

SOME OBSERVATIONS ON HIV/AIDS EPIDEMIOLOGY

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The mighty wall, atop which sits what I and a few other “insurgents” call the Humpty Dumpty of all biomedical hypotheses, was made from two kinds of bricks — fashioned from the stuff of virology and epidemiology, and held by what we contend is scientific cement of the most dangerously thin consistency. — Harvey Bialy

Epidemiology is like a bikini: What is revealed is interesting; what is concealed is crucial. — Peter Duesberg

We thought that we had the answers; It was the questions we had wrong. — U2, “11 O’Clock Tick Tock”

It’s no secret that the strongest evidence, if not the only evidence, in favor of the HIV hypothesis is epidemiological.

In his 1991 book *Virus Hunting*, Robert Gallo gave 7 reasons why he and his group of researchers in early 1984 concluded “HIV is the sole primary cause of the epidemic called AIDS” (1). All but one (#6) of Gallo’s 7 reasons are based purely on epidemiology and correlations:

1. “Finding of a new virus in AIDS patients...”
2. “The virus was also found in...’pre-AIDS cases’ and [in groups] at high risk...but only rarely in healthy heterosexuals...”
3. “[HIV] was a new...virus. AIDS as an epidemic was clearly new.”
4. “Wherever the HIV was found, AIDS was present...Conversely, no HIV — no AIDS.”
5. “Studies of blood donors showed...[a] perfect correlation.”
6. “The virus infected T4 lymphocytes.”
7. “We commonly found HIV in the brains of people who had died of AIDS.”

When challenged by Peter Duesberg in the pages of *Science* in 1988, William Blattner, Robert Gallo, and Howard Temin flatly admitted, “The strongest evidence that HIV causes AIDS comes from prospective epidemiological studies that document the absolute requirement for HIV infection for the development of AIDS.” (2) Note that this quote was made a full four years after HIV was announced as the cause of AIDS.

“The Evidence That HIV Causes AIDS”, an anonymous document produced by the National Institutes of Health, relies almost entirely on epidemiological arguments (3). The only direct claim of virologic evidence is the following vague plea:

CD4+ T cell dysfunction and depletion are hallmarks of HIV disease. The recognition that HIV infects and destroys CD4+ T cells in vitro strongly suggests a direct link between HIV infection, CD4+ T cell depletion, and development of AIDS. A variety of mechanisms, both directly and indirectly related to HIV infection of CD4+ T cells, are likely responsible for the defects in CD4+ T cell function observed in HIV-infected people. Not only can HIV enter and kill CD4+ T cells directly, but several HIV gene products may interfere with the function of uninfected cells.

Recent investigators have not been as sanguine about our knowledge of HIV's pathogenic mechanisms:

We still do not know how, *in vivo*, the virus destroys CD4+ T cells... Several hypotheses have been proposed to explain the loss of CD4+ T cells, some of which seem to be diametrically opposed. (4)

Despite considerable advances in HIV science in the past 20 years, the reason why HIV-1 infection is pathogenic is still debated... There is a general misconception that more is known about HIV-1 than about any other virus and that all of the important issues regarding HIV-1 biology and pathogenesis have been resolved. On the contrary, what we know represents only a thin veneer on the surface of what needs to be known. (5)

Twenty-five years into the HIV epidemic, a complete understanding of what drives the decay of CD4 cells — the essential event of HIV disease — is still lacking... The puzzle of HIV pathogenesis keeps getting more pieces added to it. (6)

It is thus necessary to confront epidemiological arguments directly. One immediately faces a problem — all the evidence is presented in the context of a web of assumptions concerning the ontological status of HIV and the meaning of antibody, viral load and lymphocyte count tests. Consequently, this web of assumptions itself frames epidemiological data collection and questions.

For example, it is now impossible to answer, "What is the distribution of AIDS-indicator diseases among different risk groups?" because the data needed to answer this question are no longer routinely tallied. Similarly, it is impossible to answer, "What is the relationship between specific protein band patterns on the Western blot test and HIV/AIDS demographics?" because data on such patterns are not routinely tallied, let alone related to other demographic data.

The philosopher of science Paul Feyerabend posited that sometimes the only way to demonstrate the irreparable inadequacy of a theory is to collect and interpret data within the context of a completely incompatible set of assumptions regarding the most fundamental ontological and epistemological issues (7). My own opinion is that this is the current case with regard to HIV — the hypothesis will never be rejected until a comprehensive, substantial theory giving a positive explanation for the data gains widespread acceptance. (See footnote 1.)

