Paleodermatoses: Lessons learned from mummies

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Mummies, the preserved remains of living beings from former times, bear witness across millennia to the maladies plaguing humankind. Disease, older than humanity, is better understood when examined in the context of history. Paleopathology, literally meaning “ancient suffering”, is the study of disease through evaluation of ancient remains. This area of increasing medical interest offers insights into the management of public health issues and disease epidemiology. This article provides an introduction and overview to paleodermatology, the branch of dermatology concerned with the evaluation of diseases associated with the integument by examination of ancient human remains. Mummy sources, how they were made and used throughout history, and the multidisciplinary approach used to study skin diseases found in mummies is briefly described. Despite pervasive pseudopathology, a remarkable array of diseases are well substantiated in the paleorecord, including infectious, heritable, nutritional, hormonal, acquired, iatrogenic, and neoplastic disorders. Legitimate ethical concerns have been raised in the use of human remains for any purpose, with the lack of informed consent eliciting accusations of exploitation. While these studies are undertaken with certain risks, such as the acquisition of potentially dangerous or extinct infections, paleodermatology offers a unique and historical perspective on the afflictions of the skin and the way of all flesh. (J Am Acad Dermatol 2004;50:919-36.)

“Far from being mute, ancient remains bear eloquent testimony to those who know how to listen.”

A mummy is a human or animal corpse (soft tissue and skeleton) preserved from decay, either naturally or artificially by embalming. The etymology of mummy is something of a historical accident. Early visitors to Egypt, observing mummies coated by a black, tarry resin, erroneously presumed that they were preserved by being dipped into pitch.2 The Persian word mummia, signifying wax, pitch, or bitumen, was thus ascribed.3 While mummies have been in existence for thousands of years, and certainly humans have been digging them up for almost as long, most of the scientifically valuable information derived from mummies have been accrued in the last century. Paleomedicine (palaios is Greek for old) is the medical field of observation through evaluation of ancient human remains. This field offers information of medical and historical significance.

Albert Kligman used the term “paleodermatology” to refer to anything done by dermatologists before the advent of hydrocortisone.4 I propose an alternate definition. In line with the definition of paleopathology coined by the ‘father of modern paleopathology’, Sir Marc Armand Ruffer,5 paleo-dermatology is the study of the integument and associated diseases as demonstrated in the remains of former times. One might arguably extend this definition to include literary and artistic substantiation of disease in former times. Such evidence, however, is indirect and less reliable, and therefore, not the subject of this article. Here reviewed are published findings relevant to paleodermatology.

WHY STUDY MUMMIES?

While mummies have always attracted public attention, writing about mummies is hardly a sound tactic for a young dermatologist trying to build a clinical practice or garner academic grants. Still, “...the nature of diseases prevalent thousands of years ago... is not solely of academic interest, but is of practical importance, for in many instances the eradication of disease may not be achieved until the way in which it evolved has been determined.”

Through studies of preserved remains, insight has been gained into the management of public health
issues, disease epidemiology, and medical practices of the past. For instance, the paleo-record attests to the prevalence of bilharzia in ancient Egypt, with coprolites (mineralized feces) containing *Schistosoma hematobium* larvae and eggs recovered from mumified human corpses and cesspits dating back over 3,000 years. With the institution of modern irrigation upon the building of the first Aswan Low Dam in 1902, an expanded habitat for the freshwater snail vector of schistosomiasis resulted in an epidemic. Another bilharzia epidemic was experienced upon the building of the second Aswan High Dam, with *Schistosoma mansoni*, more pathogenic to humans, becoming dominant since the 1960s. Similarly, the paleorecord confirms that land clearance for agricultural use and dense human settlements produced an environment favorable to the *Anopheles* mosquito, vector for *Plasmodium falciparum*, resulting in an increase in malaria in endemic areas. Understanding the historical patterns of these diseases might help to predict and prevent outbreaks.

Paleopidemiologic data have also been gathered on the effects of industrialization on public health. In a study of 273 mummies from an upper class population of ancient Egypt's New Kingdom period (1550-1000 BC) found in the Tomb of the Nobles, researchers noted an increased incidence (compared with modern day rates) of premature death, chronic disease, infection, dental caries, and accidental and violent trauma, especially in females. Finally, mumified remains harbor evidence of ancient medicinal and surgical skills, such as the greatly lauded skills of ancient Egypt, the knowledge of which might enlighten us even in our modern day. Thus, by studying our past, we may learn from our mistakes and strive to improve the future of humanity. For, as was most poignantly stated: “Those who cannot remember the past are condemned to repeat it.”

Paleopathology relies on a multidisciplinary approach. Dermatology offers unique insights in evaluating paleopathologic findings. For instance, the many blackheads on the face of Ramses II are not likely to be an indication of his dislike for washing, but rather a manifestation of chronic sun damage. Similarly, the 34 cm horn found overlying a 2.5 cm parietal bone defect obtained from a 74-year-old woman’s remains is not likely to be a burst sebaceous cyst, but rather, a large neglected squamous cell carcinoma. Likewise, the suggested diagnosis of Sneddon-Wilkinson’s disease based on histopathologic findings of neutrophilic pustules on an Egyptian mummy disregards more likely entities in the differential diagnosis and relies heavily on specula-

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One cannot discuss the value of paleomedicai studies without considering the ethical pitfalls involved in the study of mummies. This issue has received only cursory attention in the medical literature, with the rights and access to ancient materials remaining a source of controversy. Recent legislation, such as the Native American Graves Protection and Reparation Act in 1990, resulted in a dramatic tapering off of human remains exhibits. This, however, fueled further controversy, with accusations of an apparent double standard at the many American museums continuing to exhibit human remains from elsewhere. Universities sensitized about these issues have in some cases re-interred bodies. While paleopathologists argue the potential health benefits from this research, scientists have not always shown due respect in handling human remains, with reports of body parts being used crudely as souvenirs even in our modern day. Media humor reflects this, with former President Clinton’s comments about the well-preserved remains of Juanita (a sacrificed Inca girl) that if he were single, he “might ask that mummy out.” The Egyptians imposed great importance on their bodies. Can the knowledge acquired through these studies offer sufficient “benefits” to justify the intentional disregard of the wishes of these ancient peoples? Any societal benefits and “literary immortality” obtained through these studies of human remains may seem to us a worthwhile compromise, but may be completely antithetical to the wishes of the deceased.

