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Randall C. Thompson^{*,†}, Adel H. Allam[‡], Albert Zink[§], L. Samuel Wann^{||}, Guido P. Lombardi[¶], Samantha L. Cox^{#,**}, Bruno Frohlich^{††}, M. Linda Sutherland^{‡‡}, James D. Sutherland^{§§}, Thomas C. Frohlich^{††}, Samantha I. King^{*}, Michael I. Miyamoto^{||||}, Janet M. Monge^{††}, Clide M. Valladolid^{¶¶}, Abd el-Halim Nur el-din^{##,***}, Jagat Narula^{†††}, Adam M. Thompson^{*}, Caleb E. Finch^{‡‡‡}, Gregory S. Thomas^{§§§,|||||}

Kansas City, MO, USA; Cairo, Egypt; Bolzano, Italy; Milwaukee, WI, USA; Lima, Peru; Cambridge, UK; Philadelphia, PA, USA; Washington, DC, USA; Newport Beach, CA, USA; Laguna Hills, CA, USA; Williamstown, VT, USA; Mission Viejo, CA, USA; 6th of October City, Egypt; New York, NY, USA; Long Beach, CA, USA; and Irvine, CA, USA

ABSTRACT

Although atherosclerosis is widely thought to be a disease of modernity, computed tomographic evidence of atherosclerosis has been found in the bodies of a large number of mummies. This article reviews the findings of atherosclerotic calcifications in the remains of ancient people—humans who lived across a very wide span of human history and over most of the inhabited globe. These people had a wide range of diets and lifestyles and traditional modern risk factors do not thoroughly explain the presence and easy detectability of this disease. Nontraditional risk factors such as the inhalation of cooking fire smoke and chronic infection or inflammation might have been important atherogenic factors in ancient times. Study of the genetic and environmental risk factors for atherosclerosis in ancient people may offer insights into this common modern disease.

Atherosclerosis is commonly considered to be a disease of modern man and related to modern lifestyles. However, although diet, cholesterol level, and controllable environmental factors are important, known risk factors explain no more than 70% of the burden of this disease [1]. In other words, there are major gaps in our understanding of the genesis of atherosclerosis with important implications for prevention and therapy.

Many people are surprised when they learn that ancient people had atherosclerosis. There is such a large (and appropriate) public health effort to educate citizens about healthy cardiovascular lifestyle choices that many seem to conclude that the condition must be completely avoidable and completely caused by our unhealthy modern diet and factors such as cigarette smoking, trans-fats, and inactivity. As reviewed by others [2,3], autopsy studies over 100 years ago demonstrated that this disease was indeed present in ancient times. However, they seem to have been nearly forgotten. Starting shortly after the introduction of x-ray computed tomography (CT) scanning, investigators have found it interesting to perform these studies on mummies to noninvasively gain knowledge about the culture, anthropology, health, and disease of ancient people [4–6].

CT scanning is used in modern medicine to diagnose a wide range of diseases. One of these diseases is atherosclerosis. Contrast-enhanced CT scanning can diagnose arterial stenoses, as well as a variety of cardiovascular conditions. However, even noncontrast CT scanning can definitively diagnose the presence of atherosclerosis and semiquantitatively measure the atherosclerotic burden of disease [7,8]. The deposition of calcium hydroxyapatite into the arterial wall is part of the atherosclerotic disease process and the presence of densities compatible with calcifications in the arterial wall on CT scan are considered virtually pathognomonic for this disease [9,10].

A fairly large number of mummies from various cultures from around the world, some dating back thousands of years, have now been subjected to CT scanning. A review of the reports of these scans demonstrates that atherosclerotic calcifications have been found in many of them. A picture is emerging that this disease has been afflicting mankind for a very, very long time. In this article, we review the CT evidence of atherosclerosis in ancient people and explore possible insights into risk factors and etiology.

