asymptomatic (sic), HIV-positive people, which (sic) are treated with new anti-HIV drug cocktails (sic), is 8.8%...and the Hogg-study found it is 6.7% (sic) [7]

Palella and colleagues document a steady decline in death rates from 35.1/100 person-years in early 1994 to 8.8/100 person-years in the second quarter of 1997. These strikingly high death rates are seen because the authors restricted their study to HIV+ individuals *with CD4+ T-cell counts below 100 per microliter (ul)*, meaning that these patients were already severely immunocompromised. Many had CD4 counts below 50/ul. Analysis was *not* restricted to “initially asymptomatic” individuals. Some patients did not take antiretrovirals at all (the highest mortality rate in the second quarter of 1997—51.6/100 person-years—was in this group), while still others were on monotherapy (i.e., *not* the “new anti-HIV drug cocktails”).

In the FJ Hogg et al paper, 6.7% is *not*, as implied by Duesberg et al, an annual mortality rate; the estimated annual mortality rate is 2.9%, as stated in the paper. 1219 HIV+ patients were followed for a median of 28 months. During the study, a total of 82 patients died of AIDS. 73% of the deaths occurred in patients (36% of the total) with CD4 counts below 200/ul. As in the Palella et al study, the patients were *not* all “initially asymptomatic”: 158 had been diagnosed with AIDS (73% with opportunistic infections, 17% with malignancies, others with neurological symptoms or wasting) prior to enrollment.

These mistakes are grave and indicate, at best, the low standards of scholarship to which Duesberg, Koehnlein, and Rasnick adhere. Even worse is an example of what can only be described as true scholarly misconduct—the following misquote from the Palella article, truncated to leave the impression that all study participants were “initially asymptomatic”:

Patients with a diagnosis of cytomegalovirus retinitis or M. aviarum complex disease before study entry or during the first 30 days of follow-up and patients with active P. carinii pneumonia at the beginning of follow-up were excluded. (Note the period here—KW) [7]

In the original paper, this sentence does *not* end with a period. Instead, it continues:

...from the analyses of the incidence of that opportunistic infection. [83]

Thus, all patients were *included* in the overall study, including the mortality calculations, but patients with pre-existing or early-presenting conditions were not counted as having developed *those specific conditions* during the course of the study. Duesberg, Koehnlein, and Rasnick manipulate the quote to make it say what they want it to say, in effect lying about the patients’ health status and the study’s methods to support their own assertion that most deaths reported here were due to drug toxicity. It is unfortunate that Culshaw looks to this class of scholars for her information and inspiration.

2. Antiretroviral drugs do not exist; they just kill or change cells, not viruses (pp.28, 86)

Although Culshaw does not attribute these ideas, they were popularized by Peter Duesberg beginning in the late 1980s. It is true that at doses much higher than those administered to HIV-infected people, “chain terminators” like AZT can at least theoretically act as anti-cancer drugs, which is what Duesberg (via Culshaw) describes here. But AZT did not work well as a cancer drug, even at doses higher than those administered to AIDS patients in the mid- to late-1980s. AZT does not kill cells efficiently. It has a much higher affinity for HIV’s reverse transcriptase (RT) enzyme than for most cellular enzymes and thus has a disproportionately inhibitory effect on virus replication. However, AZT can also inhibit mitochondrial enzymes (mitochondria are found in the cytoplasm), contributing to the muscle wasting and fatigue seen in AIDS patients on AZT monotherapy. These side-effects, combined with rapid selection of drug-resistant mutants during monotherapy, necessitated the development of new treatment strategies.

Of course, AZT is far from the only antiretroviral drug. Duesberg, as repeated by Culshaw, makes no distinction between the nucleoside analogs (such as AZT) and non-nucleoside reverse transcriptase inhibitors (NNRTIs). These drugs also target RT, but even more specifically than AZT and its structural relatives; in addition, their mechanism of action is different. Further classes of antiretrovirals target stages of replication before or after reverse transcription, including protease inhibitors, fusion inhibitors, and integrase inhibitors. Fortunately for patients who have benefited from these drugs, Duesberg was absolutely wrong when he wrote that “an antiviral drug may never be possible” ([11], pp.307-308)—and laughably so, since antivirals already existed when he made this statement. Culshaw would do well not only to attribute properly the sources of her ideas, but also to find a more reliable and accurate source than Peter Duesberg.

3. A true antiretroviral drug would necessarily eradicate its targeted virus from the body (p.86).

“Antiretroviral” means simply that a drug acts against retroviruses in a specific manner. Eradicating HIV from the body is not currently possible and may not be possible for the foreseeable future [84]—mainly because of long-lived, latently-infected cells [85] that no currently known treatment can eliminate selectively and effectively—but proper antiretroviral treatment can control viral replication, keeping patients alive and relatively healthy. Culshaw’s argument here is akin to my disputing the global existence of insecticides because I still, occasionally, see ants on my porch.

4. “...if these drugs were truly HIV-specific, much smaller doses would be necessary than those that are currently prescribed” (p.29).

From a mathematical and scientific perspective, this statement is without support and largely empty of meaning. Culshaw does not quantitate the “currently prescribed” doses, nor does she explain how much smaller a “much smaller” dose would be, why less drug should be needed, or what comprises “true” HIV specificity.

An appropriate treatment of drug specificity must present a binding model (e.g. competitive inhibition, noncompetitive inhibition, irreversible binding) and detail the kinetics of drug-enzyme interactions. The kinetic constants obtained in this manner suggest the proper inhibitory dose (ID) for given concentrations of enzyme. While Culshaw cannot be expected to include in her book lengthy kinetic analyses of the various anti-HIV drugs, she could at least demonstrate that she understands these issues, give some

insight into her reasoning, and perhaps even cite several studies on the topic (such as [86] or [87], an early review of AZT and a related compound).

Yet, had Culshaw established theoretical effective doses for one or more of the antiretroviral drugs, she could not validly claim, without substantial further evidence and reasoning, that “smaller doses” should suffice. The “specificity” of an inhibitor does not, on its own, dictate the dosage required clinically for inhibition of a disease-related process. Bioavailability, elimination kinetics, processing and modification, administration route and distribution, and affinity for proteins or lipids are some of the many pharmacologic parameters that must be considered when calculating a theoretically effective dose. The amount so derived must then be tested experimentally and clinically.

5. If antiretrovirals were specific for HIV, one would be enough; combination therapy would be unnecessary (p.29)

Combination therapy is needed because monotherapy selects for drug-resistant viruses, not because the drugs are non-specific.

6. Antiretrovirals likely cause birth defects, stillbirth, and cancer and should not be used by pregnant women

7. The most toxic antiretrovirals are reserved for babies

Culshaw writes, sarcastically, that “apparently the risk of giving birth to a child carrying HIV antibodies is greater than that of any deformity, cancer, or even stillbirth” (p.30).

Culshaw presents no evidence for risks associated with anti-retroviral therapy and also fails to quantitate the very substantial health risks of HIV infection in children. Numerous studies have demonstrated that adverse events are rarely associated with prenatal anti-HIV therapy. There is some evidence to suggest that mothers on combination therapy may have a slightly elevated risk of pre-term birth; research is ongoing to explore this possibility.

In contrast, mother-to-child transmission (MTCT) of HIV occurs in approximately 25% of natural births when no antiretroviral therapy or other preventive measures are employed. Pediatric HIV infection often progresses to AIDS more quickly than HIV infection in adults. With no proven major adverse effects of prenatal antiretroviral therapy, it makes sense to treat mother and child and prevent transmission.

The encouraging results of this approach are seen in the CDC’s 2005 HIV/AIDS Surveillance Report [88], Figure 1 (p.13): the reported case-based estimated number of new US AIDS cases in children under 13 has declined steadily from 894 (1992) to 58 (2005)—a reduction of about 93.5%.

As for “toxic” drugs, Culshaw ignores all evidence for the safety of antiretroviral drugs in pediatric patients presents (for example, [89]) and presents anecdotal evidence of *one* possibly nevirapine-related death. Emphasizing this single death without giving any details, she fails to mention the thousands of patients who have received extra years of life because of nevirapine...and the thousands of children who have escaped HIV infection because of this very same drug. Culshaw’s reasoning here could just as well result in a book about cardiac bypass surgery, arguing that since at least one person has died during the procedure, it is harmful, lacks any benefit, and should be banned.

8. AZT's side effects are symptoms of AIDS, so many "AIDS" cases are caused by antiretroviral drugs (p.31)

Interestingly, Culshaw does not specify which of the CDC's diagnostic criteria she feels are caused by AZT: Recurrent pneumonia? Kaposi's sarcoma? *M. avium* complex? Prolonged AZT use at the higher doses prescribed when few or no alternatives were available can often be associated with severe side-effects, and partly for this reason, new drugs were sought and found. But these side-effects hardly constitute AIDS. (For more information on the benefits of antiretrovirals, see [AIDSTruth](#).) AIDS was described long before AZT came into use. HIV, not AZT, causes AIDS.

9. The stories of antiretrovirals giving patients a new lease on life are fiction (p.27)

AIDS deaths in the United States have fallen from over 50,000/year to 17-18,000/year today. This is not fiction. It is inconsistent that Culshaw should find fault with supporting anecdotes ("stories"), particularly when they are backed up with statistics, since she relies exclusively on anecdotes without any supporting statistics for "proof" in other settings (e.g., concerning nevirapine in points 6 and 7, above, and on p.34, referring to anecdotes about "healthy," untreated people with AIDS).

10. Antiretrovirals can have temporary benefits, but only because they kill the agents of opportunistic infection faster than they kill most host cells; "...opportunistic infections are fairly efficiently killed (sic) by these drugs" (p.28).

Although Culshaw gives no references for this claim (it seems to have been taken with minor modifications from a 2006 article by denialist Janine Roberts [90], [link](#)), it would be partially true if appropriately modified. Reverse-transcriptase inhibitor AZT, for example, can inhibit the RT activity of the Klenow fragment (Kf) of *Escherichia coli* Polymerase I. However, whereas significant HIV-1 RT inhibition occurs at concentrations normally achieved in patients at therapeutic doses of AZT, inhibition of recombinant *E. coli* Kf, or Kf RT activity in *E. coli* lysates, requires drug concentrations tens of thousands to hundreds of thousands of times higher [91]. In terms of actually *killing* bacteria, some investigators report that several *Enterobacteriaceae* family members are affected by physiological doses of AZT, while "*Pseudomonas aeruginosa*, gram-positive bacteria, anaerobic bacteria, *Mycobacterium tuberculosis*, nontuberculosis mycobacteria, [and] most fungal pathogens" are not affected [92]. Other investigators observe even anti-enterobacterial effects only at much higher concentrations than are achieved with therapy in vivo [93].

