the engineers, after two hundred years, have learned to straddle the contradictions built into our nation state" (p. 207).

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Workings of HIV

HIV and the Pathogenesis of AIDS. JAY A. LEVY. ASM Press, Washington, DC, 1994. xiv, 359 pp., illus., + plates. Paper, $49; to American Society for Microbiology members, $39.

That human immunodeficiency virus causes AIDS has long been evident from its global and detailed epidemiology; for example, about 50 percent of HIV-infected hemophiliacs have developed AIDS thus far, whereas no HIV-negative hemophiliac has done so. Just how HIV causes AIDS has seemed more mystifying, although the salient clues have been there from the beginning. In 1981 Michael Gottlieb reported that AIDS patients exhibited a severe depletion of CD4-positive T-helper lymphocytes, and in 1984 David Klatzmann showed that these very cells are selectively sensitive to infection by HIV. Thus their depletion is explained by HIV infection, due either to the cytopathic effects of the virus itself or, more likely, to destruction by HIV-specific CD8-positive cytotoxic T lymphocytes. At first it seemed puzzling how few HIV-infected cells were detectable in peripheral blood at any one time. But by 1986 Klara Tenner-Racz had shown that the lymph nodes of asymptomatic HIV-positive people are actually chockablock with HIV, which is not a latent infection at all. In fact, the viral burden is high in many individuals. As George Shaw's and David Ho's groups recently reported, the turnover of HIV and HIV-infected cells is so rapid that it is a wonder how the immune system maintains its integrity for many years in the face of this viral onslaught. We may ask, therefore, why such an effective immune response is not successful in clearing the virus altogether? Yet if it cannot, why does it keep the more severe effects of HIV at bay so long, and what co-factors herald progression to AIDS? These questions about HIV pathogenesis are germane both to vaccine development and to therapeutic strategies to prevent or delay AIDS.

Jay Levy's monograph on HIV and the pathogenesis of AIDS tells you everything about HIV infection you might wish to find out without tackling the daunting literature on AIDS, which generates thousands of new research reports each year. It is a considerable achievement that one scholar could grasp the entire subject and distill our knowledge of it in 12 concise chapters and some 2000 references. Levy was a pioneer of HIV isolation and characterization, and he and his colleagues at the University of California at San Francisco have made signal contributions to the understanding of HIV in the brain, of HIV tropism, and of the role of CD8 cells in controlling infection. In this volume he has kept abreast of the ever-burgeoning field in a remarkably informed and balanced way. Indeed, I would have preferred him to be more opinionated about controversial aspects of HIV infection, as he can be in informal discussions, for that is a privilege of the single-author book amid so many multi-author volumes.

Levy moves from a description of HIV to features of transmission, the cell and molecular biology of infection, the enormous genetic and phenotype heterogeneity of HIV and its variable tropism for lymphocytes, macrophages, and dendritic cells, to the host's immune responses. He describes the pathogenesis of HIV not only in the immune system itself but also in the central nervous system, gastrointestinal tissue, and other organs. He does not dwell in detail on the various opportunistic infections that result from AIDS but includes a useful chapter on AIDS-related cancers. The final chapters deal with the prognosis for long-term survival featuring non-progressors and how antiviral approaches linked with immune modulation might form the pattern of future treatment.

The text is clearly illustrated with mainly black-and-white diagrams (and some colorful histopathology), useful boxed tables and lists, and appendixes on the clinical categories and classifications of AIDS. This volume will be valuable to the seasoned virologist, immunologist, or physician and to the newcomer to AIDS research alike.

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Patterns of Peopling

The History and Geography of Human Genes. L. LUCA CAVALLI-SFORZA, PAOLO MENOZZI, and ALBERTO PIAZZA. Princeton University Press, Princeton, NJ, 1994. xiv, 1032 pp., illus. $150 or £150.

In 1978 the authors of this volume, in a paper in this journal, helped reinvigorate interest in the analysis of geographic patterns of genetic variation as a method for inferring pattern and process in the evolution and history of human populations. The paper, and the cover of the issue of *Science* that contained it, became well known as having introduced the method of synthetic gene-frequency maps. The present volume is the culmination of a 20-year collaboration to document the extent and patterning of human genetic variation using classical markers. According to the authors, the "book was started with the desire to analyze the geography of human genes, using new techniques we have developed for the purpose of studying ancient human migrations."

