NEWS

Clinical research: Infertile women should be tested for fragile X

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Warning sign: Women diagnosed with infertility may carry a mutation that can lead to fragile X syndrome.

Women with a mild version of primary ovarian insufficiency, a disorder that mimics the symptoms of menopause, should be tested for a mutation that can lead to fragile X syndrome, according to a study published 15 June in *Human Reproduction*[1].

Women with primary ovarian insufficiency, or POI, have abnormally functioning ovaries, leading to infertility. Those who have the classic form, called overt POI, have elevated levels of follicle-stimulating hormone and irregular menstrual cycles. Women with occult POI, a milder version of the disorder, are generally infertile, but have regular menstrual cycles.

Fragile X is a syndromic disorder related to autism, and is caused by a lack of the fragile X mental retardation protein, or FMRP. In the full-blown syndrome, a three-nucleotide region of **FMR1**, the gene that encodes FMRP, is duplicated more than 200 times, shutting off its expression.

If this region is duplicated between 55 and 200 times, it is dubbed a premutation. The premutation can expand into the full mutation in one generation and also leads to its own set of symptoms, by making too much FMR1 mRNA — the message that codes for protein — which can be toxic to the

cell.

About 20 percent of women with the premutation have overt POI, compared with 1 percent of the general population. In the new study, researchers explored whether women with occult POI are also more likely to carry the fragile X premutation.

Of 535 women with occult POI, 7 have the premutation, compared with 1 of 521 controls, the study found. Another 17 women with occult POI have an intermediate form of the premutation — between 45 and 54 repeats, which can lead to the full mutation in two generations. Among controls, seven women have the intermediate premutation.

The researchers did not include women with a family history of autism, intellectual disability or diagnosed fragile X syndrome.

References:

1.

Karimov C.B. *et al. Hum. Reprod.* Epub ahead of print (2011) **PubMed**