Nevertheless, some of the epidemiological arguments put forward in favor of HIV can be dismissed by a few thought exercises. Here, I want to address what is perhaps the most common epidemiological argument one hears: "The drugs are working. Death rates have fallen. People are living longer." (See footnote 2.)

First it should be noted that epidemiological evidence by its very nature is indirect and weak, particularly when evaluating drug therapies. Epidemiology establishes associations which require additional criteria to be met to demonstrate causation (8). It is strongest when combined with other forms of evidence. In this case, the form of evidence is that much weaker, since it is not based on the proposed pathogen itself but on therapies given. One has to be especially vigilant of not committing the classic post hoc fallacy: B follows A; therefore, A causes B.

I expounded much the same argument in my previous article, "AIDS Case Fatality Rates" (9), and here I want to extrapolate my observations to a few hypothetical thought experiments, in order to expose the essence of the faulty logic.

Consider the following hypothetical disease, for which I will give the incidence for each calendar year, and deaths/survival for those year-specific cases. In Table 1, "INC" means annual incidence, the total number of cases diagnosed that year, "D n " means the total number of deaths occurring in year n out of all cases diagnosed that year, and "D15+" means the total number of AIDS patients remaining alive at the end of year 15 out of all cases diagnosed that year. I am also assuming, without loss of generality, that all diagnoses occur on 1 January.

TABLE 1
Incidence and Death
Due to a Hypothetical Disease

YEAR	INC	D1	D2	D3	D4	D5	D6	D7	D8	D9	D10	D11	D12	D13	D14	D15	D15+
1	100	70	30														
2	200		180	20													
3	500			400	50	50											
4	1000				800	100	100										
5	2000					1400	400	100	100								
6	5000						3000	1000	500	500							
7	10000							5000	1500	1500	1000	1000					
8	15000								8000	2000	1500	1000	1000	500	100	100	800
9	10000									4000	500	300	200	200	200	100	4500
10	8000										2000	1000	500	300	150	50	4000
11	6000											1000	500	250	150	100	4000
12	5000												500	300	150	50	4000
13	5000													750	500	250	3500
14	5000														500	200	4300
15	5000															500	4500

Suppose that two therapies are given for our hypothetical disease: Therapy X, which is introduced and available to all on 1 January of year 6; and Therapy Y, which is introduced and available to all on 1 January of year 9.

First let's look at the annual mortality rates of this hypothetical disease, assuming 1,000,000 people in the susceptible population, constant over all years. (This would not be true in practice, due to population growth and other factors, but this would not affect the overall trend much.) The units are "deaths per hundred thousand":

TABLE 2

**Annual Mortality Rates
of a Hypothetical Disease**

YEAR	MORT. RATE
1	7
2	21
3	42
4	85
5	155
6	350
7	610
8	1010
9	800
10	500
11	430
12	270
13	230
14	175
15	135

From the data in Tables 1 and 2, it would appear the epidemic “peaked” in year 8. Proponents of the therapies would point to the fact that *both* annual incidence *and* mortality fell dramatically immediately following introduction of therapy Y, and that although mortality increased after therapy X, it might have been much greater than it turned out, and anyway we shouldn’t be too hard on therapy X, because it was our “first attempt” and its toxicities were much greater than therapy Y.

But wait a minute. Go back and look at the data in Table 1. The annual incidence increased 15-fold and then decreased 3-fold. Does it therefore really make sense to consider absolute mortality rates?

Now let’s look at one-year “case-fatality rates”. By “case-fatality rate” in this instance, I mean 100% minus the 1-year survival rate, in other words, out of all cases diagnosed in a given year, the proportion of deaths in that cohort after a single year times 100%. For example, in year 10, there were 8000 cases diagnosed, and of those, 2000 died within one year, so the one-year case-fatality rate for year 10 is $2000/8000 = 25\%$. (See footnote 3.)

Here are the one-year case-fatality rates:

TABLE 3

**One-year Case-fatality Rates
of a Hypothetical Disease**

YEAR	1-YEAR CFR
1	70%
2	90%
3	80%
4	80%
5	70%
6	60%
7	50%
8	53%
9	40%
10	25%
11	17%
12	10%
13	15%
14	10%
15	10%

This certainly paints a different picture of the epidemic. The severity of the epidemic reached its peak around year 2 to year 3, when survival was lowest and case-fatality was highest. Ever since then, except for some minor blips, severity has been decreasing steadily. Note that the peak severity of the epidemic was reached long before either therapy X or therapy Y was put on market, so any appeal to “falling death rates” as support for these therapies is shaky.

