Don't forget about hydrogen sulphide

SIR, I read with interest Dr Edirisinghe's comprehensive review on homocysteine-induced thrombosis.[1] Elevated blood homocysteine levels are also associated with other complications in the cardiovascular system and in pregnancy,[2] although the pathophysiological mechanisms are not clear.

It is now well established that hydrogen sulphide acts as a signalling molecule in the body, with some similarities to nitric oxide and carbon monoxide,[3,4] and is produced endogenously from L-cysteine by two enzymes, cystathionine beta-synthase and cystathionine gamma-lyase.[5-7] These enzymes are quite widely distributed in the body, and cystathionine gamma-lyase is particularly expressed in the cardiovascular system.[5-7] As shown by Dr Edirisinghe's review in Figure 2, there is a biochemical pathway by which homocysteine can be converted to cysteine 1.

It is possible that under conditions of elevated homocysteine there is increased conversion to L-cysteine, leading to increased production of hydrogen sulphide. Hydrogen sulphide could be involved in the pathology of hyperhomocysteinaemia, and its important role may be under-appreciated at the moment. More research is required into the effects of and mechanisms of action of endogenously produced hydrogen sulphide.

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Dr Carson introduces an interesting possibility in his response to my paper[1] but high levels of endogeneous hydrogen sulphide (H_2S) can be produced in many other ways, including in the brain[2-4] as a response to neuronal excitation. Also, different enzymes can either suppress (e.g., amino-oxyacetates) or enhance (e.g., adenosyl-L-methionine) H_2S production. Therefore, although it could be indirectly related, there is insufficient proof at present to implicate H_2S in thrombosis caused by homocysteine elevation. A recent paper by Eto *et al*.[5] provides some insight into the role of endogeneous H_2S in regulating some aspects of synaptic activity.

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