Cavalli-Sforza and colleagues have compiled an unprecedented array of genetic data on the world's populations. The original database consisted of over 76,000 allele frequencies from 6633 separate samples. The authors exercised a mixture of culling and pooling strategies to reduce the database to a more analytically manageable 491 populations with observations on over 120 alleles. Although the criteria applied in this culling and pooling of samples are left frustratingly vague, the appendixes make clear which populations are used in the basic analyses presented throughout the book.

The largest section—the second half—of this compendium consists of more than 500 gene-frequency maps. For each allele for which sufficient observations are available there is a map reflecting the world distribution of its frequency, as well as separate maps displaying the allele frequency diversity on separate continents: Africa, Asia, Europe, America, and the Pacific Islands, including Australia and New Guinea. The maps include the geographic location of each population from which data are used, symbols intended to help the reader judge the fit between the original data and the map, and three small graphs, one summarizing the descriptive statistics of the distribution of the allele frequencies, one showing the sample sizes, and a variogram, a standardized method of indicating the relationship between geography and genetic variation. In addition to these single-gene maps, color maps reflecting the conjoint distribution of the first three principal-component scores of allele frequencies are also given for the world and the five continental areas.

The single-gene maps are an impressive summation of genetic data. Valuable as I believe they are, however, they should be viewed with considerable caution. The map of *HLAA*2* for the Americas is illustrative. The portion of the map of North America north of Mexico is based on only 10 data points: two in western Alaska, two on the Arctic coast of Canada, one in the U.S. southeast, and five clustered closely in the U.S. southwest. Additionally, Greenland is represented by a single observation on the

east coast. The map of this gene indicates a regular clinal pattern emanating from the core of high frequencies in the U.S. southwest to lower frequencies in the Arctic and eastern Greenland, yet for most of this vast geographic expanse no data are actually available. All six of the displayed levels of variation in this map are represented in this geographic space, including three separate levels in Greenland, where only a single population is represented for this allele. In some of their other maps, admittedly with a more uniform distribution of data points, such clinial distributions are used as a basis for inferences regarding ancient migrations and settlements. Though in general such inferences are reserved for the interpretation of synthetic maps of principal components, they amplify the problem of visual geographic display from sparse data.

The authors are most familiar with this problem, which invariably arises in analyzing geographic variation in gene frequencies. Should one opt for maximizing number of genetic systems (alleles) or number of populations sampled? It is not possible to do both; maximizing one inevitably reduces, usually dramatically, the other. This asymmetry stems from the fact that there has never been a standard set of markers to be typed in all groups studied. Haphazard data collection has made it impossible to directly compare large numbers of populations for the same (large) set of genetic polymorphisms. The authors recognize and lament this fact and use the opportunity to lobby for greater coordination, and standardization, in the collection of population data on the DNA polymorphisms now being carried on worldwide. They have attempted a compromise in this book by initially maximizing the number of genes available for analysis, critical for many types of genetic (for example, phylogenetic) analysis, and then not eliminating populations just because they lack data on one or more systems. The authors argue that comparing populations differing in the systems available should not introduce substantive bias so long as the number of genes is large, the overlap of systems between populations compared is substantial, and the lack of observations on any particular system is essentially random. This is a cogent and practical argument, I believe, but the 24% missing data in the full data array should give pause.

Whatever deficiencies may obtain in the individual gene maps, they are usually clearly acknowledged. Questions raised by the peculiarities of the geographic distribution of alleles are frequently the subject of more detailed analyses and hypothesis tests in the other major portion of the volume, eight chapters of description and analysis of the data upon which the maps are based. The first of these chapters is essential reading, since it delineates the nature of the data employed and analytical methods used. The last, an epilogue, provides less a summary of what has gone before or an introduction to the maps to follow than a position statement on the nature of multidisciplinary genetic research and where it may, and should, go, including a reiteration of the authors' support for the Human Genome Diversity Project.

Between these chapters are summaries of the analysis of the pattern of diversity of allele frequencies on a global scale and treatments of each of the continental areas. The format of these chapters is uniform: an archeological and linguistic introduction is followed by a genetic distance analysis (F_{ST} is used as the distance statistic throughout). The genetic distances are used as the basis of a phylogenetic analysis with an average linkage tree as the core. Finally, a series of principal-component and synthetic gene-frequency maps are displayed and discussed with respect to the previous analyses and observed gene frequency patterns.