Now let’s put on our magic-hats and pretend we work for a hypothetical government agency, and we want to really give the impression that therapy Y is a life-saver (or at the least, a life-extender). Let's conjure up 4 survival rates. Here "survival rate" means 100% minus the case-fatality rate. In other words the one-year survival rate is the proportion of patients surviving one year after diagnosis, the 2-year survival rate is the proportion of patients surviving 2 years after diagnosis, and so on.:

Group 1: Diagnosed “pre-therapy Y”, say, years 1-7.

Group 2: Diagnosed immediately around and following therapy Y, say, years 8-11.

Group 3: Diagnosed after therapy Y was available for a substantial period, say years 12-13.

Group 4: Diagnosed during years 14-15.

We get the following numbers:

Group 1 Survival Rates after 1, 2, and 3 years respectively: 42%, 27%, 14%
Group 2 Survival Rates after 1, 2, and 3 years respectively: 62%, 51%, 45%
Group 3 Survival Rates after 1, 2, and 3 years respectively: 88%, 80%, 76%
Group 4 Survival Rates after 1, 2, and 3 years respectively: 90%, N/A, N/A

Based on these data, as well as the annual incidence and mortality rates above, it certainly seems like therapy Y has been a smashing success: just look at those plummeting incidence and mortality rates and steadily increasing survival rates, *all of which occurred immediately following introduction of therapy Y*. Anyone who denies therapy Y is working must be a “therapy Y denialist” who thinks the earth is flat and the moon landings were faked. The only data which cast doubt on therapy Y are the case-fatality rates.

So which should we believe, the mortality rates and survival rates above, or the case-fatality rates?

I’ve already discussed why the absolute mortality rates are not too meaningful: the incidence of the disease has varied by more than an order of magnitude over the years, increasing and then decreasing, so comparing absolute mortality rates over a period of several years is like comparing apples to oranges to kumquats. The problem with the survival rates is clear once you look closely at the case-fatality rates: by lumping the first 7 years together into a single group,

- (1) it obscures the fact that survival reached a low point around year 2 to year 3; and
- (2) it disproportionately favors those diagnoses made in year 6 and year 7, because there were simply many more of them.

Together, the annual incidence and absolute mortality rates and the group-generated survival rates above give the false impression that therapy Y is working. Or to be more precise, they give the false impression that they are valid evidence that therapy Y is working.

POSTSCRIPT:

There is one other way around considering absolute mortality rates, and that is to scale the mortality rates to the population consisting only of AIDS patients. This is essentially the approach I took in my article a year ago (9), when I scaled death rates to AIDS prevalence, and it is the same measure that appears in some papers examining changes in death rate from the mid-1990s, with the units being “deaths per person-year” and the populations being *cohorts of AIDS patients*, not the total population. Again, in these papers, they note that death rate declined dramatically while HAART was rolled out and conclude HAART caused the decline. They fail to consider that the decline may have begun far earlier, even before AZT monotherapy was available. My analysis a year ago concluded that this is in fact the case: the AIDS epidemic, as measured by mortality rate among AIDS patients, peaked in the US around 1984-1986. It is instructive to see what a similar analysis yields for my hypothetical disease above.

To compute mortality rate scaled by AIDS prevalence, look at Table 1. Consider year 6. The total of all the numbers in the columns D7 to D15+ at or above the row of year 6 represent those patients who were alive at the beginning of year 6 and remained alive throughout year 6. They are thus each weighted with a single person-year. There are $100 + 1000 + 100 + 500 + 500 = 2200$ such patients, so they contribute 2200 person-years. The total of all the numbers in column D6 represent those patients who were alive at the beginning of year 6 but died during year 6. Assuming that deaths are uniformly distributed throughout the calendar year, these patients are thus each weighted with half a person-year. There are $100 + 400 + 3000 = 3500$ such patients, so they contribute $3500/2 = 1750$ person-years. The numbers in columns D1 to D5 represent

patients who died before the beginning of year 6 and are thus do not contribute to either deaths or person-years. For year 6, therefore, we get 3500 deaths divided by $2200 + 1750 = 3950$ person-years, yielding $3500/3950 = 89\%$ deaths/person-year. Calculating this for each year gives the following table:

TABLE 4

**Annual Mortality Rates
of a Hypothetical Disease
(scaled to AIDS prevalence)**

YEAR	MORT. RATE
1	108%
2	168%
3	135%
4	126%
5	105%
6	89%
7	67%
8	63%
9	47%
10	24%
11	22%
12	13%
13	10%
14	7%
15	4%

Again, for our hypothetical disease, it is clear the *severity* of the epidemic peaked around year 2 or year 3. And because of the wide variation in incidence over the years, either this measure of mortality rate scaled to disease prevalence, or of survival rates among patients diagnosed in a given year, must be used rather than absolute mortality rates. It is true that mortality among patients declined and survival among patients increased after therapy Y was introduced, but in *both cases, these trends were already occurring long before therapy Y was put on market.*

