Evolution of osteoporosis

Osteoporosis is not exclusive to the Caucasian peoples nor to the female sex, but it is upon the elderly white female that the principal burden of morbidity and mortality continues to descend. In contrast, the relative freedom from the disease among peoples of African origin or ancestry is a consistent observation that requires explanation. Some recent observations within the disciplines of anthropology, molecular genetics, and linguistics, which have served to illuminate the origin and dispersal of Homo sapiens, may now begin to contribute to our understanding of the differential prevalence of osteoporosis among the races of humankind. From these data, it may be hypothesised that the clinical problem among Caucasians may derive from an evolutionary response to certain selection pressures operating in the higher latitudes of Europe and Asia to which ancestral populations of H sapiens migrated from a homeland in the continent of Africa.

Osteoporosis has now been defined qualitatively as: 'a disease characterised by low bone density and microarchitectural deterioration of bone tissue leading to enhanced fragility and a consequent increase in fracture risk.' With approximately 60,000 femoral neck fractures occurring in England and Wales during 1995, the disease is now a major problem for the public health, and also for the public purse, with an estimated £750 million of NHS expenditure required to deal with the acute and aftercare of osteoporosis related fractures.

The proximate causes of primary osteoporosis in women are already well established. A central problem would seem to be the obligatory midlife ovarian failure that reduces plasma oestadiol by an order of magnitude. Far from being purely reproductive hormones, the oestrogens are now known to contribute to normal function, not only in the skeletal but also in the central nervous and cardiovascular systems, having proved to be physicochemically useful molecules for which a broad range of activities has evolved. In bone, through a complex interaction with bone cells, cytokines, and calcitropic hormones, oestrogen restrains bone turnover and has a pivotal role in balancing bone resorption with bone formation. Menopausal ovarian failure shifts the pivot, allowing the increased turnover to cause an imbalance in favour of bone resorption. The skeleton thus embarks on a decade long decrease in bone mineral density (BMD), which is the prime determinant of fracture risk. After the age of 60, rates of loss decline and, at least at the spine, tend to become asymptotic with the underlying age related decrease seen in both sexes.

Climacteric ovarian failure is obligatory for both black and white women. However, the age specific rates of osteoprotic fractures are substantially lower in the former compared with the latter. Examination of vertebral BMD in the young of both races shows similarity until the time of puberty, when black children begin a greater accretion of bone than whites and establish a greater peak bone density when compared, site for site, with age and gender matched white controls. This advantageous bone density is still present at the menopause, and is sufficient to sustain the obligatory bone loss imposed by current longevity. Peak bone density in young females, a key variable, is largely determined genetically, with smaller environmental contributions.

A phenomenon that may reflect a racial difference in skeletal mass is the marked contrast observed in the relative performance of black and white athletes in water and in air. There is a dearth of scientific data on the subject, but it is common observation that in events such as the 100 and 200 metres on the track, black athletes predominate, while over similar distances in the pool, white athletes are consistently the more successful. One factor that could account for part of this difference might be the heavier black skeleton imposing an adverse power to weight ratio in water. In other words, black athletes may not be able to drive their relatively heavy skeleton through water at a velocity comparable to that achieved by whites driving a lighter skeleton. This might be mediated either through a difficulty in sustaining lower limb alignment with the trunk—essential to reduce drag—or through the diversion of propulsive energy towards the maintenance of buoyancy.

How may a racial difference in bone mass have evolved? For this we must turn to the substantial advances made recently by physical anthropologists in describing the evolution and dispersal of H sapiens. All humans alive today belong to the same species. It is accepted that this species evolved from hominin precursors and that they, in turn, evolved from hominoids, with the key separation between the line leading to man and the line leading to our nearest genetic neighbour Pan troglodytes, the chimpanzee, occurring some 5–8 million years ago. However, there has been major disagreement as to whether modern man evolved in Europe, Asia, and Africa, or in one location with subsequent transcontinental migration. This argument is not finally settled, but the archaeological and anthropological debate has recently received interesting contributions from two additional sources, namely molecular genetics and linguistics.
The amount of genetic variation among contemporary human populations is small, suggesting a relatively recent origin of the species. With regard to the site of origin, it has been found that nuclear genetic variation is greatest among African peoples, suggesting that H. sapiens has been established there for longer than in other locations. Similarly, mitochondrial (mt) DNA may be used as a genetic clock to estimate how long two populations have been separated. An individual's mitochondria are derived solely from the ovum and the mtDNA, consisting of some 16,500 base pairs, descends without paternal admixture to the offspring. One analysis of mtDNA in Papua New Guinea suggested a mean age of the original H. sapiens population at circa 200,000 years before present, and within the range 100,000–500,000 years. In general, the mtDNA evidence tends to support an African site of origin for humankind, but the issue is not finally settled. However, it may be postulated that at a time yet to be precisely determined, H. sapiens evolved in Africa, perhaps along the eastern division of the Great Rift valley in what is now Kenya, Tanzania, and Ethiopia, later migrating into Europe, Asia, and across the then dry Bering Strait, into the Americas. Tentative dates have been fixed for the arrival of the species in each continent, that for Europe being circa 35,000 years before present, when it encountered and then displaced with, or possibly exterminated, the resident population of H. sapiens neanderthalensis.

