

## **SRF PUBLIC LECTURE SERIES 2017**

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### **PROGRAMMED FOR SEX – A SYNOPSIS**

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The reason that each of us exists is to reproduce. Our bodies are simply vehicles via which our germ cell DNA can be passed on to the next generation and thus remain 'immortal'. As a consequence, every aspect of our body (its physiology and even its shape), mind and behaviour are fashioned for this one purpose. This 'programming for sex' is amongst the earliest events to occur in fetal life, and gives rise to the greatest pleasures and distresses of our adult lives and dictates our behaviour, especially in males. Faults in this programming appear to underlie the commonest human male reproductive disorders. Most animals are seasonal reproducers, and use environmental cues (eg daylength) to optimally time reproduction – this alters appetite and metabolism as well as sexual behaviour. More recently, evidence has emerged to suggest that environmental cues (mainly dietary) may be used to (epigenetically) adapt the next 1 or 2 generations to their perceived environment (?via germ cells) – nature's fetal programming. If this thinking is correct and applies to humans, it could be that the unprecedented 'over-nutritional' changes to our modern diet/lifestyle are distorting Nature's plan so as to result (inadvertently) in inhibitory changes to reproduction in the present and next generation.

Clues to the central importance of reproduction are evident from development. Germ cells are set aside like jewels before a body exists, and as soon as a body is formed, its sexual differentiation is actioned. The set-up is for the body to follow the female reproductive blueprint. To switch this to the male pathway involves hormonal intervention, especially via androgens. Androgenic intervention then hard-wires the sexual behaviour and associated physiology. The necessity for adequate hormonal/androgenic intervention in males may explain why disorders of this process are remarkably common in comparison to females. The discovery that both the ultimate (adult) size and function of all male reproductive tract organs are determined by the level/duration of androgen exposure in a 'masculinisation programming window', which is thought to occur in humans when the fetus is 3-5cm long, highlights just how much we are prisoners of our reproductive development in the womb. Some evidence points to an increasing incidence of disorders of this process ('faulty programming').

It seems clear that a modern Western 'over-nutritional' diet, and its associated metabolic sequelae, have a universally adverse effect on reproductive function of both male and female adults. Perhaps this is an unintended consequence of Nature's underlying plan for keeping reproduction and nutrition in harmony, but of more concern is whether it results in 'reprogramming' of germ cells such that the next one or two generations are affected in ways that are unprecedented in human history. The potential for such effects is evident from the way in which fetal germ cells develop, and experimental studies in animals, and limited evidence in humans, all support the concept. How important this actually is, only time and the reproductive and general health of future generations will be able to tell us. It seems unlikely that it will alter our fundamental programming for sex.

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