Beyond ethical concerns, the study of mummies may actually pose a health risk to society. Such concerns, for instance, of the potential risk posed in working with tissue containing live tubercle bacilli have limited studies of pre-Columbian mummies. These concerns are further explored in the discussion of smallpox.

Mummies have been classified as accidental, intentional, or artificial. Accidental mummification involves the unexpected mumification of remains as a result of nature’s chance circumstances, such as heat, cold, or chemical soil composition. Intentional mumification involves the purposeful preservation of human remains by enhancing natural processes involved in the mumification. Artificial mumification involves purposeful preservation of remains by unnatural means, including embalming or the emersion in preservative fluids. Successful preservation of a mummy is not dependent on its age, but rather depends on the growth of bacteria and fungi, tissue desiccation, freezing, an anaerobic environment, exposure to antimicrobial agents, and the
and Ming Dynasty “wet mummies” are unique in that they were embalmed in mercury. Japanese 17th-19th century Buddhist priests intentionally abstained from certain foods during the last years of life to promote post-mortem mumification.

The “bog bodies” of Northern Europe were preserved naturally, with skin tanned to leather by the peat, where the anaerobic, acidic environment of sphagnum moss prevents microbial growth. Many bog bodies, some intentionally and some accidentally mumified, show evidence of violent, even sadistic deaths at human hands. The Incorruptibles are a unique group of over 100 mummies of Christian saints. These preserved bodies, some mumified incidentally and some intentionally, were capitalized upon to inspire the faithful and advance the church’s political agenda. The Pantheon collection of 119 naturally mumified remains in Guanajuato, Mexico was assembled in 1896 when perpetual care fees were not paid. The dramatic display at a local museum of these disinterred cadavers was described as a “little shop of horrors.”

A curious form of mumification is known as adipocere, grave wax, mortuary fat, or corpse cheese. Composed predominantly of 10-hydroxystearic acid, adipocere is a by-product of the natural process of chemical soft tissue decomposition similar to saponification. Adipocere forms only under alkaline, humid, and cool conditions of low oxygen tension in bodies buried under water, or in moist crypts or caves. Adipocere is more common in babies, females, and obese corpses. While not uncommon to find some adipocere on corpses, it is rarely a complete process. Today’s modern embalming practices result in improved tissue preservation and greater adipocere formation. (Thus, people may become ‘incorruptible’ in death, something they may never have achieved in life.)

The best known and studied mummies are those from ancient Egypt. Only a few thousand of the theorized 70 million Egyptian mummies have been found, with more being exhumed every year. In Egypt, the process of intentional mumification was first developed around 2600 BC as a solemn expression of their religious belief that the human spirit cannot exist after death if the physical body is destroyed. Ironically, it is mostly the Egyptian climate, rather than the lauded skill of embalmers, that is responsible for mumification. In fact, the oldest known Egyptian mummy, Ginger (circa 3500 BC), was created incidentally. The Egyptians first mumified their royalty, and with time, increasingly the upper and middle class, until the process became almost universal by Ptolemaic times (circa 330 BC).

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**Table I. Principal regions where mummies have been found and estimated dates of origin**

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<th>Region</th>
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<td>Andes (4000 BC-1700 AD)</td>
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<td>Egypt (2600 BC-present)</td>
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<td>Southwestern United States (500-1400 AD)</td>
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<td>Aleutian Islands and Alaska (600-1700 AD)</td>
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<td>Japan (1100-1900 AD)</td>
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<td>Australia and Melanesia (1800 AD)</td>
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The process of mummmification in Egypt evolved into a 70-day multistep process, with the methods varying from dynasty to dynasty, but also between clients, based on affordability. The body was eviscerated through a left abdominal incision, with the stomach, liver, lungs, and intestines placed in Canopic jars and buried with the mummy. The brain was removed via a trans-sphenoidal approach used by neurosurgeons today. The corpse was dehydrated for about 5 weeks under hundreds of pounds of dry natron, a naturally-occurring salt. The body was then washed and anointed with a fragrance designed uniquely for each mummy. Finally, the mummy was wrapped in over 375 m² (about 20 lb.) of linen strips derived from anything from old sheets to ship sails and placed in a sarcophagus, where it was intended to rest undisturbed forever. Ironically, despite great efforts taken to protect the bodies, the remains of many of the ancients were disturbed soon after their interment. Over centuries, grave robbers broke into tombs and tore apart mummy remains in their eagerness to obtain valuable artifacts, jewelry, or amulets. Medicinal properties were ascribed to bitumen and mummies about 800 years ago, with mummy trading becoming popular. While Paracelsus used the word mummia to express natures power to heal disease, this “medicine” made people sick, and ultimately fell out of use. Artists used mummy powders for hundreds of years in their paintings. The Canadian 19th century paper industry was reported to have imported thousands of mummies for use of their linen wrappings in the manufacture of high quality paper. A contemporaneous cholera epidemic caused a public outcry and an abrupt halt to the manufacture of paper from mummies. While the burning of mummies for light and heat in ancient Egypt is well established, the reported use of mummies to fuel the Egyptian railway in Mark Twain’s writings remains unsubstantiated. Finally, in the 18th and 19th centuries, Egyptian mummy “unwrapping” performances were popular social events feeding the public’s “primitive urges for gruesome thrills,” with parts kept as souvenirs or simply thrown out with the trash. Findings at these events were not recorded in any manner of scientific value. Only in the past century have more standardized and scientific approaches to the study of mummmified remains been developed.