Similarly, numerous studies have demonstrated the effectiveness of *some* HIV protease inhibitors (PIs) against *some* agents of opportunistic infection (OI) in the laboratory, in some instances even at normal therapeutic doses. However, this is not the case for *every* HIV PI, nor do these findings necessarily apply in vivo. For example, under highly specific culture conditions, ritonavir has been reported to inhibit protease activity of some *Candida* isolates and also retard growth; saquinavir did not exert this effect [94]. A higher-throughput screen confirmed ritonavir as having some inhibitory effect on three *Candida albicans* proteases [95]. However, a patient-based study found only limited antifungal effects of ritonavir [96]. In sum, several HIV protease inhibitors appear to act against some agents of infection in vitro, but have few if any measurable effects in vivo [97]. Interestingly, (and contradicting Culshaw), the drugs without any anti-OI effects in vitro still have therapeutic benefit in HIV infection and AIDS: PIs are effective as therapy whether or not they inhibit the enzymes of parasites. Of course, if HIV PIs were to act against infections as well as HIV in vivo, this would constitute yet more support for continued (and expanded) therapeutic use.

(As a quibbling side note, it is unfortunate that Culshaw and her publishers apparently chose not to show her manuscript to a biologist before publication. A drug does not “kill” an infection, but, rather, the agent of infection, thereby ending or clearing the infection.)

11. More AIDS patients are killed by HIV protease inhibitors than by AIDS itself (p.29).

An extensive body of research has probed the toxicities of antiretroviral drugs, including the protease inhibitors, and has shown that protease inhibitors are not at all the base poisons Culshaw imagines. Acute reactions occur occasionally, resulting in liver enzyme imbalances; although these tend to stabilize, serological monitoring of liver enzyme levels is standard for patients taking these drugs (as it is for patients taking many other, non-HIV-related drugs). This monitoring permits prompt treatment modification if necessary. In some patients, HIV protease inhibitors may upregulate lipid biosynthesis or make the patient less responsive to insulin [98]. These changes may in turn be associated with accumulation of fat in the liver, or hepatic steatosis. HIV PIs may be associated with such effects only under specific conditions, such as in combination with particular RT inhibitors. HIV-positive individuals who are co-infected with Hepatitis C Virus (HCV) are at relatively greater risk for hepatic steatosis [99]. Hepatitis B and cirrhosis and other liver conditions associated with alcoholism or injection drug use are further potentially confounding factors. Exposure to multiple insults makes it difficult to determine the precise effect of HIV PIs on liver conditions, but they rarely play the exclusive (or even a leading) role. Investigators who publish on this subject emphasize their support for the continued use of PIs in combination antiretroviral therapy (cART), since, except in rare cases, their positive effects far outweigh the negatives. (For more information, see also [100, 101].)

Liver-related deaths do, however, claim an increasing share of lives among AIDS patients as these patients live longer with treatment. In the large D:A:D Study, the “Data Collection on Adverse Events of Anti-HIV Drugs Study Group,” consisting of hundreds of doctors, scientists and technicians, followed **23,441 HIV-infected individuals**, most of whom had taken cART, through 76,893 person-years ([102] and [a related abstract](#)). The effectiveness of cART, already well-known, is again demonstrated in this study. The authors observe that mortality has declined from 20-30/100 person years to 2-5/100 since cART became available; in this study, the rate is even lower, 1.62/100. At one time, opportunistic infections killed most HIV-infected individuals, but today, over half of the mortality is due to non-AIDS causes.

In the D:A:D study, **the two-times-over most common cause of death was AIDS (30.1%), contradicting on its own Culshaw’s claim that protease-inhibitor-mediated liver failure kills more HIV patients than AIDS itself.** Liver failure (**not** mediated by HIV PIs) was responsible for 14.5% of deaths. Among the 181 patients who died liver-related deaths, most had apparently contracted HIV through intravenous drug use. At least two-thirds were also Hepatitis C-infected. At least half had active or inactive Hepatitis B. Only 3.8% had tested negative for both diseases. 76% of the liver-related deaths were attributed to viral hepatitis. Importantly, in only 5 of the 181 liver-related deaths was “medication toxicity” presumed to be a major factor. The presence of confounding factors in these cases (such as alcoholism and IDU) is not given. Nor is it clear which medications were presumed toxic, whether only anti-HIV drugs were involved, if proper doses had been taken and for how long, or if the presumed toxicity was an acute or long-term phenomenon. The authors conclude,

There was no definite relationship between mortality and ART. The possibility of increased medication-related mortality cannot be excluded, but the CD4 cell count increases with cART seem to balance any adverse effects that exist [102].

In summary, for 388 people who died of AIDS, five died of medication toxicity, and it is not even clear what this medication was or whether there was significant confounding. Even if all five deaths were in fact due to protease inhibitors alone, only 0.4% of deaths in this study would be medication-related. Protease inhibitors and other antiretrovirals do much more good than harm, although research still continues into ways of even further reducing drug-related toxicities.

12. Recent reductions in AIDS deaths are the result of lower doses of toxic drugs (p.32)

Culshaw does not explain exactly what she means by this curious claim or support it with references. Reductions in AIDS deaths are due, among other causes, to cART, better overall treatment, and reduced MTCT, not to fewer drugs or lower doses.

13. Immune Reconstitution Disease (IRD) happens when the immune system is “confused” by antiretrovirals (p.29)

Culshaw gives no references for what she calls the “official dogma,” and her misleading description of IRD ignores inflammation as its main cause. IRD occurs in some patients after the initiation of antiretroviral therapy. As viral loads are suppressed, the immune system has a chance to recover. In some instances, this includes inflammatory responses to existing opportunistic infections; this inflammation can cause problems and can expose the presence of other subclinical infections. The immune system is not “confused;” an analogy is to a homeowner trying to clean house a little too vigorously after a long sickness and finding the effort a bit too taxing (maybe even knocking over a vase or two in the process). In most patients who suffer from IRD, the syndrome clears up on its own within several weeks. For others, temporary immunosuppression with steroids is necessary to lessen inflammation. Elsewhere [103], Culshaw cites a recent and accurate review of IRD [104]; perhaps she simply did not read it, or perhaps she lacks the immunological expertise to understand the underlying causes of IRD.

14. There is no evidence that any anti-HIV drugs prevent AIDS

15. The efficacy of antiretrovirals was established by “pure faith,” not by science

“It is worth noting at the outset that there are still no significant studies that actually demonstrate the statement (sic) that “anti-HIV drugs stop AIDS. There is simply no evidence, and this conclusion appears to have been reached as a matter of pure faith rather than being based on any real solid science” (p.27).

In the United States, after the introduction of antiretroviral treatment, pediatric AIDS cases quickly dropped to about 5% of pre-HAART levels. Overall, AIDS deaths in the U.S. stand at a third of the mid-1990s figures, despite the fact that more people are living with HIV infection today. While thousands of peer-reviewed articles from around the world (for just one recent example, see [105]; more information and references available at [AIDSTruth](#)) have shown the positive effects of antiretroviral therapy based upon drug trials, individual cohort studies, and meta-analyses, these reductions are perhaps the greatest and most easily-understood testimonial to the effectiveness of anti-HIV drugs.

Concerning HIV Tests

1. The positive predictive value of HIV tests is “less than 2 percent!” in the general population (p.42)

Culshaw does not describe how she arrived at this figure.

2. Half of all adults have been tested for HIV (p.36)

Culshaw gives as her source a non-peer-reviewed publication by Henry Bauer, an amateur expert on the Loch Ness Monster and editor of a delightfully quirky pseudoscientific circular called the “Journal of Scientific Exploration.” Unfortunately, the original data actually come from the Kaiser Family Foundation ([106] or [pdf](#)), are based on a survey of 2517 persons, and are restricted to the United States. Somehow, Culshaw converts “one-half of adults in the US between the ages of 18 and 64” to “nearly half of all adults”...without any geographic restriction. Half of all adults would be over two billion people.

3. At least one million people in the United States have tested false-positive for HIV at least once (p.36)

“Clearly, testing outside the risk groups would mean that almost everyone who would test positive would be a false positive, and, extrapolating to the general population, tens of thousands of people would be terrorized (sic) and put on poisonous drugs (sic) for no reason—a medical disaster” (pp.42-43).

If the Kaiser Family Foundation survey is correct [106], over 100 million people have been tested for HIV in the United States alone. Using Culshaw’s own figures and math (“testing ten thousand non-risk group Americans would yield...approximately one hundred false positives”), over one million non-risk group Americans should have already tested false-positive for HIV, with an additional twenty thousand being true positive. Since most of the over one million estimated HIV infections are found in members of various risk groups, this would mean that well over two million Americans should have tested positive for HIV already. This has not happened. Although Culshaw acknowledges that “repeat testing” would eliminate some of the false positives, there is no indication that massive numbers of Americans have falsely tested positive for HIV. Where are the newspaper reports, the lawsuits against test manufacturers, the mass panic, the loss of public confidence in the safety of the blood supply? They are nowhere to be found. The simplest conclusion is that Culshaw’s positive predictive value estimation is faulty, not the epidemiological data.

4. Pregnancy commonly causes false-positive HIV test results (p.31)

Many governments insist on high standards for screening tests that are used during pregnancy. As just one example, the United Kingdom Department of Health (in [107], Section 4, “HIV”) states that “any assay used for antenatal screening has a sensitivity >99.9% and a specificity >99.5%”. Pregnancy does not seem to increase greatly (if at all) the chance for false positives in high-quality, properly-administered tests.

5. HIV-seropositive babies are presumed positive for HIV even though “more than half” of them will eventually “revert” (p.31)

Because the natural and normal presence of passively transferred maternal antibodies can confer HIV seropositivity to an infant even when the infant is not infected, the CDC’s diagnostic criteria specify that a child under 18 months of age (maternal antibodies are no longer present in the child by 18 months) be considered HIV-positive only after two separate *non-antibody*-based positive tests (antigen detection, PCR, or viral culture) [76].

6. HIV tests have abnormally high rates of false-positive results (p.38)

7. HIV tests “are some of the worst tests ever manufactured in terms of standardization, specificity, and reproducibility” (p.36)

No references or examples are given to support this statement. Checking the specifications of other diagnostic tests, it is clear that HIV tests are actually among the *best* “manufactured in terms of standardization, specificity, and reproducibility.” Many tests are far less reliable. Serologic immune-based testing for inflammatory bowel disease (IBD) in children, as just one example, was found in one [study](#) to have a specificity of only 60% and a sensitivity of 92%, far below the corresponding percentages for standard HIV tests.

