Special Communication

Farr's Law Applied to AIDS Projections

Dennis J. Bregman, PhD, Alexander D. Langmuir, MD, MPH

Farr's Law of Epidemics, first promulgated in 1840 and resurrected by Brownlee in the early 1900s, states that epidemics tend to rise and fall in a roughly symmetrical pattern that can be approximated by a normal bell-shaped curve. We applied this simple law to the reported annual incidence of cases of acquired immunodeficiency syndrome in the United States from 1982 through 1987. The 6 years of incidence data closely fit a normal distribution that crests in late 1988 and then declines to a low point by the mid-1990s. The projected size of the epidemic falls in the range of 200 000 cases. A continuing incidence of endemic cases can be expected to emerge, but we believe it will occur at a low level.

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THE CURRENT acquired immunodeficiency syndrome (AIDS) epidemic presents a major challenge to epidemic theorists to find a rational basis for projecting future incidence of the disease. Purely empirical approaches cannot be expected to provide as relevant projections as one based on epidemiologic inference. The theory of AIDS projections should have a biologic foundation supported by epidemiologic precedent. With this proposition in mind, we proposed in 1985 that Farr's Law of Epidemics be invoked.[1] Two years later, we extended our views in more detail.[2,3]

See also pp 1497, 1538, and 1539.

In the present article, we have analyzed 2 more years of experience and are able to reaffirm our previous conclusions. Our findings indicate that the AIDS epidemic in the United States crested in 1988. The incidence of new cases has started to decline and will continue downward to a still to be determined but probably low endemic level before the year 2000. The total accumulated incidence of cases of AIDS in the United States by that time will be in the range of 200 000.

From the Department of Preventive Medicine, University of Southern California, Los Angeles.

Reprint requests to Division of Biometry, PMB-B101, University of Southern California, 1420 San Pablo St, Los Angeles, CA 90033 (Dr Bregman).

FARR'S LAW

In 1840, William Farr included a section entitled "The Laws of Epidemics" in his second annual report to the Registrar General of England and Wales.[4] He begins by stating the following:

> Epidemics appear to be generated at intervals in unhealthy places, spread, and go through a regular course, and decline; but of the cause of their evolutions no more is known than of the periodical paroxysms of ague. . . . If the latent cause of epidemics cannot be discovered, the mode by which it operates may be investigated. The laws of its action may be determined by observation.

He then proceeded to analyze mortality from smallpox in England and Wales for 1838 and 1839, when a severe epidemic was on the wane. He showed that "the fall in the mortality took place at a uniformly accelerated rate."

In that earliest era of modern epidemiology and before Koch and Pasteur kindled the bacteriologic revolution, Farr described the first measure of epidemic theory. He expressed his abiding faith that epidemics were natural phenomena controlled by forces that could be divined by scientific inquiry and expressed in mathematical terms. Surely, he was one of the earliest modern epidemic theorists—if not the first.

At the beginning of the 20th century, during the years in which Sir Ronald Ross[5,6] (1908 and 1915) and William Hamer[7] (1906) developed the basis of today's classic epidemic theories, John Brownlee, an inveterate Scottish public health physician and statistician, resurrected and embellished the mathematics of Farr's ideas.[8-10] Brownlee showed how a normal bell-shaped curve is produced by following the same arithmetic calculations used by Farr to measure a constant deceleration in the mortality rates of smallpox. He studied the records of large epidemics from various parts of the world over several centuries and was impressed by how many tended to be symmetrical in shape. He struggled rather unsuccessfully to derive a rational biologic process that explained either the prominence of the bell-shaped curve or the pattern of epidemic transmission it may represent. Others have since confirmed Brownlee's mathematical derivation of the normal curve.[11-13] We simply reiterate the relationship between Farr's Law of Epidemics and the normal curve in contemporary epidemiologic terms: in large epidemics, the incidence of new cases tends to rise to a crest and then fall in a manner so that the entire curve forms the shape approximately described by a normal curve.