The treatment of world genetic diversity in chapter 2 is based on a subsample of only 42 populations, albeit with a large number of alleles analyzed. Fourteen of the samples are from Asia, but no other continent is characterized by more than seven. Nevertheless, "the most important conclusion in this section is that the greatest difference in the human species is between Africans and non-Africans . . ." (p. 83). This conclusion is at variance with some earlier analyses from these authors but concordant with a growing number of studies based on DNA markers and sequences, briefly reviewed here. The reasons for the discrepancy with earlier studies are examined and the discrepancy is attributed to the inclusion of too few genes in prior analyses.

The authors are at pains here and in the chapters on individual continents to document the correlation between patterns of genetic and linguistic variation. It is unquestionably true that language may both facilitate and impede genetic exchange, thus imposing a similarity on genetic and linguistic distributions. However, the use of linguistic affinity as one of the criteria for pooling separate samples from local geographic areas would seem to weaken the analyses demonstrating close association of genetic and linguistic variation.

Space precludes accounts of the analyses and conclusions for all continental areas, but the chapter on the Americas may serve as example. In general, analytical results illustrate a reasonably clear relationship of gene frequency variation to geography for North American groups, whereas South America is characterized by extreme genetic diversity, with little correlation with geography or linguistics. This pattern is interpreted as reflecting extreme drift among populations of this continent, in accordance with results by earlier workers. In North America, Athapaskan groups are shown to be more similar to Eskimos than to other Amerinds, a confirmation of earlier work of these authors and others. The greater correspondence among genes, geography, and language in North Amerinds is taken to reflect the discrete nature of early migrations. The authors clearly adopt and support the three-migration theory of Amerindian origins, based in part on the tripartite linguistic classification of Amerinds by Greenberg: Amerind, Na-Dene, and Eskimo-Aleut. Moreover, the au-

Vignettes: Comestibles

My meal . . . was very agreeable, surpassing anything found at the table of the wealthy. Good, fat, well-boiled venison, taken with pure honey, is as great an excitant of the power of the *sensorium commune* in the human species as a pure solution of sulph[uric] copper is to excite the power of a clean galvanic battery.

—*Gideon Lincecum*, in *Adventures of a Frontier Naturalist: The Life and Times of Dr. Gideon Lincecum* (Jerry Bryan Lincecum and Edward Hake Phillips, Eds.; Texas A&M University Press)

I would ask anybody to name some attribute of milk besides purity. Yes, whiteness is bound to be one. "Whiteness" and "purity." Atoms would be way up at the top, but an atomic description of milk is still a long way beyond us. . . . As to the scientific account of cheese-making, until recently the way you learned to make cheddar or brie was to go and apprentice yourself to the best brie-making farmer in Brie. There wasn't any way to go to Cornell and find out. You could go there and make cheese all right, but by God it was sure not brie.

–*Philip Morrison*, in *Nothing Is Too Wonderful to Be True* (AIP Press)

thors argue that the analysis of gene-frequency diversity in America is rather more consistent with an earlier Amerind entry (15,000 to 30,000 years ago) than many American archeologists are ready to acknowledge.

The book contains three appendixes. The first two provide allele frequencies for the 42 populations used in the global analysis, and for the 491 populations in the full database. Appendix 3 lists the primary sources from which the gene frequency data were obtained.

There is much to relish and much to challenge in this volume. Many will question the use of specific analytical methods (choice of distance statistic, tree-construction method, and synthetic map surface construction methods) or be frustrated at the ambiguities of sample pooling or the limitations of the analyses presented. For many, the lack of clear-cut criteria upon which a number of analytical decisions, such as the deletion of samples due to admixture, were made will be troubling. Similarly, "when points for calculating variogram curves were too few, the variogram was omitted from the gene maps" (p. 124). The criteria employed to make this judgment are not obvious, nor is the rationale for producing a map from what may be presumed to be very sparse and irregularly distributed observations.

These reservations, however, are modest. This is an impressive display of synthesis and analysis. Arguments regarding methods and approaches will be trivial if the original data are made available to other researchers as is implied in chapter 1. This is the most comprehensive treatment of human genetic variation available. If it provokes many to challenge its conclusions and hypotheses with increasingly sophisticated analyses, and I believe it will, it will likely play an important role in future research in anthropological genetics. It is especially appropriate that such a complete summary of the classical blood-group, serum-protein, and enzyme markers appears now, as we are rapidly generating the next generation of human genetic diversity data at the nucleotide level. Many of the deficiencies to be found in this volume are the deficiencies of data collection, of standardization, and ultimately of comparability. As the authors clearly note, we should learn from these deficiencies and coordinate, to a much greater degree than in the past, the nature of the genetic data now being accumulated on DNA markers. This is a lesson worth learning, and one that is clearly presented here.

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