8. HIV RT-PCR probably does not work and is not reliable (pp.13, 46-48)

9. Unless RT-PCR is perfect, it is worthless as a quantitative tool (p.47)

10. Scientists are well aware that RT-PCR has never been “validated” (p.20)

Quantitative RT-PCR works, is quantitative, and has been properly validated both as a technique in general and specifically for each assay (primer-probe-target combination). Carefully-produced standards are the key to successful RT-PCR, yet it is precisely of these crucial controls that Culshaw and her source, Australian math instructor Mark Craddock [108, 109], seem to lack any knowledge. The standards consist of serial dilutions of a known number of copies of the RNA being assayed. Since they are amplified in exactly the same manner and with exactly the same efficiency as the unknown samples, it is valid to compare the unknowns and the standards to determine an unknown copy number. Any error will not be specific to the unknown or to the control; all will be affected. Further to ensure accuracy, all samples, including controls, are amplified at least in triplicate. Some well-designed and expertly-performed quantitative PCR assays can accurately and reproducibly quantitate as few as 10 copies of a particular RNA in a sample. Quantitative PCR has quickly become an indispensable tool in biology and medicine. It seems that the only doubters of PCR are concentrated in the field of HIV denial.

Culshaw seems to dispute not only RT-PCR, but the validity of all molecular biology and genomics-based science. She writes that HIV tests look “for fragments of DNA (sic—viral load tests start with RNA) believed, but not proven, to be components of the genome of HIV—but there is no evidence to say (sic) that these fragments don’t exist in other genetic sequences unrelated to HIV or to any virus.” In fact, the Human Genome Project constitutes persuasive evidence that HIV sequences are not found in the human genome of uninfected individuals.

11. HIV viral load RT-PCR overestimates infectious virions by 60,000 times or more “Even the mainstream literature...admits that viral load testing overestimates infectious virus by a factor of at least sixty thousand” (p.47)

This is a misreading of the paper in question [110], a misrepresentation of the literature as a whole, and a misunderstanding of viral load, infectious virus, and RT-PCR. Culshaw again relies on the uninformed speculations [108, 109] of Mark Craddock in supporting her claims, rather than performing the analyses herself or even checking Craddock’s writing for flaws (and there are many...see [this review](#) of Culshaw and Craddock).

The “mainstream” paper to which Culshaw refers says nothing about “at least.” Piatak et al [110] state that viral load exceeds virus titer *in their study, using their methods* “by an average of [not ‘at least’] 60,000-fold.” If one reads beyond the paper’s abstract (or beyond Craddock’s summary of it), the average is “nearly,” i.e., slightly less than, 60,000. Although virus could not be cultured from all 66 HIV-positive patients examined (all did have detectable viral loads), the authors did not calculate their average only from those patients whose virus grew in culture; instead, they assigned a non-zero (but negligible) titer of ‘1’ to each of the tissue-culture-negative patients, greatly increasing the “overestimation factor.” Finally, for positive cultures, the viral load overestimate varied widely, from 16-fold (JOJI 0070) to 121,000-fold (DUSE 1021). If we look at patients with T-cell counts below 200 who had culturable virus, we find that the average overestimate of viral load is under 22,000; the median, however, reflecting the distribution, is below 4000. Indeed, there are many interesting ways of looking at these data, but one thing is clear: Culshaw does not seem to have considered what the data mean in any way, and may not even have read the paper. She seems to trust Craddock’s flawed analysis as infallible.

In any case, Culshaw’s inaccuracy and exaggeration is irrelevant. The point she tries to make is that quantitative PCR is flawed, therefore unreliable and useless; her evidence is that viral load does not equal TCID₅₀ x 2 (two RNA copies in each virion). But the discrepancy between viral load and infectious free virus has nothing to do with the accuracy of qRT-PCR (which is well-established). If PCR were as capricious as Culshaw and Craddock suggest, we could expect viral load to underestimate infectivity just as often as it overestimates infectious virus. This is not the case. Instead, the apparent discrepancy between viral load and infectivity involves constraints of the experimental system and characteristics of the cells and virus assayed.

A recent publication on this topic has the following to say:

The majority of retroviral particles in cell-free supernatants do not produce an infection...When the number of physical particles is compared with the infectious titer, one sees that the apparent ratio of infectious to noninfectious particles is typically between 1 in 1,000 and 1 in 60,000 [111]

It has also long been thought that a large portion of virus particles, perhaps even the vast majority, do not produce infection because they are somehow defective. Many virus particles may well be defective; the high mutation rate of retroviruses is just one factor that no doubt contributes. However, other potential influences on the ratio (which is quite real [110, 112]) include virus tropism, cell type of origin, and host immune system success against free virus (e.g. neutralizing antibody). Cell density in standard in vitro systems is also far lower than that found in lymphoid tissue [113]. Combine this with diffusion limits, and many infectious virions simply never encounter a target in culture. Elegant experiments in which infectious supernatant is applied serially to different cultures have demonstrated little loss of infectivity with repeated application [114, 115]. Spinoculation, an infection technique in which virus diffusion limits are partially overcome by centrifugation [116], enhances the apparent infectivity of an inoculum,

revealing the presence of more infectious particles than standard TCID or moi assays would suggest. Indeed,

...the ratio of particles to infectious events is not the same as the ratio of physical particles to infectious particles, as virions that do not have a chance to infect are not inherently defective. The true ratio of infectious to defective particles is likely... 1 in 8 to 1 in 20 rather than 1 in 1,000 to 1 in 60,000 [111]

Given the many vagaries and difficulties of infectivity measurement, viral load is a far superior tool in the clinic—a quick, sensitive, accurate, and relatively simple measure of HIV replication levels. Fortunately for HIV-positive individuals and those living with any of the host of pathogens monitored by qPCR assays, Culshaw and Craddock do not have a veto against the use of this important method.

12. If HIV ELISA gives false positive for undiluted serum, the test is worthless (p.39)

Using undiluted serum in an optimized ELISA means that the technician abusing the assay in this way is worthless, not the assay itself. In citing the results of an “experiment” by denialist technician Roberto Giraldo, Culshaw shows that she does not understand the underlying principles of the enzyme-linked immunosorbent assay (ELISA). Any such assay, when performed outside of its optimized range, is inaccurate at best. Dr. John P. Moore explains further on [this page](#).

13. Using “positive” and “negative” to describe an ELISA result is ridiculous; using “reactive” and “non-reactive” would be better (pp.39-40)

While Culshaw criticizes + and –, the alternatives she proposes—“reactive” and “non-reactive”—are also polarities and thus contribute nothing. But this semantic criticism is beside the point: ELISA results are never truly “negative” or even zero. There is always a readout. Careful optimization of each ELISA determines a cutoff level: if above, samples are considered “positive;” if below, “negative.” It is also wrong to suggest, as Culshaw does, that the assays are interpreted in the clinic as black or white. Instead, the absolute value of the readings is taken into account. Samples that read near the cutoff level may suggest to the clinician that further testing is needed, i.e. the patient may be testing false negative or false positive. Very high absolute values, on the other hand, have correspondingly high positive predictive values. Similarly, a very low readout is unlikely to be a false negative.

14. A truly HIV-positive sample should show antibody reaction with all bands on HIV Western blot (p.40)

The adaptive immune response to any pathogen will vary from person to person. Responses to specific proteins will vary by strength, type, and epitopes recognized. Some proteins of a pathogen may not elicit a response at all in some individuals. Some antibodies to specific proteins may not function under the conditions of the Western blot assay. The viral epitopes recognized by some antibodies in vivo may have slightly different sequences from those of the corresponding protein immobilized on the WB membrane. There are indeed many reasons for the lack of all-band Western blot positivity. The messy biological nature of the immune system may be unfamiliar and even “shocking” to some mathematicians, but we cannot disqualify HIV science as a result.

15. Antibodies to human endogenous retroviruses (HERVs) cross-react with HIV and are probably responsible for “true” positive test results on HIV tests (pp.44-45)

Culshaw presents no evidence for this claim. Do endogenous retroviruses share epitopes with HIV proteins? Is there evidence for cross-reaction in patients? Several HERV sequences, provided they are ever transcribed and translated, would indeed give rise to proteins with a distant relationship to several HIV proteins. For example, some enzyme catalytic sites in pol and portions of the env proteins have limited similarity to corresponding HIV entities. However, to my knowledge, there is at present no evidence that anti-HERV antibodies generated in vivo cause false-positive HIV test results. Nor is there any proof that anti-HIV antibodies would recognize epitopes from any of the hypothetical HERV proteins even if the HERV proteins were present. (The few studies that have explored the role of HERVs in possible immune system reaction to exogenous viruses are sometimes intriguing [117] and at other times rather questionable [118], but they usually share a reliance on peptide recognition, so a view of the big picture remains elusive.)

Undisputedly, antibody cross-reactivity can occur. Some viruses have even evolved “molecular mimicry” of host proteins. Specific epitopes of HIV proteins that can elicit cross-reactive antibodies have been found and mapped ([119, 120]; see also this [LANL](#) site for an extensive database of HIV epitopes), and this knowledge can guide the development of antibodies that are less likely to cross-react. As regards the postulated anti-HERV/anti-HIV antibodies, one group has suggested that several anti-HIV antibodies react with proteins in *baboon* trophoblast, although these proteins are not identified and no link to ERVs is established [121, 122]. Members of this same group have also reported that human trophoblast cells contain epitopes reactive with two antibodies against two HIV proteins [123]—although, again, these epitopes are not traced to any specific HERV proteins or other proteins. Indeed, the only evidence that these antibodies recognize ERV products seems to be circumstantial, consisting of the well-established presence of ERV particles in placental tissues [124, 125]. There is currently no support for Culshaw’s attribution of positive HIV test results to anti-HERV antibodies (nor is this idea hers).

16. “(A)ll laboratory tests used to assess the severity of HIV infection are virtually worthless” (p.48, original italicized)

CD4 counts and viral load measurements are not at all “worthless.” They have high predictive value. Of course, since we are complex biological entities with complex biological diseases, for some patients these measurements are more predictive than for others. Culshaw again traffics in absolutes: in her view, either a specific measurement correlates 100% with a specific outcome, or the test behind it is useless and must be discarded. Following this standard, most of modern medicine would come to a halt.

17. “All the (sic) epidemiological evidence to date strongly indicates that whatever testing HIV-positive signifies, it clearly is not a reliable indicator of the risk of ever developing AIDS” (p.57)

HIV infection is a shared characteristic of all properly-diagnosed AIDS patients. In the absence of treatment, most HIV-positive individuals will eventually progress to AIDS. It is unclear how all “epidemiological evidence to date” disproves the association of HIV and AIDS; rather, the evidence *proves* that HIV causes AIDS. The bold yet questionable nature of this particular statement is not surprising when we consider its source: Henry Bauer (see point 2, above). Bauer’s comical *Journal of Scientific Exploration* has published a good deal of nonsense. For example, one article makes the case that massive, body-wide “jumping DNA” transposition events “in the blood cells of individuals undergoing...advanced meditation, near death experience (NDE) or close encounter experiences with UFOs” lead to “sudden reversal of aging, emergence of a light body and observed bodily ascension into

the sky,” even “attainment of...nirvana” [126]. Unfortunately, denying the link of HIV to AIDS, while just as ridiculous and nonsensical as the other pseudoscientific flights of fancy in Bauer’s journal, is not so harmless.

HIV Virology, or Whether the Virus Exists

1. “A retrovirus is nothing more than RNA with an outer protein shell” (p.53).