Human populations, as they diverge and migrate, carry with them not only their genes, but also their speech, and hence a study of the similarity and distinctions between vocabularies and grammars of different languages may furnish data on their evolution in space and time. Applied to contemporary human languages, the north-east Asian origin of the Amerind languages in the Americas has been established, as has the relationship between, for example, Asian language groups such as Uralic or Altaic and the Indo-European group which includes English. A superfamily of languages, the Nostratic, has been proposed which includes the Indo-European and certain African groups.

If we accept, for the moment, the genesis of humankind in the tropical plains and highlands of Africa, it is likely that our ancestors there would have had, as Africans today have, highly pigmented skins in order to accommodate the high incidence of ultraviolet photons found at low latitudes. At a wavelength of 290–315 nm, ultraviolet light induces photolysis of 7-dehydrocholesterol to previtamin D₃ in the stratum spinosum of the skin. Excessive production of vitamin D is restrained in part by the absorption of ultraviolet photons by the pigment melanin. As our ancestral human populations left Africa, the first moved into the Middle East where, at Qafzeh in Israel, the earliest extra-African fossil H. sapiens have been found and dated to circa 100,000 years before present. Proceeding on into the higher latitudes of Europe, individuals would have experienced a decrease in the number of ultraviolet photons arriving per unit of skin surface area. This would have been compounded by a progressive need to cover exposed skin because of the colder climate. These factors would have created a tendency for vitamin D deficiency in melanin rich skin. Vitamin D₃, in its dihydroxylated form (1,25(OH)₂D₃), is, with parathyroid hormone and calcitonin, an essential regulator of plasma ionised calcium, the stability of which is essential for normal cellular function. Hence any compromise to the availability of vitamin D would be likely to exert selection pressure towards lighter skinned individuals lacking ultraviolet photon competitive melanin. This is believed to represent a mechanism whereby contemporary H. sapiens populations manifest a broad spectrum of skin pigmentation. It has recently been shown in a case-control study that individuals who lack melanin production in hair follicles and who as a result are prematurely grey, exhibit a significantly lower bone mineral density at hip and spine when compared with age and gender sex matched controls. Prematurely grey subjects also reported an excess of osteoporosis related fractures among first degree relatives than did controls with normal hair pigment. The authors of this work proposed a genetic basis for the apparent correlation of their epidermal and bone densitometric observations.

In conclusion, it may be hypothesised that the northerly migration of H. sapiens from an African location presented the ancestors of the European peoples with selection pressure for lighter skinned individuals. The consequent progressive deletion of dermal melanin, achieved by the suppression or attenuation of a gene or genes, may have interacted with the genetically controlled accretion of bone mass in postpubertal adulthood. The proposed bone mass changes associated with melanin suppression are unlikely to be related to polymorphisms of the vitamin D receptor gene, which may influence bone mass but which have been shown to be similarly distributed among black and white individuals. Whatever genetic material was altered, its deletion probably presented no clinical disadvantages to mankind or, indeed, its relatives, provided that the latter retained the protection of their endogenous oestrogen. However, the advent of substantial postmenopausal longevity has now exposed the lighter European skeleton to a prolonged attrition of bone tissue sufficient to reduce BMD into the range where spontaneous vertebral or low trauma limb fracture may occur. This problem is itself unlikely to be corrected by evolution because, by the time that osteoporosis is manifest, one, two, or even three generations of offspring may be alive.

A hypothesis seeking to link evolved epidermal and skeletal changes in the adaptation of H. sapiens to high latitude habitats might be tested in several ways. If the hypothesis were true, one would expect to observe a downward trend in site specific bone mineral density among homogenous populations at increasing latitudes, after adjustment for confounding environmental variables. Examination of individuals of mixed race, together with their parents and first cousins of unmixed race, would provide further data on a putative correlation of bone density and dermal pigment. Finally, the data cited above suggesting an association between hair pigment loss and low BMD first require independent confirmation. This area might be further examined, through densitometric assessment of patients exhibiting vitiligo which is unassociated with an autoimmune process known to affect BMD—such as thyrotoxicosis or premature ovarian failure. The hypothesis linking BMD and skin pigmentation predicts that a gene coding for a protein involved in the development of peak bone mass will be found at a site contiguous to a gene or genes involved in the elaboration or deposition of epidermal melanin. Alternatively, it predicts that a gene product associated with dermal melanin production will be found to confer an advantage in the physiological process of bone accretion and in the achievement of peak bone mass.

Thus the ultimate cause of osteoporosis may lie, not in our bones themselves, but in our history. It may lie in those unique skills of verbal communication, tool manufacture, and cultural organisation which collectively took us on our long journey out of the warm homeland of Africa and into the paler embrace of Europe.

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The author thanks Professors Anthony Horsman, University of Hull, and Bernard Wood, University of Liverpool, for their comments on the text.