The numbers for my hypothetical disease are not much different in terms of general trends from US AIDS data. The time period is stretched out over a few more years, and mortality isn't quite as high as my hypothetical example, but the general pattern is qualitatively the same. And so the same argument applies to AIDS mortality throughout the years: the severity of the epidemic peaked around 1984-1986, before AZT and HAART, in other words, the trends in declining mortality, as measured by mortality scaled to prevalence or by survival rates, began long before HAART was introduced and even before AZT was introduced, so these cannot be used as even indirect evidence for the HIV hypothesis.

The general conclusion is quite sobering: Without the expansions of the definition of AIDS and the introduction of AZT in the late-1980s and early-1990s, *the AIDS "epidemic" in the US clearly would have petered out on its own by the mid-1990s.* For the past 15 years, "AIDS" has largely been prolonged by iatrogenic factors, in other words, the viral hypothesis itself has prolonged the epidemic.

FOOTNOTES:

1. An extended passage from Feyerabend is especially relevant here: “The concentration upon the theory will now be reinforced, the attitude towards alternatives will become less tolerant. Now if it is true... that many facts become available only with the help of such alternatives, then the refusal to consider them will result in the elimination of potentially refuting facts. More especially, it will eliminate facts whose discovery would show the complete and irreparable inadequacy of the theory. Such facts having been made inaccessible, the theory will appear to be free from blemish... By now the success of the theory has become public news. Popular science books... will spread the basic postulates of the theory... More than ever the theory will appear to possess tremendous empirical support. The chances for the consideration of alternatives are now very slight indeed. At the same point it is evident... that this appearance of success cannot in the least be regarded as a sign of truth and correspondence with nature. Quite the contrary, the suspicion arises that the absence of major difficulties is a result of the decrease of empirical content brought about by the elimination of alternatives, and of facts that can be discovered with the help of these alternatives only. In other words, the suspicion arises that this alleged success is due to the fact that in the process of application to new domains the theory has been turned into a metaphysical system. Such a system will of course be very ‘successful’, not, however, because it agrees so well with the facts, but because no facts have been specified that would constitute a test and because some such facts have even been removed. Its ‘success’ is entirely man-made. It was decided to stick to some ideas and the result was, quite naturally, the success of these ideas. If now the original decision is forgotten, or made only implicitly, then the survival will seem to constitute independent support, it will reinforce the decision, or turn it into an explicit one, and in this way close the circle. This is how empirical ‘evidence’ may be created by a procedure which quotes as its justification the very same evidence it has produced in the first place.” [italics as in original] (7)

2. I will not address here in detail the clinical evidence proposed in favor of combination therapy. There are many shortcomings of this evidence (inadequate trial duration, inadequate study size, reliance on dubious surrogate markers), but the most important point to remember is that a particular combination therapy is always tested against another “standard care” therapy, most often by simply adding another drug to an existing therapy. For example, a combination of 3 drugs is tested against a standard care combination of 2 drugs. The combination of 2 drugs is presumed to be standard care because it, in turn, has been previously tested against a standard care of monotherapy, which itself has been previously tested against a “true placebo” (inert drug). The point is that the claim that a combination therapy of 3 drugs is better than true placebo is dependent upon a chain of clinical comparisons, just as the proof of a mathematical theorem is dependent upon a chain of logical implications. So if even a single clinical comparison is invalid, the entire chain falls apart, as a mathematical proof falls apart if even a single logical implication is invalid. What this means for HIV therapy is that we must look very closely at the original studies comparing AZT monotherapy to true placebo. If we find these original studies to be unsound or fraudulent, then we have no basis for claiming combination therapy is better than true placebo.

3. One important note for those who choose to read the previous article “AIDS Case Fatality Rates”: There I use a different definition of “case-fatality rate”. Part of the problem is that after reading some standard university epidemiology textbooks, I’m a bit mystified about the precise definition of “case-fatality rate”, as you can find out by reading the “Notes on Definitions and Computations” from that article. This confusion compels me to make my own computations, spelling out precisely what it is I’m computing. If my choice of using the term “case-fatality rate” in both that article and this one causes confusion, I don’t care to accept the charge it’s my fault. If you wish, just ignore the term “case-fatality rate” everywhere you see it, and go by my own explanations of my computations, which are not imprecise at all.

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