OVARIES: UP IN A POF OF SMOKE

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Premature ovarian failure (POF) or premature menopause is a common disorder, defined by the occurrence of menopause under the age of 40 years and is characterised by amenorrhoea, hypoestrogenism and elevated gonadotrophins. Worldwide it affects 1% of all women and occurs in 0.1% before the age of 30 years. The major problems associated with POF are the loss of fertility at an early age and the psychological problems associated with this. In addition there are the physiological effects of reduced oestrogen, which include an increased risk of osteoporosis. POF is a heterogeneous disorder and the cause of most cases is unknown. A significant proportion (20-30%) of women with POF have a genetic predisposition. Our primary goal is to identify genes involved in POF. In most cases, the menopause is due to the loss of follicles, and it stands to reason that suitable candidate genes for POF development would be genes that regulate the rate of follicle loss. We have identified two common gene mutations, a 769G>A transition in the inhibin alpha gene in approximately 5% of POF patients associated with POF at a very early age, and mutations in FOXL2 in approximately 5% of patients. FOXL2 is thought to act downstream of inhibin which suggests that other candidate genes may arise from the analysis of the activin signalling pathway. Functional studies will help us to understand more about the molecular basis of POF. Each mutation has been associated with less than 10% of POF cases and POF is likely to be caused by mutations at many different loci. It is hoped that determining the molecular basis of POF will lead to the development of genetic tests to predict the development of POF, and eventually lead to treatment that will return fertility to these women.

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