While many interesting paleomedical observations have been made, a healthy dose of skepticism is appropriate in considering reported findings. Many accounts of pseudopathology secondary to diagenesis (physical or chemical changes occurring after death) are recorded in the literature. Elevated soil pressure, poor drainage, and acidic soil conditions have resulted in long bone decalcification and warping falsely suggestive of rickets. Similarly, beetle and rodent gnawing at skulls has resulted in “rodent ulcers” suggestive of antemortem disease or trauma. In many cases, only where bone healing can be detected is it possible to ascribe damage to a disease process affecting the living. Putrefaction secondary to anaerobic gas-forming bacilli colonization of postmortem tissue caused pseudoerection, pseudohernia, and protrusion of the tongue, uterus, or rectum. The grotesque facial expressions of many mummies are the product of rigor mortis and are not true to life. Degenerative changes in bog body mummies can resemble clostridial gas gangrene. In “pink teeth phenomenon,” pink dental color is thought to be secondary to postmortem blood congestion and autolysis in dentinal tubules, not Gunther’s disease. Mortuary practices, such as excessively tight ropes around mummy wrappings causing tumor-like bulges and body part substitution by Egyptian embalmers, also cause pseudopathology. Thus, a critical and cautious open mind is important in reviewing these reports.

METHODS OF STUDY

“A mummy can be a scientific treasure chest; to unlock its secrets, a multidisciplinary approach is needed.”

Bones and teeth are the most enduring of human remains and are therefore the most informative, with measurements providing information about sex, age, stature, health, parity, and race of the individual. Over a century ago, necropsy and radiography, under standardized conditions, were among the first paleopathologic methods introduced. Computed tomography (CT) has proven invaluable in mummy studies, allowing for the study and preservation of unopened mummies. Using CT data with forensic facial reconstructive technology, 3-dimensional facial reconstruction has become possible and has been applied to such famed royalty as Ramses III and Seti II of ancient Egypt, King Philip II of Macedon, King Midas of Phrygia, and Johann Sebastian Bach. Magnetic resonance imaging (MRI) is not usually possible on mummmified remains due to dehydration and the resulting lack of sufficient hydrogen traces to obtain image data.

Histologic studies have been carried out on desiccated mummmified tissues obtained by necropsy or endoscopy, revealing good preservation of the epidermis (corneum, keratin, melanin, and nuclear caps), pilosebaceous structures, reticulum fibers, blood vessels, and subcutaneous fat. There is
been demonstrated by EM, including smallpox, agents from human remains and coprolites have preservation over a 2000-year period. Even bog mummies, which lose epidermal cellular details, show excellent collagen fibril preservation over a 2000-year period. (How ironic, when you think of the effort and money spent nowadays in search of maintaining a youthful dermis.) The architectural preservation of the skin has, in several cases, been so good as to allow for the visualization of fine details, such as eccrine orifices and fingerprints. Histopathologic features of numerous diseases have been demonstrated in mummies.

Immunologically and enzymatically intact proteins have been isolated from mummies dating back as far as 2500 BC. Immunofluorescence has been used to demonstrate pathogens such as Treponema pallidum and Trypanosoma cruzi. Immunohistochemical detection of collagen I and III triple helix domain epitopes has been described in a 1500-year Peruvian mummy and the 5300-year-old Tyrolean iceman. Enzyme-linked immunosorbent assay (ELISA) has identified a variety of infections of medical relevance, including treponemes in the 3000-year-old bony remains of a native North American, and Salmonella and Helicobacter pylori from 3000-year-old coprolites from South American mummies. Serological studies of blood group antigens have successfully affirmed kinship, such as that of Tutankhamen and his supposed brother Smenkhkare. Serological analyses using gas chromatography/mass spectrometry (GC/MS) have demonstrated preservation of protein and lipid components from mummified tissues and have been useful in reconstructing dietary components.

While initial electron microscopy (EM) findings reported in mummified skin were misleading, EM and scanning EM have been successfully applied to the study of skin ultrastructure. Infectious agents from human remains and coprolites have been demonstrated by EM, including smallpox, T pallidum, M tuberculosis, Strongyloides stercoralis, Diphyllobothrium latum, Enterobius vermicularis and Trichuris trichiura. Both Leishmania amazonensis and Borrelia burgdorferi were identified from their respective mummified arthropod vectors. EM studies of the Inuit Greenland mummies demonstrated collagen indistinguishable from that of living human skin. Blood cells have been demonstrated in ancient Egyptian and Chilean remains by EM, with ABO antigens verified by serology. Molecular biology is revolutionizing archaeology and paleontology.

“The young science of molecular archaeology provides the first absolute check on inferences drawn from the genetics of modern populations…we can now dream of catching molecular evolution red-handed.”

Ancient DNA from plants, animals, and even coprolites have been successfully used to study historic human, Neanderthal man, and extinct life from a time before history. Polymerase chain reaction (PCR) has been useful in sex determination, population migration, and kinship studies of peoples buried thousands of years apart. PCR has also been used in the identification of diverse disease agents, like smallpox, M tuberculosis, Mycobacterium leprae, T cruzi, T pallidum and Yersinia pestis. Molecular paleontology, however, is fraught with pitfalls. Numerous papers were greeted with skepticism when rigorous criteria of authenticity and contamination precautions were not met. Ancient tissues often have little to no DNA surviving after years of preservation, as is the case for bog bodies. Mummies typically have less than 1% undamaged DNA, with sequences >150 base pairs likely to be contaminants from an environment pervasive for contemporary DNA. Most DNA fragments retrieved from mummified ancient materials are mitochondrial or repetitive sequences (such as Alu repeats), since the odds of survival are best for these multi-copy DNA sequences.

