"The most important experiments are those that nature has already done for us." Judson Herrick's principle (p. 331)

A review of **DIGGING FOR PATHOGENS: Ancient Emerging Diseases—Their Evolutionary, Anthropological and Archaeological Context**, edited by Charles L. Greenblatt, Balaban Publishers, Rehovot, Israel, Copyright 1998.

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"...Kinetoplastidae contain ergosterol as a major or minor sterol. None of them contains cholesterol as was believed. Ergosterol relates Tripanosomidae to algae from which they are direct descendants... Following a toxic algal attack at sea, some algae penetrated animal blood stream through holes in the gills. If the animal recuperated, the algae became trapped in the animal. The toxins helped the algae to survive and were transmitted to their offspring. Eventually algae have degenerated to the present-day blood stream pathogenic protozoa. When fish colonized the land, they carried with them their parasites as well...."

Thus begins the Abstract of Chapter 8 by Shmuel Halvy. The entire book is like this. Each chapter captures your attention, requiring the reader to think in new ways about the evolution of microbial (broadly defined) pathogens. As an undergraduate student, I studied the African Sleeping Sickness parasites (My first publication over twenty years ago was on this work.), and I have followed much of the exciting developments of the molecular biology of the kinetoplastidae. Although I was "hooked" on this book way before I got to this chapter and the preceding one on Cellulase Enzymes and the Evolution of Trypanosomatids, this chapter and many others, forced me to think in new ways on the evolution of microbial pathogens. This science of paleobiology and its accompanying paleo-vocabulary, e.g., ancient or paleo-DNA, paleopathology, paleoepidemiology, paleopathogenesis, etcetera, deals with the area of *emerging and re-emerging diseases* in a new light, that of looking at the past to understand how to deal with these diseases in the future. *This is a book for the clinical and basic researcher, teacher, and/or student involved with all aspects of emerging and re-emerging infectious diseases and mechanisms of microbial pathogenesis.* For me, this book is a must read for anyone studying the biology of host-microbial interactions.

This may be the first book of its kind that attempts to deal with ancient DNA (aDNA) and ancient microbial pathogens in a serious yet creative way by the contributors. The book is written in such a way that the reader is allowed into the contributors' way of thinking about past societies, their collective behavior and their diseases. This subject matter is what today is needed in the teaching of this research area to students of infectious diseases who, being over-exposed to modern molecular technologies and genomics, have little appreciation about the tremendously complex biology and evolution of virulence of microorganisms. This book can be viewed as a theoretical framework about the paleodiseases of microbial etiology. While being fun to read, readers will not tire going from chapter to chapter with food for thought at every page.

The book is divided into 3 parts, comprising 18 chapters and a roundtable discussion. Following the introduction chapter (by I.R. Cohen), Charles L. Greenblatt, also the editor, presents an excellent overview in Chapter 2 in which he describes and outlines the questions posed by the contributors and contents of the book. This chapter is central to setting the mental stage for what follows. His description of the Ancient DNA III meeting held in Oxford, where only three of fifty presentations dealt with infectious diseases, provided the impetus for a "full" meeting devoted to ancient DNA and the paleobiology of infectious diseases. This book is also the inaugural publication by the new "Center for the Study of Emerging Diseases" established in Jerusalem in 1996, which further highlights, I believe, a trend in the formation of new "Centers on Emerging Diseases" within established research departments and institutions.

Dr. Greenblatt is correct to pose a series of questions to the prospective reader after his brief but accurate preamble on evolution of symbiosis, parasitism and virulence. These questions appear simple and even obvious, but it becomes clear that a certain way of thinking to find answers to these questions is required by the serious student studying ancient DNA and paleobiology. If nothing else, this book makes the reader aware of this fact. Here is a sampling of the questions: Why do some pathogens restrict themselves to a single host? Why is a plant enzyme possessed by an animal parasite? How does algal toxin relate to a similar toxin in a human parasite? What happens to a parasite family when its host population "suddenly" becomes extinct? What serotypes have *Vibrio* bacilli presented in the past which may affect planning for the developing of a new vaccine? Dr. Greenblatt motivates the reader to jump ahead to get the answers to these fundamental questions.

Part I, The Evolutionary Context, presents the conceptual framework in which this area of research must deal with the complex history of life on earth that, ultimately, influenced the evolution of infectious diseases. This section challenges the reader to imagine life on earth from 50 million years ago to the present, from a "time of plenty" to limiting environmental conditions, from mass extinctions to the appearance of animals, which were "like culture flasks" for pathogens. This first part ends with a challenge to those who have studied and are presently studying the trypanosomes and malaria parasites—indeed all complex parasite models—responsible for enormous morbidity and mortality in humans and animals. Shmuel Halevy in Chapter 8 argues, within this historical context, that "immunization against trypanosomes or plasmodium should be possible...", and the argument is made notwithstanding the known extensive antigenic variation exhibited by both of these parasites—an area of intensive investigation at present. It is difficult to disagree with him, and today's students need to be challenged with this way of thinking.

The second part, Chapters 9 through 14 introduce the reader to the diseases that have been recorded in prehistory. What can anthropology and archaeology tell us about the origin of diseases? How can we trace the origins of rheumatoid arthritis that begin in the Tennessee River Valley among Amerindians (Chapter 9)? Studying ancient cultures, their behavior and environment along with the influence of new arrivals (Europeans to the New World, for example) has been important in the evolution of infectious diseases. Dr. Ubelaker (Chapter 10) does an excellent job in educating us about the field of paleopathology and the need for a new

educational paradigm in this field. This part of the book shows clearly that the study of aDNA and paleobiology will require the development of a new terminology, improved techniques for diagnosis, and better training in interpretation of disease processes in ancient tissues.

In the last part of this book, Digging for the Pathogens, four chapters discuss more than the use of modern techniques, such as PCR, to isolate infectious disease-specific markers. The reader is treated to discussions of environmental conditions that help preserve or degrade specific molecules that might represent markers of infectious diseases. Future students studying paleobiology must appreciate the chemistry of the markers such as DNA as well as of the body sites from which they can be retrieved.

Dr. Greenblatt ends his Chapter 2 by stating that "The symposium and the resulting monograph suffer from attempting to do too much." I found myself wanting more rather than feeling overwhelmed. To be sure, there was a natural overlap between the three parts of the book and even within the chapters in each part. I found this redundancy to be beneficial, reinforcing the idea that ancient DNA and paleobiology represent a new area within infectious disease research. This book has done an excellent job in showing the multidisciplinary prerequisite for studying emerging and re-emerging diseases. Indeed, the book challenges us to develop new training and education paradigms to meet the needs for tomorrow's ancient DNA research.

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