Farr did not publish further on his epidemic theories until 1866, when a severe epizootic of cattle plague (rinderpest) struck in England.[14] Beginning in the fall of 1865, incidence grew steadily, reaching a cumulative total of 73 549 attacks by the end of December. To most observers, it was rising on an unre-

Table 1.—Incidence of AIDS in the United States Through June 1989 According to Year of Diagnosis and Major Transmission Categories and Pre–September 1987 or Post–September 1987 Diagnostic Criteria*

	Homosexual or Bisexual Male			Heterosexual IVDA			Homosexual or Bisexual Male IVDA			All Adult Cases†		
Year	Pre–September 1987	Post–September 1987	Both Criteria	Pre–September 1987	Post–September 1987	Both Criteria	Pre–September 1987	Post–September 1987	Both Criteria	Pre–September 1987	Post–September 1987	Both Criteria
1981	243	1	244	42	1	43	26	0	26	355	3	358
1982	639	4	643	181	2	183	100	0	100	1032	6	1038
1983	1786	7	1793	511	7	518	276	1	277	2832	17	2849
1984	3750	32	3782	976	6	982	511	7	518	5732	55	5787
1985	6797	212	7009	1732	181	1913	753	61	814	10 174	540	10 714
1986	10 373	686	11 059	2556	586	3142	1210	149	1359	15 627	1630	17 257
1987	13 176	2038	15 214	3401	1610	5011	1324	379	1703	20 090	4690	24 780
1988	12 158	3399	15 557	3438	2858	6296	1151	548	1699	19 195	7935	27 130
1989‡	3627	1079	4706	993	1003	1996	318	168	486	5726	2616	8342
Total	52 549	7458	60 007	13 830	6254	20 084	5669	1313	6982	80 763	17 492	98 255§
%	65.1	42.6	61.1	17.1	35.8	20.4	7.0	7.5	7.1	100.0	100.0	100.0

*Based on public domain surveillance data diskette issued with the Centers for Disease Control's *HIV/AIDS Surveillance Report* of July 1989. AIDS indicates acquired immunodeficiency syndrome; and IVDA, intravenous drug abuser.

†Includes all other categories.

‡January through June only.

§If the 1681 pediatric cases are included, the total becomes 99 936.

strained upward course. Although it was beyond his official responsibilities, Farr studied the reports of the royal commission that published cumulated figures by 4-week periods. On February 16, Farr wrote to the *Daily News of London* a letter in which he challenged the prevailing view of an impending disaster. He submitted the following analysis of the published data, which are reproduced as Farr presented them:

The number of reported cases from the commencement was:

1865.	Total.	New Cases occuring in Four Weeks.
October 7	... 11,300 ...	—
November 4	... 20,897 ...	9,597
December 2	... 39,714 ...	18,817
December 30	... 73,549 ...	33,835
1866.		
January 27	... 120,740 ...	47,191

Note: The numbers include what are called "back cases."

Farr continued as follows:

It will be observed that, although the attacks in the second period of four weeks were nearly double those in the first period, that rate of increase did not continue; otherwise on the principle of doubling, the numbers should have run up from 9,597 to 19,194 to 38,388 to 76,776. But the attacks in the last four weeks were only 47,191; and the real law implies that the ratio of increase goes on rapidly decreasing until the ratio itself is decreasing.

Thus the increase in the first interval was at the rate of 96.07 percent [18,817/9,597]—in the second interval it was 79.81 percent [33,835/18,817]—and in the third or last interval under observation it was only 39.47 percent [47191/33835].

Farr then went on to predict that the epizootic was about to crest and then decline rapidly. He was a little overenthusiastic. It crested 2 weeks later than he predicted, but then did decline rapidly.