### PALEODERMATOLOGY

Many diseases of the integument have been identified in mummies (Table II). Chronic infectious diseases are second only to orthopedic injuries in offering the most definitive disease substantiation in mummies. In paleomedicine, an “osteological paradox” prevails, where the most abnormal skeletons result from chronic disease in the most robust individuals, whereas normal skeletons belong to weaker individuals who die from acute illness. Unfortunately, most acute infections resulting in major history-altering epidemics, such as cholera, typhoid, and dysentery, leave no imprint on bones.

### Infectious diseases

Of the infectious diseases, treponemal infections are ideal for study in mummies because of the chronic nature of the infection and the characteristic skeletal changes. Infection by treponemes is thought to be an early event in human history, with pinta proposed to have evolved about 15,000 BC and
evidence of yaws dating back 8000 years.\textsuperscript{103} Whereas nonvenereal treponemes are diseases of the simple village, syphilis is comparatively new (about 2000 years), having evolved with the development of advanced urban life.\textsuperscript{103,104} Thus the expression: “civilization means syphilisation.”\textsuperscript{105}

Discussions regarding the origin of syphilis are among the most heated and long-running debates in the history of medicine, with multiple theories pro-
posed. According to the Columbian theory, paucity of Old World skeletal changes consistent with syphilis implicated the New World as the origin of the disease, with Columbus’s sailors bringing this previously unknown disease back from America to the Old World.106 There is, however, some limited evidence of treponemal changes in skeletons dated prior to 1492 AD in Britain and France, confirming its existence in the Old World before 1492.106 Furthermore, the absence of evidence of congenital transmission of the disease in pre-1492 North America argues that this treponemal disease was not the same venereal form we know today.106 A pre-Columbian theory was proposed, where syphilis existed in Europe before Columbus and was misdiagnosed as leprosy.106 Thirteenth and 14th century literary references to a highly contagious form of ‘venereal leprosy’ with short incubation periods, and later, to ‘heritable leprosy,’ probably were syphilis, since these features are unknown in leprosy today.107 Furthermore, reportedly effective treatment of 12th-13th century ‘leprosy’ with mercury-containing saracen ointment also suggests misdiagnosis, since mercury is ineffective in leprosy, but was the only remedy available against syphilis for centuries.108 A unitarian theory of syphilis has been expounded, in which a single and extremely flexible disease is responsible, whose permutations are directly related to climate, clothes, hygiene, sanitation, and sexual customs.109 A contrasting nonunitarian theory was proposed, where at least 4 mutations were theorized to have occurred in treponemal strains over the last 10,000 years.110 According to this theory, a final mutation in late 15th century Europe resulted in the most virulent venereal form of syphilis causing the epidemic around the time of Columbus’s return from his trans-Atlantic voyage.106,110 An alternative hypothesis proposed that syphilis originated in Africa, with endemic treponemes, originally acquired from apes, brought back to Europe by the Portuguese during the Age of Exploration.106 Some researchers have even suggested that the post-1492 syphilis outbreak was caused by an HIV-like immunosuppressive agent, causing an uncharacteristically severe variant of syphilis, lues maligna.106 With no biological test available to distinguish between the treponemes and diagnoses based on several non-pathognomonic bony changes, resolution of this debate is still elusive.

Skeletal evidence for tuberculosis in the Old World, with destructive spinal lesions characteristic of Pott’s disease, exists dating back to circa 4500 BC.111 While artistic and literary evidence of tuberculosis predate skeletal evidence by 1500 years, this information is indirect and inconclusive.26 Macroscopic, histologic, and molecular diagnosis of tuberculosis in bone and lung tissue specimens of ancient Peruvian and Egyptian origins have been published.20,82 Experts ponder the finding of tuberculosis in mummies of the New World 500 years before its widespread distribution to Europeans.82 Tuberculosis is well recognized in many mammals, having caused numerous zoo epidemics.112 The evidence suggests that tuberculosis did not exist as a human disease before the period of animal domestication, when a strain infecting dairy cattle is theorized to have mutated to the form infecting humans today.20,82,91,111,113 Prior to the antimicrobial era, skeletal lesions were relatively prevalent in persons infected with tuberculosis (7%), allowing for their study.114

Skeletal evidence of leprosy dates back more recently than tuberculosis. Earliest literary references to leprosy suggest the disease originated in 700 BC in China or India, whereas the earliest paleopathologic evidence for leprosy has been found in Egyptian remains dating 500 years later in the 2nd century BC.26,115 The exact nature of the disease ‘Tsara’tahl’ (translated as lepro) referred to in early biblical references (about 1500 BC) is speculative.116-119 Studies of medieval leper cemetery material demonstrated that buried occupants were primarily those with advanced disease.120 These studies elucidate previously unappreciated bone changes of leprosy, such as the rhinomaxillary syndrome (paleopathologic skull deformities underlying Bergen syndrome/facies leprosa found only in lepromatous leprosy).119,121 While in vitro culture of leprosy has repeatedly failed,107 a leprosy-like disease has been identified in rats, with theories proposed, as in tuberculosis, that a mutant form infected ancient humans.119

