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Invited Commentary

Soya protein during pregnancy – an opportunity to attenuate the progression of chronic kidney disease?

Chronic kidney disease (CKD) is becoming increasingly prevalent in the developed world, affecting an estimated 5–10 % of the UK population (de Lusignan *et al.* 2005). This rising trend is in line with the ageing population and an increasing incidence of type 2 diabetes and hypertension, both major risk factors for CKD. Whilst the prevention of CKD and associated risk factors remains the first line of defence, establishing interventions that can attenuate the progression towards end-stage renal failure provides an equally important approach to reduce the burden of this disease to public health. This is of particular relevance when considering those for whom preventative measures will not suffice, for example, those who inherit a congenital form of renal cyst disease. Dietary protein restriction has long been advocated to CKD patients as a nutritional regime that will attenuate the progression of renal disease and delay the onset of end-stage renal failure. However, evidence for its clinical effectiveness and feasibility remain controversial (Lentine & Wrone, 2004). More recently, studies have focused on the source of the protein consumed rather than the total intake. There is much evidence to suggest that substitution of animal protein with soya protein has similar effects to a low-protein diet (Anderson *et al.* 1999). This evidence includes a range of human and animal studies demonstrating a beneficial effect of soya protein consumption on renal injury and disease progression. The mechanisms by which these effects are mediated remain unknown. Further work is required to investigate the differential effects of the individual components of the dietary change, including amino acid and isoflavone composition, and the critical periods at which intervention should be targeted. The work of Harold Aukema's group at the University of Manitoba has contributed significantly to this knowledge base, and the publication of their recent work in the current issue of the *British Journal of Nutrition* (Cahill *et al.* 2006) will bring further attention to the field, by highlighting the importance of the prenatal environment to the progression of this chronic disease.

The work focuses on the Han:SPRD cy rat model of renal cyst disease, which provides an excellent model for examining intervention strategies to attenuate the progression of renal disease. The 2×2 study design assessed the effects of soya protein *v.* casein in the prenatal and weaning periods on parameters of renal injury and function at 10 weeks of age. Feeding soya in the weaning period confirmed earlier findings of reduced disease progression, including attenuation of inflammatory and oxidative damage. What makes this study worthy of note is the novel finding that feeding soya in the prenatal period only was also effective in reducing disease progression in postnatal life. Despite offspring being fed a casein diet in postnatal life, the feeding of soya *v.* casein during prenatal life led to a reduction in inflammatory and oxidative renal damage and cell proliferation some 10 weeks postnatally – a long-term beneficial effect conferred by dietary change at a critical phase of development. Of further interest, feeding soya in both the prenatal and weaning periods proved to have an additive effect on inflammatory damage, reducing macrophage infiltration by 48 %. Interestingly, some of the effects of feeding soya protein in the prenatal period were different to those observed in offspring fed soya protein in the weaning period. For example, proteinuria was only significantly reduced following exposure to a soya diet during prenatal life. This indicates that the mechanisms of action differ depending on the life stage at the time of intervention and presents very interesting hypotheses for future work, including identification of critical time periods for intervention and investigation of the differential effects of individual components of the dietary change.

The concept that treatments of relatively short duration during the developmental period can have long-lasting effects on renal structure and function is certainly not new, but the study by Cahill *et al.* makes a significant contribution to this ever-expanding field of research. Over the last decade, evidence supporting the 'developmental origins of adult health and disease' hypothesis has been widely reported in the scientific literature (Zandi-Nejad *et al.* 2005; Langley-Evans, 2006). A range of animal models have been used to support the human epidemiological evidence demonstrating a link between the prenatal environment and postnatal disease status. These models have provided a useful tool with which to examine the mechanisms by which manipulation of maternal diet can have permanent adverse effects on the functionality of systems relevant to the onset and progression of chronic disease in postnatal life. The kidney has proved particularly sensitive to relatively mild shifts in maternal nutrition, with a reduction in nephron number and progressive renal dysfunction being common outcomes of manipulation of maternal diet. A number of laboratories throughout the international research community are now examining the complex gene–nutrient interactions involved, all working towards a common long-term goal: to inform public health policy through the design of preventative and intervention treatments in early life, which will counter the onset and progression of chronic disease.

The work of Cahill *et al.* provides an excellent example of the importance of early life programming and the findings are of particular importance because they demonstrate a beneficial effect of maternal dietary intervention on disease progression in a model highly relevant to human disease. This is in contrast with the majority of traditional programming models, which demonstrate adverse effects of maternal diet on offspring of an otherwise normal disease background. These traditional models provide

an excellent opportunity to investigate the mechanisms underlying the developmental origins of disease, but are perhaps less obviously applicable to measurable improvements in health. The work of Cahill *et al.* therefore marks an important step in the progression towards our common long-term goal, by demonstrating that the sensitivity of the kidney to changes in maternal diet can be harnessed to positively influence the progression of renal injury and dysfunction.

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