THE AIDS EPIDEMIC

The analogy between Farr's cattle plague epizootic and the present AIDS epidemic in the United States is sufficiently close to warrant careful study. The annual incidence of cases of AIDS in the United States by year of diagnosis is shown in Table 1 for three major transmission categories: (1) homosexual or bisexual male, (2) heterosexual intravenous drug abuser, and (3) homosexual or bisexual male intravenous drug abuser. The data have been drawn directly from the July 1989 AIDS Public Information Data set provided by the Statistics and Data Management Branch in the Division of HIV/AIDS of the Centers for Disease Control in Atlanta, Ga. The cases are presented separately for the pre–September 1987 and post–September 1987 diagnostic criteria.[15]

The data are graphed in Fig 1 using a logarithmic scale to compare trends. The three curves rise steeply from 1982 to 1983, but already by 1984 the tendency for them to veer off to the right is evident. This trend continues progressively through 1987. The data for 1988 and the first 6 months of 1989 are not charted because the shape would be misleading. The lag in reporting would cause a greater flattening of the curves than warranted.

The effect of the change in the Centers for Disease Control diagnostic criteria introduced in September 1987 is

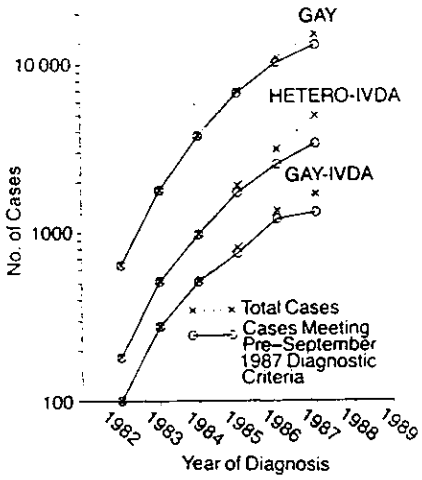

Fig 1.—Incidence of acquired immunodeficiency syndrome in the United States for three major transmission categories, by year of diagnosis, 1982 through 1987, using pre–September 1987 diagnostic criteria and total including post–September 1987 diagnostic criteria. Data appear in Table 1. GAY indicates homosexual or bisexual male; HETERO-IVDA, heterosexual intravenous drug abuser; and GAY-IVDA, homosexual or bisexual male intravenous drug abuser.

apparent. Additional cases have been reported with dates of diagnosis going back to the beginning of the epidemic in 1981. The increase in case counts became appreciable in 1984, when 1% of the total cases for that year were based on the new criteria. This percent increased steadily to approximately 30%

Table 2.—Annual Incidence of AIDS in the United States by Year of Diagnosis From 1982 Through 1987 Among Adult Homosexual or Bisexual and Intravenous Drug Abuser Groups Combined With Projections to 1995*

Year of Diagnosis	No. of Cases	First Ratio	Second Ratio
	Annual Incidence of AIDS		
1982	920	...	...
1983	2573	2.7967	...
1984	5237	2.0354	0.7278
1985†	9328	1.7812	0.8751
1986†	14 705	1.5764	0.8850
1987†	19 333	1.3147	0.8340
	Projections by Farr's Law		
1988	21 978	1.1368	0.8647§
1989	21 604	0.9830	0.8647
1990	18 363	0.8500	0.8647
1991	13 497	0.7350	0.8647
1992	8579	0.6356	0.8647
1993	4715	0.5496	0.8647
1994	2241	0.4752	0.8647
1995	921	0.4109	0.8647
Total	143 994‡	...	...

*AIDS indicates acquired immunodeficiency sydrome. The number of cases is based on using the pre–September 1987 diagnostic criteria.
†Case counts for 1985, 1986, and 1987 were adjusted upward in anticipation of cases not yet reported (see text).
‡Category includes 311 cases having dates of diagnosis prior to 1982.
§Constant ratio chosen as the mean of the three second ratios for 1985, 1986, and 1987.