Leprosy is described in archeological finds into late medieval times, reaching an estimated prevalence nadir of 1 in 200 persons, but then disappears from the paleorecord.122,123 It has been speculated that the onset of the ‘Little Ice Age’ in the mid-16th century, when people wore more clothes, limited leprosy transmission in that time, with a resultant absence of leprosy from the more contemporary paleorecord.97 Alternatively, the decline of leprosy concurrent with the increase in tuberculosis has been speculated to result from cross-immunity to the more virulent tuberculosis.124 The osteoarcheological record supports this theory with rare evidence of both tuberculous and leprous lesions in the same skeleton.125 Historically, tuberculosis was reported among leprous patients as a major cause of death in modern leprosy hospitals, whereas leprosy rarely developed in tuberculous patients.118
Several mummies with evidence of variola have been reported, spanning thousands of years of history.\textsuperscript{80,126-128} A singular case of osteomyelitis secondary to smallpox, a rare occurrence, was detected by PCR in 17th century remains.\textsuperscript{129} The most famous suspected case of smallpox was noted on the mummy of Ramses V of Egypt’s XVIII Dynasty.\textsuperscript{126} While the lesions seemed consistent, the diagnosis was contested by Unna.\textsuperscript{130} By special permission of President Anwar el-Sadat, both EM and radioimmunoassay studies were conducted on specimens obtained from the well-preserved mummy.\textsuperscript{131-134} While failing to detect virus, these studies do not rule out the diagnosis. More importantly, these studies brought to the fore the question: are archeologists and anthropologists who handle incompletely decomposed bodies at risk of unknowing exposure to smallpox? Experimentally, scabs have been shown to remain infectious for up to 13 years, with survival affected by temperature and humidity.\textsuperscript{135} In Somerset, England in 1759, several days after burial of a man in a grave next to a smallpox victim from 30 years earlier, the whole village was stricken with smallpox.\textsuperscript{136} Conversely, recent studies of frozen remains in Koltsovo, Russia failed to isolate live virus.\textsuperscript{137} Similarly, EM confirmed nonviable virus in mummified remains of a 100-year-old body from a London church crypt and a 400-year-old Italian mummy.\textsuperscript{51,138} Given the inconclusive data and theoretical possibilities of retained viral viability in exhumed cadavers, vaccination of investigators has been advised, although the circumstances have not been clearly defined.\textsuperscript{135}

Chagas disease has been demonstrated by EM and immunostaining in Chinchorro and Inca mummies from known endemic areas.\textsuperscript{95,139,140} The unique massive colon, esophageal, and cardiac dilation seen in Chagas disease has been documented in numerous incidentally mumified bodies from Chile’s Atacama desert, around 500 AD.\textsuperscript{139,141} The mummy of a 20-year-old from Tiahuanaco, Peru, sacrificed for the purpose of obtaining entrails for divinatory purposes, had generalized wart-like papules consistent with the \textit{verruga peruana} phase of Carrion’s disease.\textsuperscript{142} Giemsa stain and EM demonstrated the flagellate organisms \textit{Bartonella bacilliformis}.\textsuperscript{142} The devastating acute phase of this disease, termed Oroya fever, has been credited with the collapse of the Aztec empire.\textsuperscript{122} \textit{Coccidioides immitis} spherules and endospores have been histologically identified within skeletal remains of a pre-Columbian Sinagua adult male Indian from Arizona, circa 1000 AD.\textsuperscript{143} The earliest case of paracoccidiomycosis was substantiated in the remains of a mummiﬁed middle-aged woman from northern Chile around 290 AD, with histology and EM conﬁrmation of the organism \textit{Paracoccidiodes brasiliensis} in lung, lymph node, and kidney tissues.\textsuperscript{144} Leishmania has been documented by rodent taxidermies and not uncommonly in mummiﬁed South American skulls with uita-lytic facial lesions.\textsuperscript{8,145-147} Two Eskimo mummies with disseminated chronic granulomatous lesions suggestive of healed histoplasmosis have been described.\textsuperscript{21,148} Several possible cases of North American blastomycosis have been reported in early American Indians.\textsuperscript{114}

The first reported case of actinomycosis was described in the body remains of a 30-year-old man excavated in southern Ontario burial grounds circa 230 AD.\textsuperscript{149} Rare in modern day, actinomycosis is thought to have been more common in the past, but paleopathologic proof of this difﬁcult to isolate organism is limited.\textsuperscript{149}

Bony evidence suggestive of Madura foot was excavated from the Byzantine period (300-600 AD) in Israel.\textsuperscript{150} This condition is rare in modern-day Israel, with this case suspected to have emigrated to the region via known trade routes of the time.\textsuperscript{150}

Human T-cell leukemia virus type 1 (HTLV-1) retrovirus, closely related to the virus infecting modern Japan, has been identiﬁed by DNA analysis from 104 Chilean mummies, approximately 1500 years old.\textsuperscript{151} This ﬁnding supports the theorized but controversial Asian invasion and colonization of South America long before the Spanish conquest.\textsuperscript{151}

The mummy record suggests that parasitic infections (schistosomiasis, trichinosis, strongyloidiasis, ascariasis, dracunculosis, and echinococcosis) were among the most prevalent diseases in ancient Egypt.\textsuperscript{42,45,86,152} Malaria has long been suspected as an early agent in our paleopathologic history, with \textit{P. falciparum} antigen detected in an ELISA study in 7 of 18 Egyptian/Nubian mummies aged 1500-5000 years.\textsuperscript{153}

A destructive ulcerating facial lesion consistent with \textit{cancrem oris} (Noma) in an Egyptian mummy, has been described.\textsuperscript{154} Bubonic plague and \textit{B. burgdorferi} have also been described in mummiﬁed remains.\textsuperscript{97,155}

**Genetic diseases**

Genetic diseases are well represented in mummies, with diseases resulting in bone abnormalities, again, offering the best fossil record. An Egyptian mummy, excavated in 1907, initially thought to be a monkey, was subsequently identiﬁed as the remains of a XXI Dynasty human infant affected by \textit{osteogenesis imperfecta} (OI).\textsuperscript{156-158} A ‘tam-o’-shanter’ deformity of the reconstructed skull cliniﬁed the diagnosis.\textsuperscript{157,158} The amber color teeth and disproportionately small
crown was consistent with *dentinogenesis imperfecta*, commonly seen with OI. Two Egyptian skeletons of the Dynastic Period with findings consistent with basal cell nevus syndrome (Gorlin-Goltz syndrome) have been described. Supporting evidence includes odontogenic cysts, bifid ribs, incompletely fused sacral laminae, brachymetacarpalia, and occipital asymmetry. Several cases of ankylosing spondylitis have been reported in ancient Egyptian skeletal remains. An early 19th century British male skeleton showed bony changes characteristic of neurofibromatosis. Polyostotic fibrous dysplasia (McCune-Albright syndrome) has been described in the ancient remains of a prehistoric American Indian, with asymmetrical skeletal changes consistent with hyperparathyroidism. The mummy of an achondroplastic woman with her undeliverable fetus has been described. A mummified infant with Down syndrome was found among the Inuit mummies from Greenland dating from the 15th century. Based on the findings, the infant had apparently been allowed to die of exposure.