A retrovirus is so-named because it reverse-transcribes its RNA genome into DNA, reversing the DNA-to-RNA “central dogma” of molecular biology. Retroviruses are only a subset of the RNA viruses. The retroviruses have not only RNA and a protein shell, but also contain other viral and host proteins, various smaller factors from inside the host cell, and an outer envelope composed of lipids (including cholesterol), receptors, and surface proteins.

2. The protein shell “disappears” in the infected cell; “It is for this reason that retroviruses are called enveloped viruses” (p.53).

Retroviruses are enveloped viruses not because they have a protein shell (almost all viruses do), but because the shell is, in turn, sheathed in another coating, a lipid membrane derived from the host cell membrane. Few concepts of virology are more elementary than this.

3. In an endnote, Culshaw writes, “It is estimated that 3 percent of the human genome is retroviral in nature. This amount of genetic material is several hundreds of times (sic) larger than the genome of HIV” (p.87).

The estimate of “3 percent” predates the discoveries of the human genome project; as such, this estimate was acceptable in 1997 but not in 2007. HERV sequences alone are now known to comprise over 8 percent of the genome. Starting even from Culshaw’s outdated figure, approximately 100 million base pairs (3% of 3.3 billion base pairs in the human genome) would be “retroviral in nature.” Since HIV’s genome comprises less than 10,000 bases, endogenous retroviral sequences contain not several hundred, nor even several thousand, but over *ten thousand times* the sequence information of one HIV genome. Culshaw’s conclusion is inexplicably off by two orders of magnitude in this simple back-of-the-envelope calculation.

4. Endogenous retroviral sequences (humans are “full of” them) are activated whenever cells are growing, dying, or under stress (p.44)

There are tens of thousands of retroviral sequences in the human genome (HERVs or ERVs); most of them have been rendered defective in the last several million years of evolution. One exhaustive post-genome study found only sixteen HERVs with full env genes [127]. Even this handful of HERVs with reasonably intact genes is normally silenced in most tissues, i.e. RNA is not made. In the rare cases of viral transcription, viral proteins and particles are not necessarily produced; when particles are observed, they are not thought to be infectious. ERV research is conducted in many labs today, and for all we know, some of this research may have implications for better understanding HIV. But not a single finding supports the idea that HIV is actually an endogenous retrovirus.

5. ERV sequences are “very likely to be mistaken by the viral load PCR as fragments belonging to HIV” (pp.44-45)

6. A positive HIV PCR test probably means simply that the body is under stress and releasing endogenous sequences (pp.44-45)

Human endogenous retroviruses (HERVs), as noted before, only very rarely are transcribed to produce viral-like particles, none of which is thought to be infectious. Only those HERV viral particles that were released from the cell AND contained RNA would be available for amplification by viral load PCR. Artefactual amplification of HERV RNA, of course, would occur only if both of the primers used for any individual HIV qRT-PCR could actually recognize HERV sequences. Such erroneous amplification would be caught in the quality control process, as the fragment produced would likely be of slightly different size from the HIV fragment and, more importantly, would have a different sequence from HIV. Culshaw gives no evidence that any HERV sequence resembles any HIV sequence sufficiently to be amplified by the primers used in HIV tests, or that such sequences are found in the extracellular milieu.

Culshaw implies that PCR amplification of “HIV” is really amplifying HERV sequences. The problem is that the HERV sequences are known and publicly available, for example through the online tools of the [National Center for Biotechnology Information](#). Anyone with interest in the topic can use web-based software to check specific primers used in HIV tests for potential binding to any site in the HERV sequences. It is unlikely that an HIV primer, much less the necessary *pair* of primers, would bind to a HERV sequence and generate a product in a properly-designed and -conducted assay.

Furthermore, any such hypothetical artefact would be identified quickly during sequencing. Genotyping tests are frequently conducted for HIV patients on antiretroviral therapy. This PCR- and nucleic acid sequencing-based assay involves analysis of entire regions of the HIV genome from virions circulating in a patient’s peripheral blood...with the goal of determining whether known drug resistance mutations have arisen. The results enable clinicians to vary treatment regimens for optimal results. Importantly, *sequences* are generated, in some cases hundreds of nucleotides long. These sequences are unambiguously HIV, not HERV, providing further evidence that HIV PCR does not amplify anything other than HIV. Culshaw’s airing of the tired and thoroughly disproved HIV=HERV idea is akin to invoking spontaneous generation to explain mold on bread.

7. HIV PCR never looks for a whole genome, just small “fragments” of a retrovirus (p.45)

8. “(M)uch of the genetic material attributed to HIV is in fact DNA or RNA from decaying cells” (p.55)

Full-length or near-full-length HIV genomes are routinely amplified directly from both RNA genomes and DNA provirus from both patient samples and in vitro sources [128-132], confirming that “HIV PCR” is specific and that its target is a bona fide, intact HIV genome. In RT-PCR “viral load” assays, the target is HIV genomic RNA, not “DNA or RNA from decaying cells.” Samples are in fact treated with an enzyme to degrade DNA selectively before the RNA is reverse-transcribed into DNA and amplified. In DNA-based PCR assays, which examine either or both of unintegrated or integrated provirus [133, 134], DNA is isolated from intact cells, not from detritus in the supernatant.

PCR assays for HIV do not amplify any cellular sequences specifically. This is because no significant portion of HIV is identical with any part of the human genome, including the endogenous retroviruses. Admittedly, there is a tiny portion of the human genome that remains unsequenced. Die-hard denialist proponents of the “endogenous theory” insist that HIV or HIV-like sequences may yet be found in the human genome. They are wrong for two reasons. First, it is precisely the repetitive nature of the unsequenced genomic portions that makes them resistant to sequencing; this feature also makes it unlikely

that complex sequences such as the approximately 10,000 bases of HIV would be found within them. Second, and most importantly, hybridization experiments (in which radioactive HIV-based “probes” are hybridized with human genomic DNA) would have revealed the presence of HIV or significant HIV-like sequences long before the Human Genome Project was initiated. They did not. (One study, employing low-stringency hybridization conditions, found two sequences in the genome that contained limited regions of identity with HIV—the highest identity was 28 bases in a stretch of 31; based upon the NCBI database, it does not appear either of these sequences is located in or near an ERV [135].) HIV is absolutely not an endogenous retrovirus; in fact, no lentiviral sequence is found in the human genome [136].

9. Transposable elements, made of RNA, compose 40% of the human genome (p.44)

10. Transposable elements cleave to form endogenous retroviruses (p.44)

The implication here (so far as I can discern), is that 40% of the human genome is RNA. This is wrong. The human genome is of course exclusively DNA. The transposable elements are encoded by DNA like the rest of the genome.

Culshaw posits either that transposable elements “cleave” something else, or that they, themselves, are cleaved; her wording is vague. Whatever the intended meaning, the result is a puzzle to any biologist: no matter how much cleaving occurs—of what or by what—human endogenous retroviruses are not formed from transposable elements. One can only wonder where Culshaw picked up these uncited, curious, and biologically absurd ideas.

11. Endogenous retroviral sequences are transmitted perinatally (p.45)

12. Perinatal transmission is the most efficient means of transmission for HIV (p.45, also found above)

13. The evidence indicates that HIV is not an exogenous retrovirus (p.45)

Endogenous retroviruses, by definition, are transmitted through the germ line (i.e. at conception), not perinatally (during the birthing process). As for almost all genetic elements, approximately half of a child’s endogenous retroviruses are contributed by the father and approximately half by the mother. In modern humans, perinatal transmission of a HERV is probably impossible. There is no known HERV that is infectious even if its proteins and genome were expressed and formed a viral particle. Thus, a baby could not be infected by a HERV during birth.

If a HERV mutated and became infectious, and if this HERV were expressed and virions produced, infecting an infant during birth, there is a 50% chance that the child would already have inherited this HERV sequence from her mother through the germ line. If the mutant HERV were in fact “new” to the infant, it would represent only one sequence, as opposed to the hundreds of HERV sequences already inherited through the germ line. Thus, even in this hypothetical and extremely unlikely situation, it could hardly be said that HERVs “are primarily transmitted perinatally.”

14. HIV may not exist as a unique virus (throughout)

15. No one knows what HIV really is (p.5)

The entire genome of HIV was sequenced soon after its isolation [137-139]. Hundreds, perhaps thousands, of full-length viral genomes have been cloned from HIV-positive individuals. Hundreds of thousands of HIV sequences—full-length and otherwise—have been deposited into publicly-accessible databases

(231,490 as of April, 2007). HIV's genomic features and proteins are known in intimate detail. The virus has been photographed by electron microscope; we can discern from these micrographs the difference between immature and mature viruses. Live viruses are isolated from patients and grown in the laboratory, in both cell lines and primary cells. Scientists have watched the virus traverse a newly-infected cell. They have characterized mutant viruses that evade host defenses and anti-retroviral drugs. The relatives of HIV, the other lentiviruses like SIV and Visna-Maedi virus, have also been extensively investigated. New strains of virus are engineered routinely for research purposes. Scientists have a very good idea of what HIV is, and they understand it arguably better than any other pathogen known to medical science.

16. The existence of HIV has not been demonstrated by electron microscopy (p.46)

Not only has the existence of HIV been demonstrated by electron microscopy (HIV virions may be viewed in this [sample EM and reconstruction](#)), HIV virions from the cells of an AIDS patient were visualized by electron microscopy in 1983 by A. Karpas [140], even before the causative role of the virus was known and long before it was called 'HIV.' The first papers presenting HIV as the cause of AIDS (from Robert Gallo's group) included two with electron micrographs of HIV [141, 142]. Since then, laboratories around the world have generated untold thousands of EM images of the virus. Although HIV is routinely observed by electron microscopy, such observation is not strictly necessary to prove that HIV exists.

17. The similarity of endogenous and exogenous retroviruses by EM distinguishes retroviruses from "ordinary" viruses (p.44)

This is a very strange statement since retroviruses are defined by their use of reverse-transcriptase to create a DNA intermediate from an RNA genome during the replication cycle, not by the putative similar structural features of endogenous and exogenous retroviruses. HIV is a "lentivirus," part of a subset of retroviruses. It has numerous accessory genes in addition to the three major genes whose products are proteolytically cleaved. By EM, mature lentiviruses contain an electron-dense, "cone-shaped" or "candy-corn" core (see [here](#)). Other "C-type" retroviruses have more spherical cores (see [Figure 1](#) from [4] for typical EMs of several virus types). Since the human genome contains no known endogenous lentiviruses [136, 143], it is possible to separate mature HIV virions from HERVs by examining electron micrographs (in the rare cases when the latter are expressed).

