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BOOK REVIEWS

Digging for Pathogens. Ancient Emerging Diseases—Their Evolutionary, Anthropological and Archaeological Context. The Center for the Study of Emerging Diseases. Edited by Charles Greenblatt. ISBN: 0-86689-053-X. Rehovot, Israel; Balaban Publishers, 1998. Telephone: (+972) (8) 947-6216; FAX: (+972) (8) 946-7632. Price: $39 USD, plus $5 USD for shipping.

Up to 10 years ago, the search for pathogenic microbes had led to approximate knowledge of the origin and dissemination of infectious diseases. Medical narratives, bas relieves, paintings, and the study of bones showed the existence of rabies in Mesopotamia more than 4,000 years ago, paralytic polio in Egypt during the eighteenth dynasty, the existence of tuberculosis from remote historic antiquity, that the plague arrived in Europe from Crimea in the fourteenth century; and that venereal syphilis was exported from the New World to Europe at the end of the fifteenth century.

Technology for discerning the age of samples and the polymerase chain reaction (PCR), capable of amplifying many trillions of times the deoxyribonucleic acid (DNA) molecules present in mummies, fossils, or bones, gave birth to a specialty within paleoanthropology. Presently, there are study centers and researchers dedicated to investigating the origins of infectocontagious pathology in the most ancient sources to be found.

The immediate objectives are to find out how, when, what, and which of the consequences infectious diseases had on the first *Homo* sp. (*habílis*, *neanderthalensis*, and *sapiens*), how they evolved to change lifestyles, what their appearance and routes of dissemination were, and what the chronology of the disappearance of the relationships with their biological environment and of present technology was.

This book contains 18 essays on general themes such as geographic peculiarities and circumstances such as the microbian flora of insects trapped in amber from 20 to 25 million years ago or the dentobacterian plaque of bacteria in fossilized jawbones. Various essays discuss protocols to be developed and descriptions of the technology necessary for future work.

The novel conceptual contribution consists of Ewald's argument that the antiquity of a microbian aggression does not lead to attenuation of the clinical picture. Ewald cites a case of *Plasmodium falciparum*—as lethal in our day as it has been throughout the millennia—tempered in the carriers of hemoglobins. Host-organism mobility variants, vector transmission, and the contagiousness of the disease put forward virulence variants independent of time of initiation.

The symbiosis of bacteria and *Amoeba proteus* after more than one hundred divisions of protozoa signals the evolution of parasitism to symbiosis. The extreme case concerns our mitochondria, photosynthetic prokaryotes that "parasitized" a eukaryote 1.5 billion years ago and that, after their adaptation, are the transductor organelle of energy in all eukaryote cells.

The study of bacterian/protozoan symbiotic relationships is interesting, not only because of the phenomenon itself, but because of the possible evolutive connection in pathogenic microbes for man. *Legionella* sp. can grow symbiotically in *Tetrahymena* and *Acantamoeba.* Some chlamydias can infect protozoa, and the leishmanias can degrade cellulose, an enzymatic capacity of bacteria.

With regard to plasmodia and trypanosomes, it is postulated that they are derived from marine algae that were transitory parasites in which they adapted permanently. The modus vivendi was maintained as tolerable aggression. On colonizing the earth, they continued in the amphibians and other orders: reptiles; birds, and mammals. Eukaryotes do not express all of their genes—in addition to cholesterol, a mouse neoplasia synthesizes phytosterol, a steroid characteristic of algae.

Paleopathology studies the material available. The bones allow the researcher to explore shape, size, fractures, luxations, arthritis, vertebral pathology, porotic hyperostosis, and the *criba orbitalica.* It utilizes the equation health index = years of quality life (judged by the bone findings).

In judging environmental microbes and those present in animals hunted in the Pre-Neolithic Age and afterward and consumed raw after skinning, pathology such as the following are presumed: toxoplasmosis, hemorrhagic fevers, leptospirosis, brucellosis, anthrax, salmonellosis, gangrene, tetanus, botulism, malaria, yellow fever, sleeping sickness, leishmaniasis, and meningoencephalitis.

Twelve thousand years ago, domestication of animals brought with it zoonosis. Presently, the analogies of 65 diseases of dogs, 46 of caprines, 22 of pigs, and 26 of barnyard birds are recognized, and 32 possible zoonotic relationships have been identified in rodents.