A thyroglossal duct cyst has been observed in the remains of a young male in a 13th century Greek cemetery. An Egyptian mummy with torticollis has been reported. Probable cases of Crouzon’s syndrome in a medieval child from Sant Miquel de Cardona and a Nubian child, respectively, have been described. Anencephaly with *aplasia cutis congenita* has also been reported in an Egyptian mummy from the catacombs of Hermopolis. *Spina bifida occulta* is frequently reported, whereas *spina bifida aperta* or *cystica* is very rare. High frequencies of *spina bifida occulta* have been found in several populations, including remains from prehistoric Taforalt, Morocco (10,000 BC), Lake Titicaca, Peru (400 AD), and Guanche of the Canary Islands. Such high occurrence rates suggest inbreeding, biocultural isolation, and autosomal dominant inheritance.

The high prevalence in arctic mummies of *torus palatinus* and *torus mandibularis* (bony oral outgrowths) have spawned theories regarding a possible connection with strongly developed masticatory musculature. Studies of the prevalence of heritable tori in Chilean mummies have been used in population migration analyses. The absence of frontal sinuses in Inuit Greenland mummies is another interesting reported finding.

Steatopygia, also known as Hottentot bustle (protrusion and excessive fatness in just the buttocks region), is a common heritable trait in living and ancestral remains of the Khoisan Hottentot people of southwest Africa.

In several Egyptian mummies, alkaptonuria was suspected because of the characteristic skeletal disc pigmentation and radiologic findings. Gel filtration and spectral analysis of intervertebral black deposits demonstrated a pattern indistinguishable from ochronotic pigment. Subsequent NMR/IR spectral analysis of the pigment provided images different from homogentisic acid, but identical to that of natron used in Egyptian embalming. To date, no chemically confirmed cases of true ochronosis have been published in the paleoliterature.

**Endocrinologic disorders**

Several endocrinologic disorders have left their mark in the paleorecord. Acromegaly has been described in an Egyptian skull. Hypothyroid goiter was reported in a Peruvian mummy dated circa 100 BC. Findings suggestive of diabetes mellitus in human remains spot the literature, including soft tissue ulceration and bilateral gangrenous toes.

**Nutritional disorders**

Nutritional disorders are also described in the paleoliterature. Harris lines, radiologic opaque transverse lines on long bones, similar to Beau’s lines of the nail plate and Pohl-Pinkus constrictions of the hair shaft, represent recovery from malnutrition or generalized disease. Harris lines are more prevalent and numerous in females than males in aborigines from the Canary Islands, suggesting their secondary role in Gauche society.

Hypervitaminosis A has been suspected in fossil remains of *Homo erectus* in Kenya, East Africa. While rare, several cases of scurvy have been documented based on CT findings of subperiosteal bone formation and evidence of periodontal disease in human remains. Studies of mummified remains of Dutch sailors killed in Arctic expeditions contributed to our understanding of the lesions of adult scurvy, with evidence of joint hematomas, long bone fractures, and blackened dental roots secondary to gingival hemorrhage readily evident. One study suggests that scurvy may have been the most common Scandinavian health problem in medieval times.

Rickets, rare in antiquity, has been termed a ‘disease of the twilight,’ a consequence of the crowded, smoke-filled, perpetual dark tenements of city...
slums. Rickets can be identified in mummies by the bent long bones, costochondral nodules (rachitic rosary), and pelvic, dental, and skull evidence of disease. The unexpected finding of several Egyptian female skeletons with rickets is speculated to relate to the cultural practice of shrouding women when outdoors. Many cases of rickets were found from the Baltic and North Sea areas dating back to the early Iron and Bronze Age, with peak ‘epidemic’ levels found in 18th century Europe.

Porotic hyperostosis (cribra orbitalia) symmetrically involving the orbital bone has been documented in mummies, substantiating many cases of iron deficiency anemia. Interestingly, skeletons from pre-Neolithic times show no evidence of this disease, suggesting that in evolutionary terms, this is a recent phenomenon.

While the Egyptian ideal of beauty, as portrayed in their artwork, was that of an unrealistically thin and fit body mirroring the contemporary preoccupation with slimness, mummies of many of the pharaohs (e.g., Ramses III, Merenptah, and Thutmose II) harbor imbricated skin folds bearing witness to their previous corpulence. While the paucity of these findings suggests that obesity was uncommon in ancient Egypt, variable rates and degrees of post-mortem fat hydrolysis achieved in human remains limit our understanding. In fact, in a Peruvian mummy study, in only about half the cases could gender be determined based on breast tissue remains.

Acquired skin disorders

Acquired skin conditions have been described in mummies. Infantile eczema was described in the remains of a Utah Indian baby. Idiopathic acute vasculitis in a spontaneously mummified female from about 350 AD in northern Chile was reported. A case of hypertrophic osteoarthropathy from the Huu culture (about 1000 AD) with enormous thickened periostitis diaphyses most likely represents the primary idiopathic form of pachydermoperiostosis. Acquired cubbing in an adult male skeleton from a medieval Polish cemetery has also been described.

Facial senile comedones are prevalent in Egyptian mummies and may represent Favre de Racouchot disease. This is consistent with the documentation of light blonde hair color in Nubian mummies, as well as long bone and skull measurement studies demonstrating that the ancient Egyptian peoples were of mixed racial/physical types.

Both rheumatoid arthritis and psoriatic arthritis are rare and difficult to distinguish from other joint diseases in the archeological record. The most famous example of rheumatoid arthritis is in the mummy of Ramses II. Skeletal remains of a 30-year-old woman with changes consistent with late findings of Still’s disease (juvenile rheumatoid arthritis) were found on Kodiak Island, Alaska. A single case of probable Reiter’s syndrome has been described in the 9th century skeletal remains of a 40-year-old man from the Netherlands.

