

# Abstract

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## Heme, iron, and the mitochondrial decay of ageing.

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**BACKGROUND:** Heme, the major functional form of iron, is synthesized in the mitochondria. Although disturbed heme metabolism causes mitochondrial decay, oxidative stress, and iron accumulation, all of which are hallmarks of ageing, heme has been little studied in nutritional deficiency, in ageing, or age-related disorders such as Alzheimer's disease (AD).

**FINDINGS:** Biosynthesis of heme requires Vitamin B(6), riboflavin, biotin, pantothenic acid, and lipoic acid and the minerals zinc, iron, and copper. Micronutrients are essential for the production of succinyl-CoA, the precursor for porphyrins, by the TCA (Krebs) cycle. Only a small fraction of the porphyrins synthesized from succinyl-CoA are converted to heme, the rest are excreted out of the body together with the degradation products of heme (e.g. bilirubin). Therefore, the heme biosynthetic pathway causes a net loss of succinyl-CoA from the TCA cycle. The mitochondrial pool of succinyl-CoA may limit heme biosynthesis in deficiencies for micronutrients (e.g. iron or biotin deficiency). Ageing and AD are also associated with hypometabolism, increase in heme oxygenase-1, loss of complex IV, and iron accumulation. Heme is a common denominator for all these changes, suggesting that heme metabolism maybe altered in age-related disorders. Heme can also be a prooxidant: it converts less reactive oxidants to highly reactive free radicals. Free heme has high affinity for different cell structures (protein, membranes, and DNA), triggering site-directed oxidative damage.

**SUMMARY:** This review discusses heme metabolism as related to metabolic changes seen in ageing and age-related disorders and highlights the possible role in iron deficiency.

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