Atherosclerosis in ancient populations

We read with interest Randall Thompson and colleagues' report (April 6, p 1211),[1] and we think it requires some clarifications.

First, the percentages of diagnosed atherosclerosis (38% of ancient Egyptians, 25% of ancient Peruvians, 40% of Ancestral Puebloans, and 60% of Unangan hunter-gatherers) seem too high for preindustrial communities, especially for hunter-gatherers who did not show evidence of atherosclerosis in previous studies.[2] These civilisations did intense physical activity and followed a diet rich in vegetables and seafood, free from saturated fats, and therefore with low risk of developing atherosclerosis.

Second, atherosclerosis diagnosed as probable or definite in 13 mummies with mean age at death between 18 years and 35 years seems too high for young individuals.[3] Therefore, the age of death positively correlating with atherosclerosis (43 years for mummies with atherosclerosis *vs* 32 years for those without) could simply be linked to older age.

Third, regarding smoke, a major risk factor, Thompson and colleagues correctly note that cigarette smoking was not part of these populations, but then they suggest that fire smoke inhalation could have played a part in the development of atherosclerosis. However, the risk of atherosclerosis increases as a result of nicotine intake and not of the smoke of a bonfire. Components of tobacco smoke induce changes in the function of thrombocytes, endothelium, macrophages and smooth muscle cells of blood vessels, and antioxidant enzyme activity by inducing the production of reactive oxygen species.[4]

The development of vascular calcification is related not only to atherosclerosis but also to conditions such as disorders of calcium-phosphorus metabolism, diabetes, chronic microinflammation, and chronic renal insufficiency.

Furthermore, stating that atherosclerosis is not characteristic of any specific diet or lifestyle, but an inherent component of human ageing is not in agreement with recent studies demonstrating the importance of diet and physical activity.[5] If atherosclerosis only depended on ageing, it would not have been possible to diagnose it in a young individual, as done in the Horus study.[1]

Finally, classification of probable atherosclerosis on the basis of the presence of a calcification in the expected course of an artery seems incorrect, because the anatomy can be strongly altered by post-mortem events. The walls of the vessels might collapse, dehydrate, and have the appearance of a calcific thickening. For this reason, the x-ray CT pattern alone is insufficient and diagnosis should be supported by histological study.

We declare that we have no conflicts of interest.

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Authors' reply

Like Gino Fornaciari and Raffaele Gaeta, we found the high frequency of atherosclerotic calcifications in the bodies of ancient people to be somewhat surprising. The frequency, however, is comparable to that described by Allison and colleagues[1] in their population-based study of modern human beings. About half of our mummies[2] estimated to be older than 40 years at the time of death had arterial calcifications. Age was strongly correlated with both the presence and the severity of atherosclerotic calcifications, as one would expect. The calcifications seen in the mummies who were younger at death tended to be much less extensive.

The fact that the appearance of atherosclerotic disease on the CT scans in the mummies is virtually identical to that in modern patients is also strong confirmation.[2] While conditions of abnormal calcium-phosphorus metabolism, including renal failure, increase calcification, these uncommon conditions cannot be expected to be present in a substantial percentage of the mummies. Arterial calcifications on CT scan are widely deemed to be pathognomonic for atherosclerosis.[3]

Regarding our category of probable atherosclerosis, it was a conservative designation we might well have called highly probable. Heavy, focal calcifications along the course of an artery are almost certain to be from atherosclerosis, especially when the calcifications are dense, numerous, and in multiple vascular beds. In our sensitivity analysis, we excluded the mummies with probable atherosclerosis and found that the association with age was unchanged.

The frequency of calcified lesions across these cultures of diverse diets and lifestyles is consistent with atherosclerosis as a basic process of ageing. This underscores the need for all individuals to manage


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their own traditional risk factors, recognising that manipulation of one risk factor such as diet cannot fully protect against atherosclerosis. Our findings also suggest we should look beyond traditional risk factors and consider other factors. For example, the Aleutian Islanders and Ancestral Puebloans probably had heavy exposure to indoor smoke. Animal model responses to exposure to wood smoke specifically suggest interactions with atherosclerosis.[4]

Finally, while we cannot determine cause of death in our study, cardiac symptoms were common enough to be mentioned in ancient writings, dating as far back as 1550 BCE: "If thou examinst a man for illness in his cardia, and he has pains in his arms, in his breast and on one side of his cardia…it is death threatening him."[5]

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Computed tomographic colonography for colorectal cancer diagnosis

Wendy Atkin and colleagues (April 6, p 1194)[1] assessed the rate of additional colonic investigation in symptomatic patients after computed tomographic colonography (CTC), and found a relatively high referral rate (30%). The authors recommend a reduction in the referral rate after CTC on the basis that almost half the referrals after CTC were for small lesions (≤10 mm) or clinical uncertainty.

An important question raised by this study is whether the threshold of 10 mm for high-risk polyps is appropriate. While it is generally agreed that patients with polyps 10 mm or more in diameter found on CTC should undergo additional colonic investigation, subcentimetric lesions also bear an increased risk of progression to colorectal cancer. Frank Thomas Kolligs and colleagues[2] showed that 13% of intermediate (5–9 mm) and 3·7% of diminutive (≤4 mm) polyps contained advanced neoplasia, which is the main target of screening and diagnosis. Furthermore, increasing age and symptoms suggestive of colorectal cancer were identified as risk indicators of subcentimetric lesions containing advanced neoplasia.

Another limitation of Atkin and colleagues' study is the omission of the number of polyps. A pooled analysis showed that the number of polyps is associated most strongly with risk of advanced neoplasia, in addition to age and size of polyps.[3] The American College of Gastroenterology recommended that patients with three or more polyps of any size should be offered colonoscopy and polypectomy.[4] Therefore, ignoring the subcentimetric polyps and the number of polyps to reduce referral rates does not seem acceptable because a relevant group of high-risk individuals can be missed.

I declare that I have no conflicts of interest.

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We read with great interest Wendy Atkin and colleagues' study,[1] in which they compare rates of additional colonic investigation after computed tomographic colonography (CTC) or colonoscopy for detection of colorectal cancer or large polyps in symptomatic patients in clinical practice. The authors conclude that CTC offers a similarly sensitive, less invasive alternative to colonoscopy. However, they do not mention radiation exposure with each type of investigation.

For a radiation exposure ranging from 10 to 18 mSv at the age of 62 years, the life attributable risk of cancer incidence was one in 1336 in men and one in 614 in women.[2] The radiation dose from a CTC is equivalent to several hundred chest radiographs. Previous data[3] suggest that the estimated mean effective dose per CTC screening study is about 8 mSv for women and 7 mSv for men. The life attributable risk of cancer incidence with this radiation dose might be substantially higher than the risk of perforation from colonoscopy. The