18. The mutation rate of HIV is "unprecedented in the history of viruses" (p.55)

19. No virus could mutate as much as HIV is said to do and still survive (p.29)

20. HIV could not possibly develop drug resistances and yet survive (p.29)

HIV's mutation rate is indeed quite high [144], but HIV is by no means the only virus with this characteristic. Most RNA viruses have mutation rates as high as or higher than that of HIV, since RNA-virus-encoded polymerases lack the proofreading activity present in most DNA polymerases. As a result, most RNA viruses experience approximately one mutation for every 10^4 to 10^5 bases transcribed. HIV is no exception.

21. Influenza has a "segmented chromosome (sic)," necessary for recombination (p.29)

22. HIV, lacking the segmented chromosome, cannot recombine, leaving RT error as its only mutation strategy. "HIV...has only approximately nine thousand nucleotides and as such is incapable of mutation by any method other than transcription error" (p.29)

While the influenza virus does have a segmented *genome* (not “chromosome”), HIV, like other retroviruses, is capable of recombination. Retroviral recombination was first described by Peter Vogt (then a colleague of Peter Duesberg) in the early 1970s [145]. Recombination in HIV was proposed soon after the discovery of the virus and was demonstrated several years later [146]. Further publications quickly detailed the biochemistry and genetic consequences of recombination [147-149]. In 1995, recombination was first reported between genetically distant strains of HIV (as opposed to the relatively similar variants of a “quasispecies” [150]).

HIV incorporates two copies of its RNA genome into each infectious viral particle and as such is a diploid (or pseudodiploid) virus. These two copies facilitate recombination. After the HIV virion infects a new host cell, reverse transcription renders the two RNA genomes into one cDNA molecule for eventual insertion into the host genome. The process of reverse transcription includes “strand transfer,” in which the reverse transcription machinery switches from one RNA template to the other. If the two RNA molecules are not identical, this transfer produces recombination.

(In addition, other processes may also introduce mutations. At a very low rate, the integrated provirus will accumulate errors during replication of the host cell’s genome. Host deaminase molecules are capable of hypermutating viral genomic RNA and cDNA during or shortly after reverse transcription. This is usually lethal to the virus, but it remains a formal possibility that sublethal mutation levels could enhance viral diversity and evolution [151, 152].)

The contribution of recombination to retroviral diversity has been studied extensively and is well-understood, especially in the case of HIV. I would not leave my car with a mechanic who had never heard of a serpentine belt, or take my children to a pediatrician who was unaware of the varicella vaccine. Culshaw’s ignorance of recombination is on a similar level, betraying a comparably disturbing apparent lack of elementary knowledge of the virus she claims to have studied for over ten years.

On HIV Proteomics

1. Many “HIV proteins” are not actually HIV proteins at all, including p24, p13, p32, and gp41; “...it is known that neither gp120 nor gp41 are (sic) specific to HIV...” (pp.41,52)

Each of these proteins has a known amino-acid sequence and is translated from RNA of known sequence that is found in HIV particles in the blood of HIV-infected persons. The provenance of each protein is HIV, not another virus or (as Culshaw implies) the human cell.

2. “p80, gp120, and gp160 are all considered to be ‘oligomers’ of gp41—which basically means they consist of the appropriate number of gp41 proteins hooked together” (pp.40-41).

The gp160 protein is translated from an env transcript. It is cleaved by cellular proteases into two fragments, gp120 and gp41. While gp41 is found in gp160, it is not a part of the gp120 from which it is cleaved. In 1989, Pinter et al showed that monomeric gp41 can form dimers, trimers, and tetramers [153] under certain conditions. They did not suggest, as the denialist literature states, that gp160 and gp120 are oligomers of gp41. Subsequent work has confirmed the oligomerization of gp41 [154-156]. However, neither gp120 nor gp160 is an oligomer of gp41. (See reference 44 in [this denialist article](#) for Culshaw’s probable source, which is not cited.)

3. The “oligomer, gp41” is a “component of cellular actin” (pp.41,52)

Since gp41 is of approximately the same mass as actin (42 kD for actin, about 39 kD for unmodified gp41), it could not possibly be a “component” of actin. Nor is gp41 considered by any scientist to be a “component” of any cellular protein. Apart from their roughly similar mass, actin and gp41 have nothing in common and (today, anyway) are not easily confused. The molecular cloning of HIV revealed the genetic sequence of gp41; the actin sequence is also known. They are unambiguously distinct.

Culshaw’s reference to “the envelope protein gp120 and its oligomer (sic), gp41” (p.52) demonstrates that she is not conversant in the terms of molecular biology. If gp120 were composed of gp41 monomers “hooked together,” (and it is not), the large complex would be the “oligomer,” while gp41 would be a “subunit” or a “monomer”—not the converse.

4. “...gp41 is presumed by Luc Montagnier’s group to be cellular actin...” (p.52, see also p.41)

Luc Montagnier’s group speculated in a 1983 paper that an uncharacterized band observed on a radioactive gel could have been actin, a cellular contaminant of their viral preparation. As Montagnier stated in an interview with a denialist publication [157], the protein he observed was not the viral gp41 described by Gallo. The two groups, using different methods, obtained slightly different results; as such, there is no contradiction. Montagnier does not equate gp41 with actin, and subsequent genomic, proteomic, and functional studies have shown conclusively that gp41 is not actin.

5. “p24 is frighteningly common among individuals at no risk of HIV infection” (p.41)

6. p24 cannot be found in numerous AIDS patients (p.41)

p24, too, is a protein uniquely encoded by HIV. It is not encoded in the human genome, or by any other known virus. Even the closest viral relative of HIV-1, SIVcpz, encodes a protein that, while homologous with p24, has a mass of 27 kD, is thus known as p27, and is fairly easily distinguished from p24 on a protein gel or otherwise. The HIV-1 p24 protein can be found only in individuals infected with HIV; it is not found in uninfected people.

Contradiction: Culshaw argues extensively that the identification of multiple antibodies to HIV by specific ELISA or Western blot diagnostic assays does not prove that a patient is HIV+. Yet here, the presence of antibodies that cross-react with p24 proves to her that p24 is found in HIV-negative individuals, despite the absence of p24 RNA or DNA sequences in all HIV-negative individuals.

HIV-negative individuals do not contain HIV p24 or any other HIV protein. Sometimes, antibodies will cross-react with an antigen other than their real target, particularly when the different proteins have similar epitopes of antibody recognition. There are some examples—rare ones—of antibodies to other retroviral gag antigens cross-reacting with HIV-1 p24. This is why a reaction with only a single HIV-1 protein on a Western blot (e.g. with p24 only) is not an unambiguous confirmation of HIV-1 infection. The official diagnosis requires reaction with multiple bands. HIV assays (and assays for other disease agents) are continually being refined to reduce the chances of cross-reactivity.

Culshaw does not cite her source for the lack of p24 in AIDS patients. Extremely low viral replication, made possible, for example, by combination therapy with antiretrovirals, can make p24 detection difficult in some patient samples when older assays are used. However, recently improved, ultra-sensitive p24 antigen assays can be at least as sensitive as PCR-based techniques, able to detect viral proteins even when viral RNA load is quite low [158-161]. (Importantly, these assays are also considerably easier and cheaper to perform than quantitative PCR.) Such tests are likely to detect viral antigens in most or all AIDS patients.

7. gp120, tat, and nef are not “specific” to HIV, but are found in endogenous retroviruses (p.52)

8. These proteins supposedly induce apoptosis; but since HERVs do not cause apoptosis, HIV should not, either (p.52)

HERVs do not induce apoptosis for good reason: they are transcriptionally silent and are not thought to make infectious particles even in the very rare case of HERV transcription, translation, and viral particle formation. Some HERVs do encode potentially functional envelope proteins, but these are only remote relatives of HIV gp160 and its cleavage products ([162] and see [this e-textbook figure](#) for a graphical representation of envelope proteins from numerous viruses). The different sizes and sequences of these proteins distinguish them from HIV proteins.

No HERV has ever been shown to encode a homologue—even a functional (as opposed to sequence) homologue—of Tat or Nef. Although unlikely, it is formally possible that, as retroviruses, some HERVs have as-yet undiscovered proteins that play the accessory roles of Tat or Nef; if these hypothetical proteins do exist, they are sufficiently divergent from HIV Tat and Nef, even at the protein sequence level, to have evaded discovery until now. Culshaw seems to have invented this entire idea (or taken it unreferenced from a piece of denialist literature I have not read); to my knowledge, no such claims are present in the literature, and Culshaw gives no references.

On HIV and Pathogenicity

1. “HIV...is not highly active at any point during final AIDS stages...” (p.86)

HIV often increases to its highest level in the blood during late-stage disease, sometimes surpassing even the high levels of replication during acute infection. (For a graphic representation of virus titer at various stages of disease, see figure 5 from “Pathogenesis of HIV and SIV” in [4].)

2. HIV antibodies are not protective (p.35)

The immune system is apparently incapable of eliminating HIV infection entirely, even with pharmacological aid. This does not mean that anti-HIV antibodies do not protect against HIV. Neutralizing antibodies, for example, can help to limit the spread of HIV within the body and delay disease progression [163-165]. The generation of escape mutants shows that these antibodies exert selection pressures on HIV-1 env.

3. HIV antibodies are supposedly a sign of “imminent doom” (p.35)

No scientist or doctor considers anti-HIV antibodies to spell “imminent doom.” The denialist community simply seems fond of setting up such “straw men.” HIV is a “death sentence” only in the mischaracterizations of authors like Culshaw...or when Culshaw’s anti-treatment advice is followed.

4. No one know how HIV works (pp.3-4)

To the purist, this may be true. No one really understands how an atom works, how the sun works, or how the brain works, either. To the realist, it is somewhat inaccurate. Scientists understand how the HIV virion is assembled and processed. They have learned how it gets inside various cells, sheds its coat, and makes its RNA genome into DNA. Researchers have followed the trip of HIV cDNA into the cell’s nucleus, and its occasional successful insertion into host cell DNA. They understand much about how the virus becomes latent, and how it “reawakens” to make new, infectious virus for another round of replication. They know well some of the ways in which HIV harms the immune system and causes AIDS, and are aware of or have hypothesized others. There is much science does not know, but tremendous strides have been made. The HIV literature from 1985 alone reveals more about HIV and its workings than Culshaw seems to be aware of today. (Culshaw implicitly admits this on p.62: “So how do we know anything about what HIV really does, where it came from, and even what it is?...The answer is: we don’t, anymore than we did back in 1984.”) But does any branch of science stand still for a quarter-century?

5. There is no mechanism for HIV-mediated T-cell death (p.52)

There are many mechanisms for HIV-mediated T-cell death, both direct and indirect. Culshaw seems to assume that if the virus does not directly lyse the cells (as in a classic lytic bacteriophage infection), then it cannot possibly be contributing to cell death. This assumption is wrong.

6. HIV does not kill T-cells directly (p.51)

The direct killing of T-cells by HIV was first reported nearly twenty-five years ago ([141] among many others), and has been demonstrated in many subsequent experiments and papers. However, many other mechanisms for cell death are known.