Classic tophaceous gout, with radiographic and chemical verification of urate crystal deposits, has been described in a male Egyptian mummy. Findings consistent with gout in 5.6% of 250 examined skeletons dated about 950-1450 AD from Guam are consistent with modern Pacific islanders markedly high prevalence of gout. Other acquired skin conditions described include skeletal sarcoidosis, varicose veins, plantar callus, foot ulcer, decubitus ulcers, frostbite, lichenoid eruption, and connective tissue disease.

Iatrogenic disorders

Iatrogenic disorders have been observed in mummies, with the pubertal male ritual of circumcision frequently demonstrated in Egyptian mummies, largely as a result of embalmers’ considerable efforts to preserve external genitalia. Castration and limb amputation with prosthetic replacement have also been found in exhumed Egyptian mummified remains. Extensive mummy evidence for trepanation (surgical removal of a portion of the skull vault) in the context of trauma, infection, or neuropsychiatric disease, is available from prehistoric South America, Neolithic Egypt, and western Europe. A significant percentage survived even multiple procedures, as demonstrated by the healing and bone remodeling around surgical sites. Osteological consequences of scalping have been described in the remains of an Arikara Indian who survived the experience.

The mummy of the 5300-year-old “Tyrolean Ice-man” harbored skin tattoos overlying joints with arthropses. These tattoos were in striking proximity to classical acupuncture points, implying that knowledge of the science of acupuncture was in use long before its previously known period of use in ancient China. The application of infrared photography, used today in dermatology to visualize photodamage, is effective in revealing mummies’ frequently faded tattoos. While no tattoos were found on Egyptian mummies, eye painting dating back as far as 4000 BC has been found. Kohl and malachite cosmetics were used for more than cosmetic purposes, with insect repulsion, photoprotection, and sun glare shielding kept in mind.
Paleopathologic findings of mercury poisoning can be subtle, with a case described in which dental enamel deposits in a renaissance Italian noblewoman were presumably the result of the then popular approach to treat syphilis.\textsuperscript{214}

**Neoplasms**

Neoplasms have generally been documented at a decreased frequency in antiquity.\textsuperscript{215,216} In experimental studies of mumification, it was found that both primary and metastatic tumors were actually better preserved than normal tissues.\textsuperscript{217} While exceptional studies exist,\textsuperscript{218} the paucity of tumor findings in ancient tissues implies a markedly lower incidence of tumors compared with modern society. A common explanation offered is that primitive people did not live long enough to get cancer. Studies of over 23 cultures, however, have shown that at least 40\% of the populations studied lived past age 40.\textsuperscript{135,146} A larger sample is needed to determine whether the incidence of neoplasia, skin and otherwise, was as low as it seems to have been in antiquity. If confirmed, industrialization would be implicated as a significant contributor to the increased incidence of cancer in modern times. This is in agreement with previously documented industrialization trends.\textsuperscript{219}

To date, at least 60 tumors have been described in mumified remains.\textsuperscript{218} Histologic confirmation is available for a squamous papilloma on an Egyptian female mummy’s hand,\textsuperscript{150} a histiocytoma on the heel skin of another Egyptian mummy,\textsuperscript{220} an angiokeratoma circumscripta on the leg of an Inca child sacrifice,\textsuperscript{221} and a lipoma.\textsuperscript{222} Dubious cases of an epidermoid cyst, hemangioma, plasmacytoma, actinic keratosis, squamous cell carcinoma, and poorly defined skin metastases have also been described.\textsuperscript{21,27,130,223,224}

Studies have found skeletal data suggestive of malignant rhabdomyosarcoma in two Peruvian mummies.\textsuperscript{225} Multiple lytic circular punched-out lesions in cranial bones from an American Indian infant are strongly suggestive of histiocytosis X.\textsuperscript{21} A solitary skull lesion consistent with eosinophilic granuloma has been reported.\textsuperscript{226} Leukemia and myeloma similarly have been suspected in skeletal remains.\textsuperscript{21} While in these cases, skeletal evidence is highly suggestive of cancer, histologic proof of malignant skin tumors in ancient materials is not available and these studies must be interpreted with caution. Reports of 9 pre-Columbian 2400-year-old Incan mummies with diffuse osseous metastases of melanoma is improbable, since no histological verification was provided (only descriptive information) and these data suggest an inexplicably high prevalence of this tumor.\textsuperscript{227} PCR application may afford us a deeper understanding of malignant neoplasia among the ancients. For instance, PCR detection of the activated K-\textit{ras} protooncogene was identified in a colon cancer specimen from the mummy of an Italian renaissance monarch.\textsuperscript{228} Interestingly, the observed K-\textit{ras} mutation is the most frequent mutation found in colon cancer today.\textsuperscript{225}

Hair has been dubbed “the keeper of history.”\textsuperscript{229} Hair and nails are frequently far better preserved than skin and soft tissue. Hair type identification has been possible based upon hair follicle angle and size.\textsuperscript{58} Hair only rarely decolorizes post mortem, and thus hair color can be determined in most cases.\textsuperscript{53} Preservation has been so good as to allow for hair-styles in Egyptian mummies to be described in detail.\textsuperscript{560} Furthermore, sex differentiation and seasonal shifts in diet have been elucidated by hair analysis.\textsuperscript{230} Baldness is a frequent finding among Egyptian mummies.\textsuperscript{160} Female hypertrichosis has been described in a mummy known as The Bearded Lady.\textsuperscript{251} Hair is amenable to x-ray fluorescent spectrometry for isotopic analysis of diet, nutritional status and exposure to trace elements.\textsuperscript{252} Nicotine, cocaine, hashish, arsenic, and the heavy metals, mercury and lead, have all been demonstrated in mumified hair.\textsuperscript{235-235} Comparative paleopathology has demonstrated a greater than 100-fold increase in hair lead levels in human remains since the beginning of civilization.\textsuperscript{236,237} Toxic lead levels (plumbism) reaching epidemic proportions were verified by hair and bone analysis (by radiographic lead lines at long bone epiphyses) in early Roman mummies, circa 400 BC.\textsuperscript{238} This coincides historically with the onset of extensive lead ore mining, with dangerous levels imbibed in acidic wines, which efficiently leach lead out from the pewter containers in which they was stored.\textsuperscript{138} Saturnine gout, a consequence of plumbe, was also described among most of the Roman emperors.\textsuperscript{239} Thus, it is conjectured that among Roman aristocracy, notorious for its abuse of wine, tales of the madness of Caligula and erratic behavior of Nero and many others were due to neurologic manifestations of lead intoxication, and may have ultimately contributed to the fall of the empire.\textsuperscript{239}