EGYPTIAN MUMMIES

Although numerous cultures across history have mummified their dead, the magnitude of scale, resources devoted, and technological achievement for mummification in ancient Egypt far surpasses all others. Egyptian mummies have fascinated the public since the time of Napoleon [11]. The level of soft tissue preservation in some of these mummies is truly amazing. The methods of embalming in

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Natural History, Smithsonian Institution, Washington, DC, USA; ‡‡Newport Diagnostic Center, Newport Beach, CA, USA; §§Saddleback Memorial Medical Center, Laguna Hills, CA, USA; ||||Mission Heritage Medical Group, St. Joseph Heritage Health, Mission Viejo, CA, USA; ¶¶Museo de Sitio Puruchuco— Arturo Jimenez, Lima, Peru; ##Cairo University, Cairo, Egypt; ***University for Science and Technology, 6th of October City, Egypt; †††Zena and Michael A. Wiener Cardiovascular Institute, Icahn School of Medicine at Mount Sinai, New York, NY, USA: ‡‡‡Biological Sciences and Gerontology, University of Southern California, Los Angeles, CA, USA; §§§MemorialCare Heart & Vascular Institute, Long Beach Memorial, Long Beach, CA, USA; and the |||||University of California, Irvine, Irvine, CA, USA. Correspondence: R. C. Thompson (rthompson@ saint-lukes.org).

GLOBAL HEART © 2014 World Heart Federation (Geneva). Published by Elsevier Ltd. All rights reserved. VOL. 9, NO. 2, 2014 ISSN 2211-8160/\$36.00. http://dx.doi.org/10.1016/ j.gheart.2014.03.2455 ancient Egypt varied over the more than 3,500 years these arts were practiced, but it is common to find the heart and blood vessels preserved in the mummified remains of many ancient Egyptians. CT scans of these bodies have demonstrated the sometimes-remarkable preservation of the aorta and major vessels. Densities compatible with atherosclerotic calcifications have been demonstrated in the walls and along the course of major arteries [12–16].

According to a recent publication by the Horus Team [14], the CT scans of 76 Egyptian mummies were systematically reviewed for arterial calcifications. Despite a wide variation in the level of preservation of the bodies, the disease was present and not hard to find; 29 of 76 (38%) had probable or definite atherosclerotic calcifications. Also, the arterial calcifications were seen in all vascular beds, including the "event-related arteries" (i.e., the coronaries and the carotids). The frequency and severity was increased in the mummies of longer-lived individuals and the appearance and location of these calcifications are virtually identical to the appearance of atherosclerotic disease on the CT scans of modern patients.

Figure 1 demonstrates an Egyptian mummy being scanned by CT, and Figures 2 to 10 demonstrate atherosclerotic disease in several Egyptian mummies. Particularly heavy coronary calcifications are seen on the CT scan of the mummy of Princess Ahmose-Meryet-Amon, a member of the royal household from the Second Intermediate Period (Fig. 5). Very heavy calcifications in the carotid bulbs and along the superficial femoral arteries are seen on the CT scan of the mummy of Hatiay, an 18th Dynasty Egyptian scribe (Figs. 2 to 4). Calcifications were seen on CT scans of mummies who lived during a period spanning over 2,000 years (Fig. 11), with varied mummification techniques. Given the CT scan appearances, there seems little doubt that these lesions are indeed atherosclerotic calcifications. Atherosclerosis has also been demonstrated histologically on autopsies of Egyptian mummies [2].

A fair amount is known about the diet of ancient Egyptians. From surviving papyri and the paintings on the walls of tombs, it is clear that the elites, at least, ate plenty



FIGURE 1. An Egyptian mummy undergoing computed tomographic scanning.



FIGURE 2. Coronal thick maximum intensity projection reconstruction of the computed tomographic scan of Hatiay, a scribe from the 18th Dynasty of Ancient Egypt. There are heavy calcifications in the superficial femoral arteries (*arrows*). Reprinted, with permission, from Allam et al. [13].

of fat and protein. Their society was an advanced agricultural one. Domesticated goats, cattle, and fowl; fish from the Nile; and cereal grains were consumed regularly. It was also highly hierarchical. David et al. [17] have pointed out that the priests in ancient Egypt would have eaten a



FIGURE 3. Sagittal thick maximum intensity projection reconstruction of the computed tomographic scan of Hatiay, a scribe from the 18th Dynasty of Ancient Egypt. There are heavy calcifications in the left carotid bulb (*arrows*). Reprinted, with permission, from Allam et al. [13].