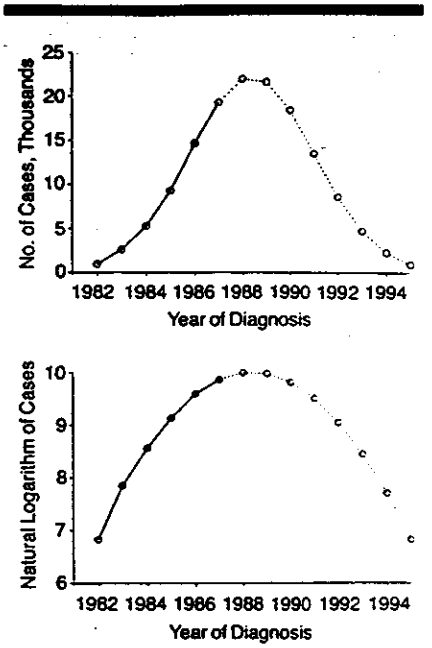

Fig 2.—Annual incidence of acquired immunodeficiency syndrome in the United States from 1982 through 1987 for combined homosexual or bisexual male, heterosexual intravenous drug abuser, and homosexual or bisexual male intravenous drug abuser categories (solid line), with projections to 1995 based on Farr's law (dashed line). The upper panel is charted on an arithmetic scale and the lower panel on a logarithmic scale. Only pre–September 1987 diagnostic criteria are used. This is a first approximation. See discussion in text and Table 2.

by 1988. The increase affected the homosexual or bisexual male group the least, 22% in 1988 and 23% in the first 6 months of 1989, whereas the comparable increases for the heterosexual intravenous drug abuser group were 45% and 50%, respectively. The increases for the homosexual or bisexual male intravenous drug abuser group fall between the homosexual or bisexual male and heterosexual intravenous drug abuser groups.

Despite the substantial and disproportionate impact of the revision of diagnostic criteria, the effect has not changed the underlying configuration of the curves. All give the impression of moving in a parallel fashion. They look a lot like parabolas—the shape of a normal curve plotted on a logarithmic scale.

In attempting to invoke Farr's law with these data, we have chosen, as our first approximation, to limit our calculations to cases in which the diagnosis was made prior to 1988 and classified by the Centers for Disease Control with the pre–September 1987 diagnostic criteria. This provides a certain degree of consistency in diagnostic standards in the cases being analyzed and eliminates most of the knotty problems created by lags in reporting cases to the health department. Based on inspection of the intervals between diagnosis and report, we found that approximately 90% of cases are reported within 18 months of diagnosis. By using cases diagnosed before 1988, the need for extensive and somewhat uncertain adjustments is minimized. The counts for 1985, 1986, and 1987 are adjusted upward by 0.5%, 4.0%, and 8.0%, respectively, to account for cases diagnosed in those years that may still be reported to the health department. Furthermore, if there is any validity to Farr's law, it should become apparent with 6 years of consecutive data.

In Table 2, we have combined the data for the three major transmission categories. During these 6 years, 1982 through 1987, these three groups have consistently made up from 89% to 91% of the total adult cases. Combining the groups provides the stablest numbers and eliminates the difficult problem of how to subdivide the homosexual or bisexual male intravenous drug abuser group between the two possible transmission categories.

In the upper half of Table 2, we have applied Farr's simple, but elegant, arithmetic method of fitting a normal curve to the combined data. The first ratio is calculated by dividing 1 year of data by that of the immediately preceding year. For example, the 2573 cases in 1983 divided by the 920 cases in 1982 give a first ratio of 2.7967. By subtracting 1.0 from this ratio, one obtains the percent increase, or 179.67%. The first ratios progressively decline with time, so that the ratio of 1.3148 in 1987 signifies that the increase over 1986 was only 31.48%. When the ratio reaches 1.0 the epidemic crests, and thereafter it declines as the ratio becomes lower.

The second ratios are calculated by dividing the first ratio for 1 year by that of the preceding year. These are also shown in Table 2. The second ratio measures the rate of change of the first ratio, or in mathematical terms the acceleration. For a normal curve the second ratio is constant, having a value between 0.0 and 1.0, which signifies a constant deceleration in the rate of change. For 1984 the second ratio is 0.7278, and for the ensuing years it varies from 0.8850 to 0.8341. To fit a normal curve to these data, we have chosen the mean of the second ratios for 1985, 1986, and 1987, which is 0.8647. By back calculation the first ratios after 1987 can be estimated and from them the projected incidence for each succeeding year.

