

## Why is Intracranial Large-artery Steno-occlusive Disease More Common in Asians? A Human Evolutionary Hypothesis and Its Implications

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Atherosclerotic disease is the most important cause of premature mortality. The susceptibility to many diseases is determined by genetic traits. Intracranial (IC) large-artery steno-occlusive disease occurs more frequently in Asians and other non-White races than those with a European ancestry. An alternative interpretation is that IC large-artery disease occurs in all races, but is uncommon in Caucasians. Over 70% of present-day Caucasians are descendants from Middle East or central Asian nomadic hunters who diversified to settle in Europe during the Upper Palaeolithic period and lived there in relative isolation until recently. We postulate that, through an evolutionary process of allopatric speciation, these Europeans had acquired a genetic trait which increases their resistance against atherosclerosis, but with protection restricted to IC large arteries. The modern unhealthy Western lifestyle accelerates development of atherosclerosis. In Caucasians, it involves the whole vascular system but the IC large arteries, being protected by the underlying genetic mechanism, are relatively unaffected. Conversely, people living in non-Western countries generally have a healthier diet. These non-Whites usually have less severe but more generalised atherosclerosis. Nevertheless, they will still develop major vascular disease after adopting a Western lifestyle but, unlike the Caucasians, their IC large arteries will not be spared. This speculation has two implications. Firstly, as human evolution advances, if this anti-atherosclerotic mechanism extends to protect the rest of the vascular system, a new *Homo sapiens* (*HS*) subspecies that can tolerate an unhealthy diet but without developing premature vascular death will emerge. They may eventually replace the original *HS* populations through natural selection. Secondly, if the mediator of this anti-atherosclerotic mechanism can be identified and applied therapeutically, we will have an ultimate “vaccine” against atherosclerosis.