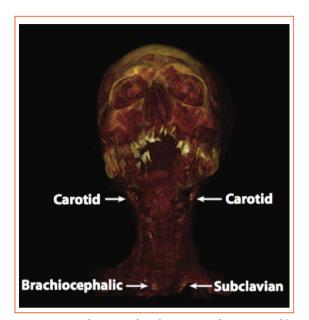


FIGURE 4. Volume-rendered computed tomographic image of the mummy Hatiay, a scribe from the 18th Dynasty of Ancient Egypt. There are heavy calcifications in the carotid bulbs, the brachiocephalic artery and the left subclavian artery (*arrows*). Reprinted, with permission, from Thompson et al. [14].

particularly rich diet because they consumed the sacrificial offerings. They hypothesized that these individuals would have been prone to atherosclerosis because of this rich diet, just as a high fat diet is thought to be a risk factor for modern heart disease. Most Egyptian mummies are thought to be of individuals who were well-to-do in life. Although considerable resources were expended toward mummification during the latter centuries of Pharaonic Egypt, the wealthiest were most likely to be mummified and most likely to be mummified using the best techniques. Relative physical inactivity and a high fat diet may well have been common in the Egyptians whose mummies survived to modern times. However, tobacco smoking was unknown and the average level of physical activity in those pre-industrial times was probably greater on average than it is today, except for the very elite. As with other ancient cultures, chronic inflammation from infections and parasites was likely common, and this inflammatory state might have contributed to atherogenesis [2,3].

ANCIENT PERUVIAN MUMMIES

In a recent report, the Horus Team described the cardiovascular findings on CT scans of 51 ancient Peruvian mummies (dating from about 200 CE to 1500 CE) housed at the Museo Puruchuco [14]. Almost all of these mummies were still wrapped in mummy bundles, and, therefore, the state of preservation could not be ascertained prior to the CT scan. Peruvian mummies are also



FIGURE 5. Coronal thick maximum intensity projection image of the computed tomography of Princess Ahmose-Meryet-Amon, a member of the royal household in the 17th Dynasty of Ancient Egypt. There are heavy calcifications at the aortic bifurcation and in the common iliac arteries (*arrows*). Reprinted, with permission, from Allam et al. [13].

almost always in a crouched position (Figs. 12 to 15). Some were indeed not well preserved and contained very little soft tissue. Still, atherosclerosis was present and not

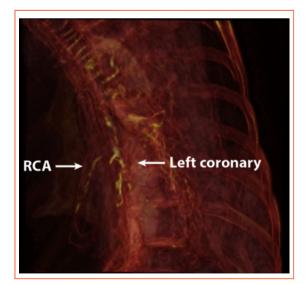


FIGURE 6. Volume-rendered computed tomographic image of the mummy of Princess Ahmose-Meryet-Amon, a member of the royal household in the 17th Dynasty of Ancient Egypt. There are heavy calcifications in the right and left coronary arteries (*arrows*). RCA, right coronary artery. Reprinted, with permission, from Allam et al. [13].



FIGURE 7. Sagittal view, thick maximum intensity projection reconstruction of a computed tomographic scan of the Egyptian mummy Djeher. There are heavy calcifications in the left coronary artery (*arrow*). Reprinted, with permission, from Allam et al. [12].

hard to find in this series of mummies. Some atherosclerotic calcifications were seen on CT scans of 13 of 51 individuals (25%), including the following beds: carotid, n = 2 (4%); aorta, n = 7 (14%); iliac-femoral, n = 8(16%); and distal lower extremity arteries, n = 7 (14%). As was the case with the Egyptian mummies, these calcifications were more common and more extensive in the longer-lived individuals-as would be expected in atherosclerotic disease [14]. Figures 16 and 17 demonstrate atherosclerotic calcifications in the abdominal aorta and iliac arteries and aortic arch vessels of ancient Peruvians, and Figure 18 demonstrates arterial calcification in an arch vessel. As is the case with the Egyptian mummies, the calcifications in these locations appear virtually identical to the calcifications of atherosclerosis seen on the CT scans of modern patients.

The ancient Peruvians were as advanced in many ways as the ancient Egyptians were; they were as hierarchical and had a sophisticated system of agriculture adapted to difficult landscapes. They domesticated alpaca, Muscovy ducks, and guinea pigs, and it is known that they consumed fish, birds, deer, corn, hot peppers, potatoes, sweet potatoes, and manioc. Nevertheless, their lack of a written language limits our knowledge about their

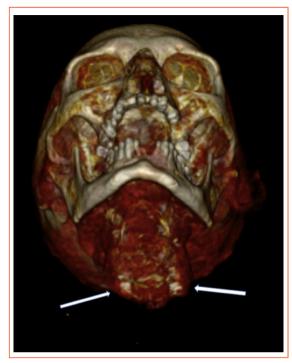


FIGURE 8. Volume-rendered computed tomographic reconstruction of the Egyptian mummy Lady Hudson. There are heavy calcifications in the carotid bulbs (*arrows*).