The reports of cocaine and nicotine in hairs from dozens of 3000-year-old Egyptian mummies, including that of Ramses II, has baffled scientists. While it is known that the Egyptians grew hemp (the source of hashish) and the blue lotus flower, cocaine and nicotine came from the New World, and were not introduced into the Old World until the 15th century AD.\textsuperscript{42,240-242} Using the GC/MS, high levels of these drugs were elicited in The Cocaine Mummies, a finding deemed inconsistent with contamination.\textsuperscript{245}
This discovery has opened new and unresolved controversy regarding the possibility of transatlantic contact with South America 500 years before the accepted Viking contact with the New World. The detection of arsenic in hair retrieved from Napoleon’s corpse supports theories of his murder.229 Nits and/or head lice have been found on mummies from ancient Egypt, prehistoric southwest American-Indians, pre-Columbian Peruvians, mummies from the Aleutian islands, Peru, Greenland, Mexico, and Inca sacrifices, and on Neolithic hair combs from Israel.244-248 The oldest intact Pediculus humanus egg recovered dates back 10,000 years, with infestation prevalence as high as 44% in a small North American Indian mummy series.249 Considered by many to be an ancient disease that evolved from a louse species infecting monkeys, prevalence increased with crowded housing, in populations such as the Chiribaya mummies of southern Peru, whereas open nomadic hunter-gatherer populations remained relatively louse free.246,250 Studies of Peruvian mummies demonstrated that despite the apparently effective therapeutic modalities available at the time, infestations became more severe as a chronically ill person neared death.249,251 Very heavy head lice infestations were documented in the Greenland and Xinjiang mummies, with nits deposited as much as 20 cm from the hair root indicative of a long-lasting cohabitation and perhaps, poor hygiene.252 The finding of nits in corporets from the Greenland mummies is thought to reflect their efforts to eradicate the vermin.252 Herodotus commented on the eating of head lice by a central Asian population in the fourth century BC.244 Nit combs, full body shaving, and the wearing of wigs were implemented by ancient Egyptian priests to manage infestations.253 Interestingly, I could find no paleoliterature on body or crab lice, although plague and other body louseborne illnesses played a prominent role in human history.252

Little research has been done on mummy nails, although they are durable. Beau’s lines of the nail plate, a presumed consequence of cyclic anemia from trichuris infection, has been reported.254 Mee’s lines (transverse leukonychia) secondary to arsenic poisoning have also been recognized in mummified remains.186 Nails are also informative of ancient occupations, with patterns of wear on the nails of the fishing Inuit confirming their vocation.31

Paleodontology is mentioned since teeth, harder than bone, provide a most enduring physical record. Linear dental enamel hypoplasia, like Beau’s lines, serves as a permanent record of acute episodic malnutrition or other physical stress.255 Teeth are one of the best indicators of age.255 Among the Inuit, teeth were heavily worn down by their practice of chewing seal skin.31 The presence of sand in crudely prepared food is responsible for dental abrasion among the ancient Egyptians and the Chinchorro.256,258 Generalized dental attrition found in dynastic upper class Egyptian mummies is linked with dietary intake of honey, sweets, and beer.257 In the 2800-year-old remains of Djedmaatesankh studied by CT scan, severe dental disease was presumed to have resulted in her premature death.256 Conversely, the Greenland and Chinchorro mummies diet of seafood, lacking free sugars, is reflected in their absent dental decay.

CONCLUSION

While the ancient literature, hieroglyphics, and art abound with references to skin diseases, the study of human remains offers singular scientific proof of previously described or suspected medical conditions. With modern societies’ increasing respect of interest in the management of excavated mummies, and with the benefit of advancing technologies, we are now acquiring more scientific and medically useful information from mummies.

The study of disease and health in mummies provides a tool in addressing fundamental questions about the nature of life. Pathogenic organisms, and the diseases they cause, have evolved just as humankind has. The history of life, death, and disease are inexorably intertwined. “It is often forgotten that life, the continued survival of the physiologic materials...are but vehicles of its progress...They die, but life goes on. Disease...is as old as life itself.”255 To understand the history of disease is to fathom the survival of a species and the perpetuation of life itself.

Humankind has long viewed its mortality with a profound sense of loss: “Like water spilled on the ground, which cannot be recovered, so we must die.”258 Yet, more often than not, the mark men leave behind testifies to their hubris and is neither laudable nor memorable. The poem by Percy Bysshe Shelley makes this point:

“My name is Ozymandias, king of kings
Look on my works, ye mighty, and despair!
Nothing beside remains...”259

Humanity leaves a sobering paleorecord of violence that perseveres throughout the centuries, from Neolithic to modern day. Fortunately, evidence of our humanity also persists from earliest civilizations, with the Chinchorro mummies, prepared and preserved with evident egalitarian veneration, attesting to the magnanimous society from which they originated. In what light will we be viewed, I wonder, when we become history?
The field of paleomedicine is not likely to die. Scientists continue in their quest for and study of mummies. Questions of great historic and medical significance remain unanswered. Only time will tell what benefits and insights may be gained through the study of mummies.

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