7. Low CD4 counts are found in healthy individuals as a result of normal fluctuations, so CD4 count is invalid as a diagnostic tool (p.26).

As support, Culshaw refers to a publication from 1992 [166]. In this study, ten distance runners are examined; the authors do not directly address CD4+ T-cell counts. Instead, they report ratios of total T-cells to total lymphocytes, as well as helper/suppressor ratios. The proportions, when depressed, are still within normal range. Again, it appears that Culshaw either has not read this paper, or has read it and willfully misrepresents its conclusions. In any case, CD4 counts below 200 are rarely seen in “healthy” individuals. In a study of 864 HIV-negative Nigerian miners and pregnant women, CD4 counts were found in a reference range of 528 to 1330 cells/microliter, with a mean of 838 cells/microliter [167]; similar results have been obtained in countries around the world.

8. No retrovirus kills cells “outside of the laboratory” (p.53)

Culshaw takes Duesberg at his word that all retroviruses are harmless by nature. They are not. Even the avian viruses (on which Duesberg did some of his early work) kill cells in vivo, promoting anemia, wasting, and other disorders in birds. EIAV, afflicting horses, causes anemia. Feline Immunodeficiency Virus and other mammalian lentiviruses can produce the same sorts of cell death seen in human AIDS. (For an overview and more information, see this [page](#) from [4].)

9. “In laboratory experiments where apoptosis has been demonstrated in HIV-infected cell cultures, apoptosis is detected only after the addition of powerful chemical stimulants called mitogens” 10. But the same cells die in the absence of HIV when these chemicals are added, so HIV does not induce apoptosis (p.52)

Which laboratory experiments? Were they published? Did these investigators fail to use appropriate controls? I.e., did mitogen by itself result in apoptosis? Culshaw provides insufficient information to make her case (and no references).

11. HIV virions are not present in sufficient numbers to cause disease (pp.19,54)

12. Very little HIV is found in the blood of AIDS patients (p.19)

These false claims were originally popularized by Peter Duesberg and repeated by Alexander Russell, Christine Johnson, David Rasnick, and other denialists. Culshaw presents no reason for why a virus present at these levels should not be pathogenic. She further ignores the phenomenon of cell-to-cell virus spread, which is not reflected in plasma TCID levels and is much more efficient than infection by free virus. Importantly, the numbers given here are inaccurate. When viral replication is effectively suppressed, infectious particles might not be culturable at all. In the absence of suppression, the number of viral infectious particles per milliliter might vary greatly; one early paper found anywhere from 10 to 10 million infectious particles per milliliter [168] in patient samples. Culshaw’s misunderstanding of viral

load vs. infectivity was discussed above (“HIV tests,” point 11). Besides, much HIV-mediated immune system destruction occurs in the lymphoid tissues, e.g. the gut-associated lymphoid tissue (GALT—see [169, 170] and this IAVI [report](#), also linked from [AIDSTruth](#)).

13. Only one in 10,000 CD4+ T-cells is infected with HIV (p.53)

14. Lymph node infection is also low (p.19)

One in 10,000 represents the extreme lower bound of available measurements or estimates for one bodily compartment, the peripheral blood. Peter Duesberg quotes the literature selectively to give this figure, and Culshaw, as elsewhere, repeats after him without citation. The proportion of CD4 cells infected varies during the course of infection, from patient to patient, and by compartment. Recent findings suggest that the peripheral blood may not necessarily indicate the extent of cell death in the rest of the body [169]. In some compartments, such as in the GALT, but also in the peripheral blood by some accounts, the *majority* of CD4 cells may be infected and even killed early in lentiviral infection [171, 172]. (See also this early paper on lymph nodes [173].)

On the Adaptive Immune System

1. “The subset of CD4+ (‘helper’) T-cells” consists of two subpopulations (p.33)

Culshaw’s insistence that CD4+ T-helper cells are divided into two distinct camps is an oversimplification: **there are at least three types and probably several more.** According to Culshaw, CD4+ cells are either Th1 or Th2. In fact, Th0 precursors (which give rise to both Th1 and Th2 types) also exist and exhibit a cytokine secretion profile that overlaps those of Th1 and Th2. Th0 cells have been studied for two decades. Even if Th0 cells are excluded as precursors from consideration, several additional subtypes have been classified. Th3 “suppressors” are well-established; Th17 cells (sharing some characteristics of Th1) have been demonstrated, and it appears that Th25 helpers also exist [174].

Nor are these distinctions necessarily absolute. Th1 and Th2 have been described as two ends of a cytokine-secretion “spectrum.” And cells that are not terminally differentiated may even “revert.” Recent work from Lena al-Harhi’s group, for example, demonstrates that some Th2 cells may assume a Th0 phenotype upon HIV infection [175].

It is likely that further subpopulations of T helper cells will be characterized as the scientific understanding of helper T-cells expands with continuing research. The review article Culshaw cites as the source of her information on T helper cells [176] predicts in its introduction (in 1989), “Further divisions of helper T cells may have to be recognized before a complete picture of helper T-cell function can be obtained.” It is unclear why Culshaw would ignore 18 years of progress in the rapidly moving field of human immunology.

2. Th1 cells lend help against intracellular pathogens, such as “fungi and yeasts (sic)” (p.33) Th2 cells stimulate antibody productions and are effectors against bacterial infection (p.33)

Culshaw’s assignment of functions is simplistic and symptomatic of her apparent unfamiliarity with immunology. The authors of the review Culshaw gives as her source on this subject specifically caution against this oversimplification [176]. Both Th1 and Th2 cytokines stimulate production of antibodies (not just Th2, as Culshaw claims). Th1 responses can act against bacteria, not just “fungi and yeasts (sic)” (p.33). (Incidentally, yeasts *are* fungi, so this last phrase is akin to “My two favorite animals are dogs and poodles.”) Th2 cells were originally characterized not for their anti-bacterial actions, but for their involvement in defense against multicellular parasites (such as the helminths). In any case, while Culshaw denies a Th2 role, Th2 responses are involved along with Th1 in the immune defense against AIDS-defining pathogens such as *Pneumocystis*. (See table 8.1 of [177] and accompanying text for accurate information about Th1 and -2 cells and their actions.)

3. Th1 cells circulate in the blood, while Th2 cells “remain in the bone marrow and the lymph nodes,” (p.33)

Culshaw gives no references to support this incorrect statement. In just one of many examples contradicting Culshaw’s proposed physical separation of Th1 and Th2 cells, Klein, et al [178], demonstrate that Th2-cytokine producing CD4+ T-cells are indeed present in the blood. The 1989 Mosmann and Coffman review [176] that Culshaw uses as her major reference on this topic cautions that

the Th1 and Th2 profiles observed in mouse cell culture do not necessarily correspond to previous categories of T-cells that were distinguished by tissue compartmentalization.

4. A Th1-Th2 shift occurs during the course of HIV infection (p.33)

On the whole, it appears that an increasing bias towards a Th2-like response (i.e. elevated ratio of cytokines secreted by Th2 over those associated with Th1) occurs during progression to AIDS, while long-term non-progressing patients retain relatively higher Th1 function; however, numerous studies have disputed the extent of this bias. If a Th1-Th2 “shift” occurs, it is likely to involve changes in the Th1 and Th2 subpopulations, but the *extent* to which this is true remains under investigation. Molecular markers for Th1 and Th2 cells exist and are now used experimentally, but much of the Th1/Th2 literature has measured Th1 and Th2 responses mainly by assaying levels of secreted factors. Since these factors can also be made by other cells (including CD4- T-cells and populations other than T-cells) in vivo, such results should be (and usually are) interpreted with caution when direct measurement of Th1/Th2 *cells* is absent. Note that neither of the references given by Culshaw in this section supports the Th1-Th2 shift hypothesis.

5. HIV infects only Th2 cells, not Th1 cells (p.33)

In the paper Culshaw cites as evidence [179] for this claim, HIV preferentially replicates in vitro in clonal cell populations that, upon chemical stimulation, produce cytokines characteristic of Th2 and Th0 (precursors of both Th1 and Th2) cells. The authors determine the extent of HIV-1 replication by measurements of the viral p24 protein (not multiple “markers,” as Culshaw writes). It is important to note that Maggi et al do not claim that Th1 cells are not infected in vivo, nor that they cannot be infected productively. This unsupported claim is Culshaw’s alone (unless it has been made in an uncited, non-peer-reviewed source).

Contrary to Culshaw’s claim that the virus does not infect cells that purportedly increase during disease progression (Th2 cells—p.33), **HIV does infect Th1-cytokine-producing cells**, but apparently unproductively, in the culture system used by Maggi et al. The authors suggest that interferon gamma or another soluble factor (in the absence of Th2 cytokines) may suppress HIV replication in vitro in these Th1 cells. A follow-up letter [180] from a different group proposes that the lack of IL-4 and/or other Th2 cytokines may be solely responsible. Another influencing factor is the infection protocol used (see [181] for details), consisting of coculture with PBMCs from infected patients (or uninfected controls). The tropism of the source virus(es) could determine the subset(s) of cells infected. It has been shown that CCR5-tropic (R5) virus replicates in all three broadly-defined helper cell populations, while dual-tropic R5X4 virus prefers Th0 and Th2 [182]. An article published four years after the Maggi et al paper suggests that the X4 virus HIV-1/IIIB replicates with comparable efficiency in Th1, -2, and -0 populations [183].

6. Th1 cells would not die unless HIV infected them (p.33)

As we have seen, HIV can infect Th1 cells. Of course, HIV can also kill uninfected cells by inducing apoptosis or by indirect effects involving immune activation.

Notes on Culshaw's selective use of the literature on T helper cells

Culshaw presents the 1989 review and the Maggi et al article [179] as her only references for an entire page of false or misleading statements about T helper cells. Referring to the discovery of Th1 and Th2 cells “in the late 1980s” she cites the 1989 review, not, as is customary, the original research from 1986 (also by Mosmann and Coffman). In her text (twice) and in the references, Culshaw consistently misspells the name of Dr. Mosmann as “Mossman.” She makes the same mistake in her 2006 JPANDS article.

Culshaw does not acknowledge (and may not know) that a stark Th1/Th2 dichotomy is not only controversial, but was not claimed even by Mosmann and Coffman, or that vigorous debate has characterized this issue for at least the past 10 years. While Dr. Culshaw is quick to highlight healthy HIV-related debate in the scientific community as evidence that a hypothesis she dislikes has been “discredited” and is a “failure” (see her treatment of the sister Nature papers of Ho et al and Wei et al from 1995), Dr. Culshaw fails to mention the diversity of opinion on hypotheses on which she relies (albeit through the distorting lens of her own apparent scientific misunderstandings) to make her points. Citing Maggi et al and not the various papers with differing results constitutes selective quoting: those papers that Culshaw erroneously assumes to support her intended position are used and others are ignored. For example, the results of Graziosi et al [184] diverge from those of Maggi and do not support Culshaw's position at all; does Culshaw simply ignore this important paper and others like it? Of course, it is also quite possible that Culshaw is not aware of the scientific debate concerning T helper cells, as most or all of her knowledge of this subject—as presented in her book—seems to derive at best from superficial readings of two papers, and perhaps just their abstracts. (Culshaw seems to have taken her ideas on immunology from Heinrich Kremer and his promoter/translator David Lowenfels; see these [examples](#).)