PCR has permitted recognition of the microbial DNA in human matter (mummies, bones, or skin) as well as in attire. Some examples follow:

- tuberculosis in medieval bones and, in the 19th century, pre-Colombian lung samples
- leprosy in bones of the Middle Ages

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- bubonic plague in medieval bones
- syphilis in Renaissance textiles
- malaria in the ribs of Egyptian mummies
- retrovirus in the skin of mummies over 5,000 years old

Historical sketches testify to the presence over 2,000 years ago of cutaneous schistosomiasis (*S. hematobium*), malaria, helminthiasis, tuberculosis, and leishmaniasis. The new discipline is comprised of genetics, sociology, economics, anthropology, and chemistry, among others. The most important work is being carried out in contemporary Israel, where there exists evidence of human populations from 1.4 million years ago, and pre- and protohistoric cultural traces from the Early Upper Paleolithic (32,000 years ago), to the Late Upper Paleolithic (22,000 years ago), Kebaran (18,000–4,500 years ago), Initial Natufian (12,500–11,250 years ago), Pre-Ceramic (10,200–8,500 years ago), Neolithic (8,100–6,500 years ago), Chalcolithic (6,500 years ago), and the Bronze Ages (5,500 years ago).

Dental study of fossilized jawbones shows the scarcity of cavities, their appearance, and increase, coinciding with ingestion of sweet foods—Alexander the Great introduced the cultivation of sugar cane into Egypt in 327 A.C. The Arabs and the Crusades carried it to Europe, but it was not until the discovery and colonization of America that saccharose was produced on a grand scale.

The enigma concerning the greater resistance of Jews to tuberculosis is presented with the following hypothesis: human tuberculosis, in large numbers, originated in bovines after the domestication of animals. The Jewish inhabitants of mountainous areas, of strict endogamy and relative isolation, instead raised more caprines and ovines, thereby conserving and transmitting genes for such diseases as Tay-Sachs, whose heterozygotes are 10 times less inclined to suffer from tuberculosis than other European races. Yemenite and Ethiopian Jews, who recently immigrated to Israel and converted to Judaism during the Byzantine dominion, originated from ethnic groups different from Sephardic and Ashkenazi Jews. The findings (the object of the book) are the result of modern technology: PCR; pyrolysis; high-pressure liquid chromatography (HPLC); electronic scanning microscopy; culture media, in which the intestinal bacteria of insects were trapped in amber, and microbes present at 1 km below sea level, grown in polar caps or in salt crystals.

The work is useful for historically situating microbes—basic matter to all general or specialist physicians, epidemiologists, historians, economists, anthropologists, sociologists, and demographers.

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

> . . . 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 20 years ago, was on this work), and I have followed much of the exciting development of the molecular biology of the kinetoplastidae. Although I was hooked on this book long before I got to this chapter and the preceding one on Cellulase Enzymes and the Evolution of Trypanosomatids, it 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, and paleopathogenesis—deal with the area of emerging and re-emerging diseases in a new light: they look to 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 the 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. The contributors attempt to deal with ancient DNA (aDNA) and ancient microbial pathogens in a serious yet creative way. The book is written in such a manner 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 is needed today in the teaching of this research area to students of infectious diseases who, often overexposed to modern molecular technologies and genomics, have little appreciation of the tremendously complex biology and evolution of virulence of microorganisms. This book can be viewed as a theoretical framework on the paleodiseases of microbial etiology. Because the book is fun to read, readers will not tire of reading from chapter to chapter; there is food for thought at every page.

The book is divided into three parts comprised of 18 chapters and a roundtable discussion. Following the intro-

ductory chapter (by I.R. Cohen), Charles L. Greenblatt, also the editor of the book, presents an excellent overview in Chapter 2 in which he describes and outlines the questions posed by the contributors and the contents of the book. This chapter is central to setting the stage for what follows. His description of the Ancient DNA III Meeting held in Oxford, where only 3 of 50 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 of 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.

Doctor Greenblatt is correct in posing a series of questions to the prospective reader after his brief but accurate preamble on the evolution of symbiosis, parasitism, and virulence. These questions appear simple and even obvious, but it becomes clear that the serious student of ancient DNA and paleobiology must adapt a certain way of thinking to find the answers to these questions. If nothing else, this book makes the reader aware of this fact. Here is a sample 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 that may affect planning for the developing of a new vaccine?" "Did the tubercle bacillus possess the gene for streptomycin resistance before the use of the antibiotic?" 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—presently an area of intensive investigation. 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, introduces the reader to diseases 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. Doctor Ubelaker (Chapter 10) does an excellent job of educating us on the field of paleopathology and the need for a new educational paradigm in this field. This part of the book clearly shows that the study of aDNA and paleobiology will require the development of a new terminology, improved techniques for diagnosis, and better training in the interpretation of disease processes in ancient tissues.

In the last part of *Digging for 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 of paleobiology must appreciate the chemistry of the markers, such as DNA, as well as of the body sites from which they can be retrieved.

Doctor 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 of 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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