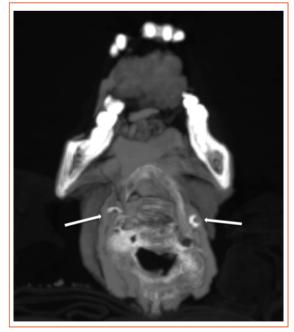


FIGURE 9. Modified axial thick maximum projection image of the computed tomographic scan of the neck of the Egyptian mummy Lady Hudson. Heavy calcifications in the right and left carotid bulb are seen (*arrows*).

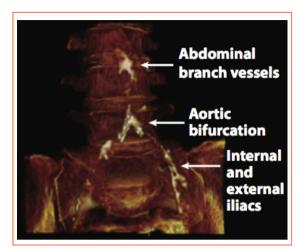


FIGURE 10. Volume-rendered reconstruction of the computed tomographic scan of an ancient Egyptian mummy. There are heavy calcifications in the abdominal aorta and the internal and external iliac arteries. Reprinted, with permission, from Thompson et al. [14].

culture and lifestyle, which stresses the importance of bioarcheological research in that part of the world. The ancient Peruvians generally lived in above-ground mud homes and cooked outdoors over fires fueled by wood or animal dung [14]. It has been generally believed that ancient Peruvians did not consume tobacco because it was not available until the Spaniards brought it to this part of South America in the 16th century. However, a very recent report demonstrating nicotine in the hair of mummies from nearby northern Chile suggests that tobacco products may have been consumed by these people after all [18].

NORTH AMERICAN MUMMIES

The Horus Study included the CT scans of 10 mummies from North America [14]. Five of these mummies were of

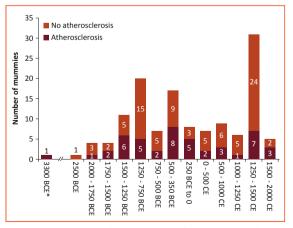


FIGURE 11. Historical distribution of mummies with and without atherosclerosis from the Horus Study and The Tyrolean Iceman (*).

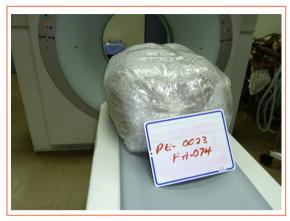


FIGURE 12. An ancient Peruvian mummy bundle being scanned by computed tomography.

ancestral Puebloans who lived about 1,000 years ago in a region that is now part of modern Utah [14]. The other 5 North American mummies in the Horus Study series were of Unangan people from the Aleutian Islands, now part of Alaska [14]. The Unangan mummies were not ancient—these people probably lived during the late 19th century—but they were hunter-gatherers who lived a



FIGURE 13. Volume-rendered whole-body computed tomographic scan image of an ancient Peruvian mummy.



FIGURE 14. Mummy of Rosita, a woman who lived in ancient Peru (Chancay culture, Late Intermediate Period, AD 1000 to 1534) and is housed at the Huando Museum in Peru.

traditional lifestyle [19]. Two of the 5 ancestral Puebloans and 3 of the 5 Aleutian Islanders had evidence of atherosclerosis. Figure 17 shows calcifications at the aortic bifurcation in the mummy of an ancestral Puebloan. Figure 18 is a volume-rendered display of the CT scan of an Aleutian Island woman who died at about age 50 years and shows heavy coronary calcifications. These calcifications are particularly extensive, and one can make out the right and left coronary arteries.

Unlike the mummies we described from Egypt and Peru, these North American mummies were not from cultures with advanced agriculture. The Ancestral Puebloan mummies are thought to have been either huntergatherers or forager-farmers in life [14]. It is very unlikely that they ate the sort of rich diet that modern Westerners and elite ancient Egyptians consumed. The Aleutian Islanders were hunter-gatherers with almost no established agriculture. They had a marine-based diet that included shellfish, sea urchins, birds, eggs, fish, and the occasional seal, sea otter, and whale. Except for some wild



FIGURE 15. Modified axial view thick maximum intensity projection image of the computed tomographic scan of Rosita, an ancient Peruvian mummy (Chancay culture, Late Intermediate Period, AD 1000 to 1534). There are calcifications in the aortic arch vessels (*arrow*).



