Cholesterol and violent death

Clinical importance is questionable

EDITOR,—I have several worries about the relation between cholesterol concentration, violent death, and mental disorder proposed by Ann Ryman.¹ Firstly, although the violent deaths referred to are due to accident, violence, trauma, and suicide,² attention rests on suicide and the reported connection between violent death and cholesterol concentration somehow becomes a link between depression and lipid neurochemistry.

Secondly, cohort studies examining cholesterol concentrations and violent death have yielded mixed findings. Selective reviews tend to put greater weight on studies that suggest that cholesterol concentration is a risk factor. When an association has been reported there is enormous scope for potential confounders, including alcohol, diet, existing mental illness, and social group.

Thirdly, although intervention studies of cholesterol lowering have minimised confounding, they have led to exaggerated certainty about causative connections. Although each of the six intervention studies systematically reviewed showed a small excess of violent deaths among participants who received the cholesterol lowering intervention (2, 3, 4, 6, 7, and 7 out of 1147 deaths in all),³ none reported that the excess was significant. Only when all the data were pooled in a meta-analysis did a significant excess of violent deaths emerge.² What is the clinical importance of this finding?

Each trial set out to record cardiovascular deaths and overall mortality, but none was designed to examine violent deaths. When pooled data suggest that treatment has affected an end point that was not considered at the start of the trials we ought to treat this finding as we should one that arose unexpectedly in a single trial. Thus we should wonder whether something is going on but should remain unconvinced until we see results from cholesterol lowering trials, with adequate power, in which violent death is one of the end points. Any subsequent meta-analysis should also start afresh; otherwise the uncertain findings from the existing pooled data will submerge authentic new results.

The pooling of data in meta-analyses has champions⁴ and sceptics: "A pragmatist might argue that when no other answers are available, the results of the pooled analyses are better than nothing; a fastidious reviewer might insist that no answer is better than one which is probably misleading."⁴ In this case we should heed the

sceptics because our only answer so far is to a question that no one has asked.

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Other studies exist

EDITOR,—In her editorial on cholesterol, violent death, and mental disorder Ann Ryman gives a balanced summary of the main studies.¹ However, it is not entirely correct that no studies so far have examined the effect of lowering cholesterol concentrations on mental state. The family heart study used dietary intervention to lower cholesterol concentrations and examined changes in mood and aggressive hostility using the Hopkins symptom checklist.² Both depressive symptoms and aggressive hostility were reduced on a low fat diet compared with a high fat "American" diet. Although these results were in the opposite direction to that predicted from the increased incidence of suicide in the large primary prevention studies, the reduction in cholesterol concentration achieved in the family heart study was only about 1% compared with around 10% in the large studies. None the less, in a small study using drugs to lower cholesterol concentration by up to 40% in hypercholesterolaemic men Strandberg *et al* found an associated decrease in anger and hostility measured by the Finnish twin study scale.³

As Ryman says, only further work can elucidate the nature and mechanism of the relation between cholesterol concentrations and mental disorder. Such a relation was described as long ago as 1935, when Brice published an article entitled "the blood fats in schizophrenia" and found evidence of low concentrations of cholesterol in association with this disorder.⁴ We have previously reported our preliminary findings of lower cholesterol concentrations in patients with treatment resistant schizophrenia than in those with treatment responsive schizophrenia.⁵ The issue of increased suicide is only one facet of this fascinating and complex subject.

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Diets, violence, and civilisation

EDITOR,—Perhaps there is more prescience in labelling coronary heart disease as a disease of civilisation than we realise. Ann Ryman adds her voice to the argument that the association between low serum cholesterol concentration and death from accidents, suicide, or violence cannot and should not be dismissed as artefactual and that it may have a physiological basis.¹

Researchers have established that the traditional hunter-gatherer diet is low in fat (about 15-20% of energy) and argue that the serum cholesterol concentrations of hunter-gatherers should also be low.^{2,3} Yet traditional Australian Aboriginal society, as one example of this way of life, is very violent, involving selective infanticide, initiation rites including penile subincision (the slitting open of the underside of the penis, which exposes the urethra), and elaborate systems of intertribal "payback" that entail culturally endorsed wounding and murder.⁴

The fact that people in Western countries have both a higher average serum cholesterol concentration and a longer lifespan than those in most non-Western countries may indicate that there is a selection advantage towards increased serum cholesterol concentrations. Perhaps the move to a higher fat, Western style diet resulted in biochemical changes that were conducive to the "civilising" process in which the unpredictability of interpersonal conflict is transformed into a regulated system of manners that reduces opportunities for violence. If higher serum cholesterol concentrations were to reduce people's depressive or violent predisposition then those people would be more likely to survive as they would be exposed to fewer risks—that is, civilised behaviour would increase survival and reproduction rates. Coronary heart disease may be the price we pay for everyone living longer in a civilised society, but since it is primarily a disease of the years after reproduction, the ability of the human species to procreate will not be affected to any great extent.

The aetiology of civilisation is, of course, multi-causal, and ascribing too strong a role to serum cholesterol concentration would be foolish. It is interesting to speculate, however, whether the Mediterranean diet was one reason why the Greeks and Romans were able to lay the foundations of Western civilisation. Maybe the public health message should be that we eat a "civilised" diet rather than a "natural" one.

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