(I also find interesting that Culshaw attempts to nitpick the minutiae of how HIV replicates in T-cell subsets in vitro, under specific culture conditions, when elsewhere in her book she doubts that HIV even exists as “a unique virus.”)

On the Early History of HIV/AIDS Research

1. “The first five men with AIDS were patients of Michael Gottlieb...” (pp.23,59).

This is a common misconception amongst individuals whose knowledge of HIV and AIDS is derived mainly from popular media reports. The first victims of AIDS are—and will always remain—unknown. Their deaths went unreported. We will never know with certainty who they were, or when or where they died. Gottlieb’s patients were not the first AIDS victims, not even in the United States; their cases *were*, however, the first to be recognized and published in the CDC’s *Morbidity and Mortality Weekly Report (MMWR)*.

2. Dr. Gottlieb first concocted a “syndrome,” then searched far and wide for patients to fill the bill (p.23)

3. The syndrome was a “clever idea” since it could include anything (p.24)

4. T-cell counting was included by Gottlieb because it had recently been invented, not because it was relevant

“It remains a matter largely hidden from the public that the first cases of AIDS did not suddenly arrive all at once, but rather were sought out by...Michael Gottlieb in 1981. After searching hospitals...for gay men suffering from opportunistic infections, he managed to find five (Brown 2001).” Then: “What is quite curious about this discovery is that the technology to count T-cells had only just been perfected” (p.23; the latter comment is expanded on p.59).

Culshaw’s language (“hidden,” “were sought out,” “searching hospitals,” “he managed to find,” “quite curious,” “clever idea”) seems to be meant to convey the impression that Michael Gottlieb invented a syndrome with characteristics that could be diagnosed only with the use of new technology...then searched for patients to pin it on. This is a scurrilous, baseless, and potentially libelous accusation, as Culshaw would know had she carefully read the Washington Post article she references [185] as her source. Gottlieb was looking not for gay men with opportunistic infections, but rather for *any* unusual cases that would be valuable for the training of his students and interns. To quote from the article, “one day in January 1981, he asked the immunologist-in-training to prowl the wards for ‘teaching cases.’” (Of course, Culshaw does not seem to be in the consistent habit of reading her given source material and has rewritten her statements here, including the accusations of impropriety, from Peter Duesberg—once again without referencing them; see [11], pp.146-148.)

Reporter David Brown continues, “In spring 1981, AIDS was waiting to be found. If Michael Gottlieb and several other Los Angeles doctors -- principally Joel Weisman and Wayne X. Shandera -- hadn't described unusual infections in gay men, someone somewhere would have within weeks.” Indeed, multiple cases were reported from New York City very soon afterwards.

As for “technology to count T-cells,” why is this “curious”? And what does “just been perfected” mean in terms of time frame? The Fluorescence Activated Cell Sorter was invented by Leonard Herzenberg and colleagues in the late 1960s [186]. T-cell “counting” had been possible for quite some time. Analysis of specific T-cell subsets had been going on since the mid-1970s. What is now known as the CD4 molecule had been used in analysis for several years by 1981. Yet AIDS would have been recognized, and HIV discovered, even if T-cell counting had not been possible. It is “curious” only that Culshaw insists on seeing nefarious processes at work here.

5. “The first five men with [described] AIDS were not sexually involved with one another, so why was a sexually transmitted cause considered to be so likely?” (p.61).

6. Alternative hypotheses for AIDS were ignored (p.19)

7. Sexual transmission of HIV was “simply assumed” (p.61)

Sexual transmission was not at first assumed, indeed quite the contrary. Many potential causes were considered, including all of the various lifestyle, chemical, or environmental stressors that HIV/AIDS denialists such as Peter Duesberg would resurrect much later despite the strong arguments that had been built against them. There was the umbrella “multifactorial hypothesis” [187-189]; the “poppers” hypothesis [190]; the corticosteroid hypothesis [191]; “antigenic overload;” rectal exposure to semen [192, 193]; CMV, EBV, and other herpesviruses, singly or in combination [194-196]; even swine fever [197]. (M. Grmek examines this history in detail in his monograph *History of AIDS* [198].) As the evidence accumulated, it became apparent that almost all of the early AIDS patients may have contracted a disease-causing agent sexually, and that many of them had previously had sexual contact with other AIDS patients, including before the onset of symptoms. Extensive sexual networks were traced, criss-crossing the United States and concentrated on New York, Los Angeles, and San Francisco. A previously unknown sexually- (and blood-) transmitted agent rapidly established itself as the only plausible explanation for AIDS.

8. Sexual transmission “was arrived at not by the traditional method of proving an infection is indeed an STI, which involves microbial isolation and contact tracing, but rather by simply assuming sexual transmission” (p.61).

HIV’s sexual transmission has been demonstrated by both isolation and contact tracing. HIV has been isolated from patients by multiple methods. Its genome has been cloned thousands of times. Genomic methods have revealed shared sequences in viruses cloned from sexual partners or those who contracted the virus in the same location [199-201]; this technique has allowed scientists to trace the spread of particular variants of HIV.

Before these molecular methods were available, “old-fashioned” contact tracing was performed all over the world. Sexual networks were traced throughout North America. Outbreaks in Europe were traced to individuals who had visited California or New York in previous months or years.

In the Soviet Union, the relatively unfettered power of the government allowed compulsory, not just voluntary, tracing. A homosexual Soviet citizen (‘Citizen K’), stationed in Africa for some time, was the USSR’s “patient zero.” The authorities traced sexual contacts he had back home in Russia: he had cultivated relationships with 22 bisexual men between 18 and 22 years of age. Five of them became infected with HIV. These five had had on average five heterosexual contacts each, and these, too, were followed. One of the five HIV+ men infected one woman; a second man infected two women; one of these women gave birth, transmitting the infection to her child; one man also donated blood that was used for six transfusions; five of the transfused patients became HIV positive. (For more on this and other instances of contact tracing, see [198].) Isolation and contact tracing, performed all over the world in the years following the discovery of AIDS, can hardly be characterized as “simple assumption.”

9. “...the announcement of the discovery of the causative agent of AIDS—via press conference, no less—was immediately accepted by scientists and citizens alike before any supporting evidence had been published or critiqued in the scientific literature” (p.8).

The press conference was held on April 24, 1984. A cursory check of the biomedical literature reveals numerous peer-reviewed, data-containing papers that were published prior to this announcement and that addressed various aspects of AIDS causation and of the virus that was eventually proven to cause AIDS. Of course, these early, pre- or early-1984 papers did not constitute “proof;” but they were certainly “supporting evidence.” In addition, a bevy of papers was published within two weeks of the press conference [141, 142, 202, 203] and many more soon after; these papers had indeed been discussed in the scientific peer review process.

Since the public has a natural interest in medical issues—and also helps to fund research—it is only appropriate that its members be kept abreast of major events in the biomedical community. AIDS was a well-known phenomenon and a source of much anxiety in 1984. Then-Secretary of Health and Human Services Margaret Heckler chose to call a press conference to assure the public that answers were available and more were on the way...as indeed they were. Does Culshaw perhaps think that members of the public should not be informed of research they support, that progress in fighting disease should be kept under wraps, or that scientific findings should be suppressed until every mechanistic detail of every biological process is understood? In a news environment where sensationalism and celebrity rule the day, we should have more news conferences on science and medicine, not fewer. In my opinion, Heckler’s initiative was a step in the right direction.

10. “By the time the supporting papers were published, the lay press had all but declared HIV to be “the AIDS virus,” and debate in the scientific arena was effectively stopped” (p.19).

The continuing scientific debate after the press conference is exemplified by the title of this paper from 1985: “The cause of acquired immunodeficiency syndrome--is it known?” [204]. Competing hypotheses of AIDS pathogenesis were entertained long after 1984. The scientific literature on HIV and AIDS has always been replete with healthy disagreements and alternative hypotheses; debate was never “effectively stopped.” On the issue of HIV’s pathogenicity, however, most scientists were convinced by the evidence published between the discovery of AIDS and the flood of papers addressing causation in 1984 and 1985. Still, the scientific community has tolerated dissent. Numerous individuals have published their opinions on “co-factors,” which they claim are necessary—in addition to HIV infection—for progression to AIDS. Leading dissident Peter Duesberg has published over 30 articles or letters on HIV/AIDS in peer-reviewed journals since 1987, although his contributions, considering the lies and misrepresentations we have seen, can no longer be seen as contributing to real debate. Culshaw’s characterization underscores nothing more than her own apparent unfamiliarity with the HIV literature.

On a final note to this section, Culshaw follows other HIV/AIDS denialists in finding fault with early HIV/AIDS research because arguments for the causation of disease did not include comprehensive descriptions of pathogenesis mechanisms. This criticism is unfair and unprecedented: the details of pathogenesis are not needed to establish causation. Biomedical science has achieved this level of complete understanding of pathogenesis for few infectious diseases. Although much has been learned about the pathogenesis of AIDS (and of many diseases), much remains to be discovered; through it all, however, the causal link between HIV and AIDS is not in doubt.

On Legal Issues Involving HIV

1. “Every state in the U.S. and every province in Canada maintain (sic) a list of ‘HIV carriers’ in that region”...these lists are used to discriminate and violate human rights (p.49).

On its own, the first part of this statement is partly correct; unfortunately, context matters, and Culshaw says that reporting HIV infection to public health authorities is a “violation in human rights,” implying that this information somehow becomes publicly available. It does not. Without giving any evidence, Culshaw says that surveillance of HIV leads to career termination, denial of insurance, a “death sentence,” and a revocation of hope.

As with other reportable infectious diseases, cases of confirmed HIV infection are not reported to the public. HIV positive status is reportable via a **confidential**, name-based system in many *but not all* US states—38 as of this [CDC report](#) [88] and 45 today [205]—and by coded identifiers or “mixed” systems in several more states. (As stated in the Summary, Culshaw possibly is once again confusing HIV and AIDS in this statement, since AIDS diagnosis is directly reportable in all states in the US.) As with other diseases, these data are reported for surveillance and disease control purposes *only*, and strict safeguards protect them. Culshaw repeatedly accuses the “AIDS establishment” of spreading terror; it is she who engages in fear-mongering here.

2-6. “Women are encouraged to abort their babies...they are forced to take antiretroviral drugs, and these drugs are forced on their babies as well. The babies themselves must be born by Cesarean section, and in many states the highly beneficial practice of breastfeeding is illegal” (p.49).

No references are given to support these truly outrageous claims. Some doctors may encourage abortion when a mother is HIV+. For that matter, some doctors advise women to terminate pregnancy when the mother is over the age of 40. Some unethical individuals may even try to coerce pregnant women to submit to certain procedures. However, none of this is a matter of public policy. No woman is legally obligated to follow such advice.