The results are shown in the lower half of Table 2. The epidemic can be seen to crest at the end of 1988 and begin its decline in 1989 to a yet to be determined endemic rate, which we believe will be low. The incidence falls symmetrically to an annual incidence of fewer than 1000 cases in 1995.

The data are graphed in Fig 2 on an arithmetic scale in the upper panel and on a logarithmic scale in the lower panel. The classic bell-shaped appearance of the arithmetic chart and the parabolic shape on the logarithmic chart are evident. The total number of cases observed from 1981 through 1987 plus those projected to the end of 1995 is 144 339, or in round figures 150 000.

COMMENT

We wish to reemphasize that this projection is a crude first approximation. Many factors must be incorporated into its evaluation. Some might lead to a reduction in the total, most will increase it. For example, the choice of 0.8647 as the constant for fitting the approximate normal curve may be a bit high. If the second ratio for 1984 of 0.7278 had been included in the estimate, or if a normal curve had been fitted to the full 7 years of data, the resulting projection would have crested somewhat earlier and the total projection would have been a little smaller.

More significantly, the projection was based only on adult cases—among homosexual or bisexual males, heterosexual intravenous drug abusers, and homosexual or bisexual male intravenous drug abusers. These make up about 90% of the total cases, which implies the projection must be increased by at least 10%. Likewise, to correct for the omission of the pediatric cases, an additional increase of about 2% is indicated.

A more imponderable problem was created in September 1987 when the Centers for Disease Control broadened the case definition, encouraging a greater variety of manifestations of AIDS to be reported. Experience during the ensuing 21-month period shows that "new criteria" cases make up about 30% of the total cases. The homosexual or bisexual male group contributes about the same numbers of new criteria cases as both the heterosexual intravenous drug abuser and the homosexual or bisexual male intravenous drug abuser groups. The impact of the new criteria still has to be evaluated. It depends on what proportion of patients who meet the new criteria go on to develop the signs and symptoms compatible with the old criteria. Two extreme contingencies can be considered. First, suppose all the patients who meet the new criteria proceed to develop old criteria manifestations. Then the effect will be to put a somewhat asymmetrical cap on the top of the curve, with a compensatory decrease on the down curve. The total projection based on the old diagnostic criteria would stand unchanged, since the effect would be to accelerate the rate of reporting, but not to affect the total recorded cases in the long run. Second, if none of the patients who meet the new criteria develop old criteria manifestations, the estimated curve should be evenly increased by about 30%. For these reasons, we stated in the introduction that the projected total would "be in the range of 200 000."

We have made no effort to calculate confidence limits for these projections. We humbly submit that we do not know how to account for the error due to biases in the reporting system. Furthermore, we believe it would be futile and meaningless to place a 95% confidence interval based on random error about the projections that extend out for a decade. To do so would suggest a greater confidence in both the method used and the data available than is justified.

By invoking Farr's law with Brownlee's expanded interpretation that many large epidemics tend to be symmetrical, we introduce a new and epidemiologically reasonable estimate into the debate over AIDS projections. The use of the normal curve was chosen partly in respect to the Farr-Brownlee tradition but more practically because of the stark simplicity of the method. Others have also discussed the complexity of modeling the infinite number of events, circumstances, and relationships that have conspired to create the epidemic of AIDS.[16-21] There is reluctance to accept simple explanations of complex phenomenon.[22]

In spite of problems with the lag in reporting of cases and the change in diagnostic criteria in September 1987, we believe the AIDS epidemic has crested and will steadily decline. However, while the number of new cases starts to decline, those who chart prevalence statistics will find the number of living cases will continue to increase as medical treatment prolongs the duration of disease.

We note with interest the recent official report of the US General Accounting Office on AIDS forecasting.[23] In it, 13 national forecasts of the cumulated total of cases through 1991 are identified. None of these considered the concept that the epidemic might crest and then decline. We believe the evidence presented is sufficient to indicate that the Farr-Brownlee ideas are worthy of consideration. The passage of time, perhaps only 1 more year, will serve to confirm or refute their validity.

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