FIGURE 16. Volume-rendered image of a computed tomographic scan of the mummy of an Ancestral Puebloan woman. Calcifications in the aorta and iliac arteries are seen. Reprinted, with permission, from Thompson et al. [14].

berries, they ate very little fruit or vegetables. Although the people of these North American cultures likely did not eat a modern (atherogenic) diet, they may have had considerable exposure to smoke from cooking and heating fires. Both of these groups of people lived in subterranean homes

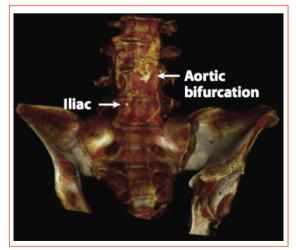


FIGURE 17. Volume-rendered reconstruction of a computed tomographic scan of the mummy of an ancient Peruvian woman. There are heavy calcifications at the aortic bifurcation and in the right iliac. Reprinted, with permission, from Thompson et al. [14].

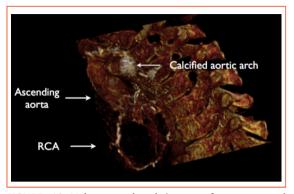


FIGURE 18. Volume-rendered image of a computed tomographic scan of the mummy of an Aleutian Island woman. Heavy calcifications are seen in the ascending aorta and the aortic arch and in the right coronary artery. RCA, right coronary artery. Reprinted, with permission, from Thompson et al. [14].

and cooked indoors. It is possible that they, especially the women, inhaled considerable amounts of smoke. This cooking fire smoke, like tobacco smoke, might be atherogenic [20,21].



FIGURE 20. Oblique coronal maximum intensity projection image of the computed tomographic scan of the pelvis of the mummy of the Tyrolean Iceman. There are calcifications in the distal abdominal aorta (*arrow*).

EUROPE: TYROLEAN ICEMAN

In 1991, 2 tourists discovered a well-preserved natural mummy of a Chalcolithic (Copper Age) man from about 3300 BCE in the area of the Tisenjoch in the Ötztal Alps, about 92.56 m on the Italian side of the border with Austria. The mummy has been nicknamed Ötzi and has been extensively studied at the South Tyrol Museum of Archaeology in Bolzano, South Tyrol, Italy (Fig. 19). He is Europe's oldest mummy, thought to have been 40 to 50 years old at the time of death. Atherosclerotic calcifications are seen in the aorta and other vessels on the CT scan (Fig. 20) [22,23].



FIGURE 19. The Tyrolean Iceman, Ötzi.

Evaluation and study of Ötzi has been extensive, and much is known about his diet and lifestyle. His last meals are believed to have included chamois and red deer meet, herb bread, einkorn wheat bran, chaff, and grains of einkorn wheat and barley, sloes (small plumlike fruits of the blackthorn tree), and various berries growing in the wild. There were also pollens identified in his intestines, which indicate the presence of wheat and legumes, which may have been domesticated crops [24]. Clearly, this individual was an omnivore with much variety in his diet.

Ötzi, having been discovered in a high alpine location, would logically be presumed to have exercised vigorously during his life. In fact, CT scan evidence indicates a skeletal structure that would corroborate this presumption [25].

As Ötzi the Iceman's diet and lifestyle did not suggest traditional risk factors for atherosclerosis, the genetic evaluation of this individual is particularly interesting and provocative. Several single-nucleotide polymorphisms associated with coronary heart disease and atherosclerosis have been identified in a whole genome analysis of this mummy. For example, he was homozygous for the minor allele of rs10757274, a major locus for coronary heart disease. There was also a homozygous minor allele of rs2383206, another major coronary heart disease and ischemic risk single-nucleotide polymorphism. The Iceman's genome also harbors endothelin receptor type B heterozygote variant rs5351, which is a risk factor for atherosclerosis in men [26]. His genome also contained single-nucleotide polymorphisms in 3 other genes-VDR, TBX5, and BDKRB1-that have been associated with coronary heart disease.

Regarding nontraditional risk factors for Ötzi, it should be mentioned that his lungs had blackened material suggesting smoke inhalation, thought likely to have been from campfire smoke. He also had pinworm and his fingernails suggested multiple illnesses during the 6 months previous to his death [27]. The Horus Team has previously hypothesized that cooking fire smoke might have been atherogenic in ancient people and that chronic infections and parasites might increase the inflammatory response contributing to this disease as well [14]. These possible risk factors would have been present in the Iceman.

