The cyanosed myocardium: evolutionary defence against reflex coronary vasoconstriction in vertebrates including man

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There are new data concerning the vertebrate evolution of defence against myocardial hypoxia. These data help explain sudden death syndromes of mammals, and question our anthropocentric views of man as an advanced species. Fish, amphibians and reptiles do not have a dedicated coronary circulation and perfuse the myocardium by direct pressure-assisted diffusion from the ventricular lumen. By contrast mammals including man post-conception develop a complex coronary circulation to overcome the greater diffusion distances within the bi-ventricular heart and in-series circulation.

The myocardium uniquely among vascular beds even at rest "lives on the edge", because of high oxygen usage and extraction from coronary blood reflected in the poor coronary sinus oxygen reserve. Extra demand in the normally cyanosed myocardium must be met by matching coronary blood flow to need. It turns out that no one has challenged the disparate literature findings of coronary control factors gleaned from Petri dish to human intervention laboratories to define the priority mechanisms governing responses in real life. The question is whether a general theory of neurovascular control exists, or whether the literature reflects true variation between species. For this reason we challenged the known baro-autonomic dilator coronary response of the awake dog (Quail *et al.*, 2000) with an exactly similar experimental approach using awake sheep. A similar response pattern in awake sheep would imply a common response exists in man. If different, it would confirm species variation and add weight to random evolutionary processing.

The null hypothesis was that an evoked baroreceptor dilator stimulus in awake dogs would be at least qualitatively the same as in awake sheep. That is to say there would be differential reflex dilator effects between right, circumflex and anterior descending vascular territories.

The null hypothesis was refuted, because not only did sheep have quantitative differences between coronary beds compared to dogs, but the right coronary bed was qualitatively different. Right coronary flow-conductance rose (dilated) in the dog to 156% of control, whereas in sheep it fell (constricted) to 82%. The evidence favours random evolutionary development, and a true species difference.

The possibility of such a counterintuitive coronary control system existing in man is supported by the variable constrictor effects to ACh noted in the diseased (Yasue *et al.*, 1990) and normal (Angus *et al.*, 1991) heart. Moreover, the ACh-dependent reflex response of vascular constriction in the highly metabolic myocardium suggests, for the first time, that the survival of the mammalian heart is heavily dependent in this case on a dynamic reflex-induced, reduction in metabolism of rapid time-constant. Such a mechanism has been suspected since Scholander's 1940's work in diving mammals, and by others working on hibernating species and why Bar-Headed Geese can migrate annually over millions of years across the Himalayas. Still others have invoked the mechanism for post-myocardial infarction (myocardial stunning), and from this time on, in stroke. These speculations demand scrutiny of real life time-constants of glycolytic and transcription hypoxia-inducible factor (HIF)1α mechanisms. They suffice for the Weddell Seal feeding submerged and Grey Squirrels hibernating, but perhaps not for predator-induced, sudden-death tachyarrhythmias in Sugar Gliders and nasopharyngeal reflexes in SIDS, nor during coronary obstruction-related tachyarrhythmias in Man.

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