British Journal of Nutrition (2006), **96**, 1169

Nutrition Discussion Forum

Fatal flaw in the fetal argument

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DOI: 10.1017/BJN20061887

Given its title above, the Invited Commentary by Dr Rachel Huxley (Huxley, 2006) is misleading in that it appears to refer to the fetal programming of adult disease hypothesis in general, whereas the 'flaw' actually discussed only concerns the programming of adult lipid disorders and CVD. There is ample evidence of a fetal (or early postnatal) programming effect on glucose metabolism and Type 2 diabetes in man (Hales & Barker, 1992).

Furthermore, the Invited Commentary does not take into account the substantial body of animal studies which provide 'proof of concept' in mammals of the hypothesis that events in fetal or early postnatal life may result in the subsequent occurrence of chronic disease in adult life. Though caution is obviously needed in extrapolating from animal studies to man, the virtue of animal studies is that it is possible to minimize confounding, so difficult to allow for in human studies, from the genetic and environmental influences listed by Dr Huxley. Adult rats whose dams have been subjected to partial protein deprivation during pregnancy and lactation exhibit glucose intolerance in the second year of life (Hales *et al.* 1996). The glucose intolerance is attributable to structural and functional changes in the liver (Burns *et al.* 1997; Murphy *et al.* 2003), which may include near-doubling of the volume of the hepatic acinus and centrilobular depletion of glucokinase, and in the pancreas, where β cells show reduced glucokinase, an enzyme essential for the glucose-sensor function of the islets (Hales *et al.* 1996).

The great virtue of the fetal programming hypothesis is that, if substantiated, it suggests practical and ethical approaches to the amelioration of some chronic diseases in adults. It should not be lightly discarded.

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