OTHER MUMMIES

In 2005 and 2006, Frohlich et al. [28,29], from the Smithsonian Institution and the Mongolian Academy of Sciences, performed examinations, including CT scans, on a group of mummies who had lived circa 1450 CE in the Gobi Desert. One partially preserved mummy is of a man, approximately 60 years old at the time of death, and CT scans show significant atherosclerotic calcifications in the aortic arch vessels (Fig. 21). A rope around his neck indicates that he died of strangulation, probably by execution (Fig. 22). A mummy from almost this exact time period from Europe, that of Ferdinand I, King of Naples, has also recently been reported to have had atherosclerosis-on autopsy, not CT scan [30]. Whereas the diet of a Renaissance nobleman was likely quite rich, the Mongolian individual would have been a nomad living in the harsh environment of the Gobi Desert. These 2 cases bring the documented breadth of atherosclerosis to include North

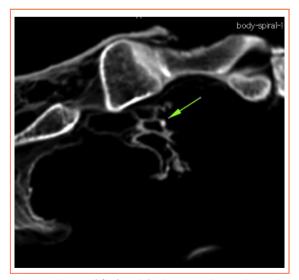


FIGURE 21. Modified axial view maximum intensity projection image of the upper chest of a Mongolian mummy (circa 1450) found in the Gobi Desert. There is an atherosclerotic arterial calcification in an aortic arch vessel (*arrow*).

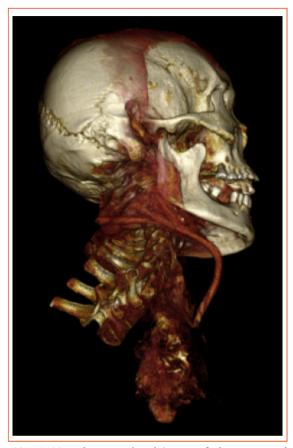


FIGURE 22. Volume-rendered image of the computed tomographic scan of the Mongolian mummy seen in Figure 21. This individual died from strangulation.

Africa, the Middle East, South America, North America, the Arctic, Europe, and Asia.

SIGNIFICANCE OF ATHEROSCLEROSIS ON CT SCAN

It should be emphasized that CT scanning is a sensitive test and most of the mummies in which vascular calcium has been detected undoubtedly had pre-clinical disease at the time of death. There are some notable exceptions, however. For example, the mummy of the Aleutian woman described previously and of the ancient Egyptian princess Ahmose-Meryet-Amon (Fig. 6) have such heavy coronary calcifications that symptomatic disease seems likely. Also the mummy of Hatai (Figs. 2 to 4) appears to have had extensive and diffuse arteriopathy-he may have had either cerebrovascular symptoms or claudication. Also, the CT scan of the mummy of Lady Rai shows changes consistent with a calcified old myocardial infarction [16]. It is also rarely possible to determine the exact cause of death from a CT scan of an ancient body. Of the mummies reviewed here, only 1 had an unequivocal cause of death-the Mongolian man who had a rope around his neck with cervical spine and hyoid bone fractures had rather

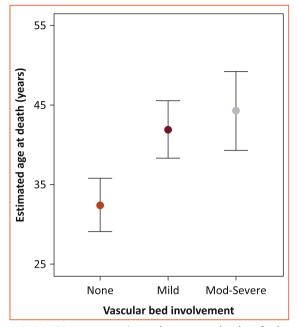


FIGURE 23. Mean estimated age at death of the mummies in the 3 categories of atherosclerosis in the Horus Study. Error bars show 95% confidence intervals. Reprinted, with permission, from Thompson et al. [14].

obviously been hung (Figs. 21 and 22). The lifespan in ancient times was also significantly shorter than it is in modern times. For example, whereas age was significantly correlated with the presence and the severity of atherosclerosis in the Horus Study, the average age at time of death was estimated to be <40 years (Fig. 23) [14]. Still, the wide presence of these atherosclerotic calcifications suggests that many of these people would have developed symptomatic disease had they lived a modern lifespan.

SUMMARY

Although atherosclerosis is widely thought to be a disease of modernity, CT evidence of atherosclerosis has been found in the bodies of a substantial number of mummiesmummies of people who lived across a very wide span of human history and over most of the inhabited globe. Atherosclerotic calcifications, which appear virtually identical to CT findings in modern patients, have been detected in all vascular beds in ancient mummies. These people had a wide range of diets and lifestyles, and traditional modern risk factors do not thoroughly explain the presence and easy detectability of this disease. We have hypothesized that nontraditional risk factors such as the inhalation of cooking fire smoke and chronic infection or inflammation might have been important atherogenic factors in ancient times. Further study of the genetic and environmental risk factors for atherosclerosis in ancient people may offer insights into this common modern disease.

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