I have found no reports that HIV+ pregnant women have been *forced* to take any medication or constrained to undergo C-section against their wishes in order to limit the likelihood of Mother to Child Transmission (MTCT). Advised, encouraged, yes, but legally *forced*, no. The legal system in the United States has repeatedly upheld the right of competent individuals to make their own medical decisions. Starting with *Roe*, it has also placed the mother’s rights above those of the fetus. Numerous landmark cases in the US in the 1980s involved court-ordered Caesarean sections, although HIV was apparently not a factor in any of these cases [206]. Courts have consistently ruled against such interventions. If Culshaw has evidence to the contrary, she should present it; the United States judiciary, including the Supreme Court, would probably be interested in hearing the case.

As for the “practice of breastfeeding,” whether beneficial or not, it has not been banned in a single state, much less in “many.” Children who escape perinatal HIV infection may have a higher risk of HIV infection if their HIV+ mothers breastfeed them. There is one reported case (from 1999, see [CNN](#) and [HERE](#)) in which health authorities in Oregon, after being alerted by the doctor of an HIV-positive pregnant woman, won a legal custody case mandating feeding by bottle; the parents retained physical custody of the child during and after the legal proceedings. In *one* state and *one* legal case, *one* woman

was ordered to feed her child by bottle. It is not clear why Culshaw sees the need to exaggerate this single case into “many states” making breastfeeding “illegal.”

7. HIV-positive children are forced to take antiretrovirals against their wishes and/or the parents' wishes (p.30)

Again, Culshaw gives no examples or citations to support her claims. Courts are generally unsympathetic towards forced prenatal interventions. After birth, there is some precedent for intervening on behalf of a child's health. However, custody cases in which HAART is the only issue (i.e. the mother is not a drug addict and abuse is not alleged) are sufficiently rare that they usually attract national media attention. Valerie Emerson's story is a good example (see a 1998 New York Times story [HERE](#)). In September of 1998, Ms. Emerson successfully won the right to withhold drug treatment from her son, the younger of two HIV+ children (a third had already died of AIDS-defining PCP). All decisions to impose treatment against parents' wishes are made on a case-by-case basis. By using vague and sensationalist language, Culshaw conjures a pervasive, treatment-imposing legal machine that does not square with the complex reality, a reality that more often than not upholds parents' rights over public health and children's health concerns.

Miscellaneous

1. Most people who deny that HIV causes AIDS are “credentialed doctors and scientists” (p.12)

One of two widely-circulated HIV/AIDS denialist internet petitions currently includes almost 2500 signatories. “Most” of these individuals are not credentialed doctors or scientists. This “denial-list” is often presented by HIV/AIDS denialists as a counter to the Durban Declaration [207], signed by over 5,000 scientists and medical doctors in the year 2000 in response to South African President Thabo Mbeki’s questionable statements and actions regarding HIV and AIDS. Unlike the Durban Declaration, the denial-list may be signed by anyone. The Durban Declaration may be signed only by MDs or PhD-level scientists. While the Durban Declaration has verification procedures in place, the denial-list does not verify that signers actually exist or have not exaggerated their credentials.

I looked at the “rethinkingaids” petition (see [here](#) or [here](#)) to assess Culshaw’s claim. Of the 300 or so names beginning with ‘A’ or ‘B,’ only about 16% even *claim* to have MDs or PhDs in biomedical science...a far cry from Culshaw’s “most.” Even including those signatories with PhDs in the physical sciences fails to boost the percentage to 25%. The list includes many journalists, authors, lawyers, students, and alternative medicine practitioners, but few “credentialed doctors and scientists.” Few if any of the scientists on this list have ever worked with HIV in the laboratory; to my knowledge, none does so today. Most tellingly, many of the professionals and more prominent individuals include statements with their names, putting their position more in line with that of the scientific community. I have been told that at least one signatory later publicly renounced his doubts after learning more about HIV and AIDS...but his name remains on the list, as do those of signatories who, tragically, have since died of the disease they denied.

I point this out to show that Culshaw did not analyze the list properly if at all, or did not perform her calculations correctly: problems found, unfortunately, throughout her book. The truth about HIV and AIDS, of course, does not depend upon how many people recognize it or what their graduate degrees may be. In the numbers game, the most we can say is that tens of thousands of inherently skeptical people with high levels of training in science and medicine, many of whom work with HIV every day, are convinced of the basic validity of HIV/AIDS science, while only a small minority of those who question its validity have similar training, and few if any have hands-on experience with HIV and AIDS.

2. The CDC speaks through Oprah Winfrey (pp.4,7)

Culshaw states this in all seriousness. Oprah Winfrey, according to Culshaw, once made an alarming and (it turns out) rather pessimistic prediction about AIDS in the US, although Culshaw does not give enough information to allow us to verify this quote. Through Culshaw’s looking-glass, if Oprah Winfrey was wrong about an aspect of the HIV/AIDS epidemic, then the CDC is also wrong, Oprah Winfrey must work for the CDC, and HIV/AIDS is a hoax.

3. Yeasts are separate from fungi (p.33)

As noted above, just as poodles are dogs, yeasts are a subset of fungi.

4. “(O)ther viruses (cytomegalovirus and herpes virus [sic], to give just two examples) were far more prevalent in AIDS patients than HIV ever was...” (p.63).

Cytomegalovirus (CMV) is one of many herpesviruses; there is no single “herpes virus.” Without evident knowledge of virology, Culshaw has most likely relied on previous denialist literature in writing this unsupported statement. The biomedical literature shows that CMV and Epstein-Barr virus (EBV, another member of the herpesvirus family) were considered as potential causes of AIDS in the early 1980s (both separately and in tandem), but study results did not support further consideration of these hypotheses. Both of these viruses (and other herpesviruses) are found in many individuals who experience no immune suppression; unlike HIV, neither is necessary or sufficient for the development of AIDS.

Inconsistencies and inaccurate use of terms

- “With the WB, the proteins are separated out according to their molecular weight...” (p.40). But HIV, according to Culshaw, has never been isolated. If the virus has not been isolated, if in “fact” no one knows “what HIV really is,” (p.5), where do these proteins come from?
- Culshaw accuses medical professionals of coercion. She states that individuals are pressured to take drugs without being informed of side effects. Yet in the same paragraph, turning to HIV-infected children, Culshaw laments, “At least adults have the opportunity to decline such medicine and are capable of gathering sufficient information to make an informed decision...” (p.30).
- Culshaw suggests that any refutation of Peter Duesberg’s denialist arguments is invalid unless it occurs *following* his publications (most of the proof he is wrong existed in the early 1980s, before Duesberg went public with his doubts) *and* is published in the peer-reviewed literature. Astoundingly, in the same sentence, Culshaw states that the “anonymously authored” refutations of Duesberg “have been thoroughly rebutted themselves”...referencing *two non-peer-reviewed essays* from a denialist website. Culshaw’s logic here is as hard to understand.
- Culshaw refers to “AIDS drugs” and “AIDS tests” (p.3, etc.) instead of “antiretrovirals” and “HIV tests,” although, elsewhere, she finds fault with the media for conflating HIV and AIDS.
- Culshaw claims that testing positive for HIV+ is, according to the scientific and medical “orthodoxy,” a “death sentence,” (49), a proclamation of “imminent death” (pp.35 and 46). From other denialists, Culshaw borrows “HIV=AIDS=DEATH” (p.62) and “HIV=DEATH” (p.67)—interestingly, two of the only equations in this math professor’s book. Culshaw writes that “an AIDS patient (whatever that means) can never recover, *by definition*” (p.63), and that “every other disease...is accompanied by some hope of recovery—not so with AIDS.” AIDS patients, according to her, are not “allowed” (p. 49) to recover. Yet in the book’s only quote in which a “mainstream” scientist addresses this issue (p.67), Luc Montagnier actually argues *against* the “HIV=DEATH hypothesis.”

The position that HIV must necessarily lead rapidly to death is held by few (if any) scientists and doctors. The use of antiretrovirals has prolonged the lives of perhaps hundreds of thousands of AIDS patients worldwide. *Untreated and unmonitored*, HIV will result in AIDS (and, eventually, death) in *most* (but perhaps not all) infected persons. But with proper and careful treatment, especially since the advent of combination antiretroviral therapy in the 1990s, many HIV positive individuals and even former AIDS patients can live full and relatively healthy lives. For most North Americans who submit to standard medical care, HIV is by no means a “death sentence.” By claiming otherwise, Culshaw attempts to characterize her chosen opponents as members of a “death cult” (p.62).

- Culshaw criticizes the use of “denialist” to describe a person who is in denial about the existence of HIV, AIDS, or the contribution of HIV to AIDS, yet she variously refers to scientists as “vultures,” (p.65); “[those who wish to keep] people supportive of AIDS,” (p.3; what can it mean to be “supportive of AIDS?”); originators of “an epidemic of low standards that is infecting all of academic scientific research,” (p.14); the “orthodox” or “orthodoxy” (pp.17, 18, 26, 27, 60, 62),

and “zealous,” (p.60); “politically motivated,” (pp.18, 25); practitioners of “circular logic,” (pp.20, 38,) who rise to a “ridiculous level of illogic,” (p.54), are “intellectually bankrupt,” (pp.60, 61), and remain unconcerned about “all questions of causation,” (p.60); supporters of “patently inept research,” (p.21); people who need “to wake up,” (p.22); perpetrators of “disastrous clinical trials” and “fraud,” (p.27); reliant on “pure faith,” (p.27); spouters of “official dogma,” (p.29); “treatment activists” who abuse children (p.30); slaves of fashion (pp.33, 52); “sinister forces” and obscurantists (p.34) who invent “farcical concept(s)” to cover up their failures (p.54) and rely solely on *ad hominem* attacks in response to criticism (p.60); inhumane (p.45); facilitators of “discrimination,” (pp.36, 49, 62, 63, 69), “weapons of terror” and “medical terrorism,” (p.48); profiteers of a “massive industry,” conducting a “campaign of psychological terror,” (p.60; see also p.70); motivated by “racism and homophobia” and a need to support the “rights that Caucasians and heterosexuals have enjoyed since time immemorial,” (p.61); bereft of “hard evidence,” (p.61); “medical” and “psychosocial” criminals as well as “death-cult” members (p.62); “the scientific ruling majority,” (p.68); people who make “slandorous accusations” but respond to debate “by quite literally running away,” (p.68); a “moral majority in-crowd,” (p.69); moral absolutists, pious moralists, and suppressors of argument (p.69); creators of a substitute religion (pp.69-70); “HIV promoters,” (p.86). Culshaw says that “the ‘scientific community’” is “emotionally attached to the idea of an HIV/AIDS pandemic,” and its members are “the high priests,” (p.70) of an “AIDS establishment” (p.69 and elsewhere).

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