What is Fragile X syndrome ?

Fragile X syndrome (FXS) is the most common inherited form of intellectual disability. FXS is caused by a defected FMR1 gene located on the X chromosome, in which there is an increased number of unstable trinucleotide repeats. Overexpansion of >200 repeats cause FXS with mental retardation and autism. Carriers with an increased repeats may have variable degree of health problems (Table 1)*.

Fragile X Carrier Screening

Table 1. Categories of Number of trinucleotide repeats in the *FMR1* gene and associated clinical disorders.

Triplet repeat no.	Category	Clinical disorders
<45	Normal	None
45-54	Intermediate	None
55-200	Premutation	Late on-set of premutation specific disorders: Fragile X-associated tremor/ataxia syndrome; Primary ovarian insufficiency
>200	Full mutation	Fragile X syndrome

Ref: Fragile X Syndrome: Diagnosis, Treatment, and Research. 3rd ed. Baltimore: The Johns Hopkins University Press. 3-109. 2002.

* Limitation of this assay includes the inability to detect mosaicism, point mutation and methylation status of the amplified allele. Point mutation may contribute up to 1% of Fragile X syndrome.

Why do we need to screen for FXS carriers?

Depends on ethnics group, FXS may affects up to 1 in 4,000 males and 1 in 8,000 females. The prevalence of premutation in female is approximately 1 in 250-1,000 and in male is approximately 1 in 250-1,600.

A premutation carrier mother is at risk to transmit her premutation allele to her babies, which may then further expand to > 200 times (full mutation), resulting in a FXS baby. The risk of such transmission is dependent on the number of repeats present in the carrier mother (Table 2). The more repeats a carrier mother has, the higher chance has a full mutation being transmitted.

Table 2. Risk of full mutation transmission from maternal premutation allele.

Maternal Repeat Size	Full Mutation Expansion (%)
55–59	4
60–69	5
70–79	31
80–89	58
90–99	80
100–200	98

Data from Nolin SL, Brown WT, Glicksman A, Houck GE Jr, Gargano AD, Sullivan A, et al. Expansion of the fragile X CGG repeat in females with premutation or intermediate alleles. Am J Hum Genet 2003;72:454–64.

For more details, please refer to your specialist or contact us at (Tel) 2632-4219 or visit our website:
https://www.fetalmedicine.hk/en/Fragile_X/leaflet.pdf

Samples required for carrier screening:

Carrier screening involves the testing of DNA sample. It could be isolated from blood, saliva or any tissues.

Who should consider carrier screening ?

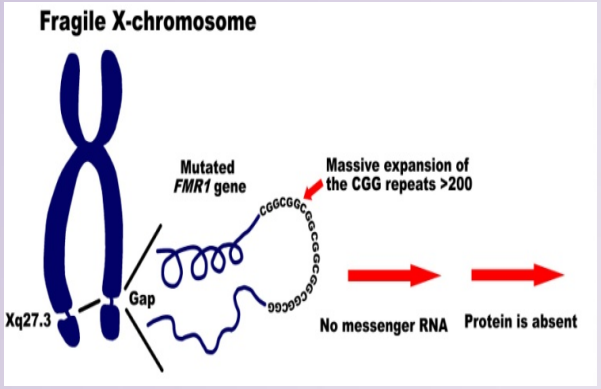
You may consider carrier screening:
if you have family history of FXS/ unexplained mental retardation or developmental delay/ autism/ ovarian failure.
If you are pregnant or planning for pregnancy and worry about FXS, you may consider the screening after counseling.

Paternal testing of FXS is not usually recommended because of the mode of inheritance.

What can I do if I diagnosed as carrier ?

Premutation carriers are at risk of transmitting the defected gene to their offsprings, and other health problems, they should be counselled by a genetic counselor. Pregnant carriers may need prenatal diagnosis. Genetic counseling and prenatal diagnostic services are available in our department.

香港中文大學 婦產科學系
The Department of Obstetrics and Gynaecology
The Chinese University of Hong Kong



脆性X攜帶者篩查
Fragile X Carrier Screening

什麼是脆性X綜合症？

脆性X綜合症(FXS)或(X染色體易裂症)為常見的遺傳性智力障礙。FXS由X染色體上*FMR1*基因不穩定三聯核苷酸重複引起。重複數>200引起FXS，表現為智力發育遲緩和自閉症，攜帶者可能有不同程度健康問題(表1)*。

* 該方法不能檢測嵌合體，點突變及等位基因甲基化狀態。脆性X綜合症可能有1%由點突變引起。

為什麼需要篩查脆性X綜合症？

不同人種FXS發病率不同， 約每4,000名男性,或每8,000名女性便有一人患有X染色體易裂症。前突變在女性的發生率為1:250-1,000，男性為1:250-1,600。

女性前突變攜帶者存在將該前突變等位基因遺傳給後代的風險，這可能引起前突變重複數增加致完全突變（>200重複數）。遺傳的風險大小取決於母體攜帶重複拷貝數的多少，重複越多導致全突變的風險越高 (表2)。

表2. 從母體前突變等位基因繼承全突變的風險

Maternal Repeat Size	Full Mutation Expansion (%)
55–59	4
60–69	5
70–79	31
80–89	58
90–99	80
100–200	98

Data from Nolin SL, Brown WT, Glicksman A, Houck GE Jr, Gargano AD, Sullivan A, et al. Expansion of the fragile X CGG repeat in females with premutation or intermediate alleles. Am J Hum Genet 2003;72:454–64.

用於做攜帶者篩查的標本:

從血液、唾液或組織中提取的DNA均可做該篩查。

哪些人應做攜帶者篩查？

有下列家族史可考慮：脆性X綜合症、未找到原因的智力障礙或發育遲緩、自閉症、卵巢早衰。如果你懷孕或計劃妊娠，同時擔心脆性X綜合症，可在諮詢醫生後考慮該篩查。

因其遺傳方式的特殊性，通常不建議父親做FXS的檢測。

表1. FXS三聯重複突變分類及相關臨床病變

Triplet repeat no.	Category	Clinical disorders
<45	Normal	None
45-54	Intermediate	None
55-200	Premutation	Late on-set of premutation specific disorders: Fragile X-associated tremor/ataxia syndrome; Primary ovarian insufficiency
>200	Full mutation	Fragile X syndrome

Ref: Fragile X Syndrome: Diagnosis, Treatment, and Research. 3rd ed. Baltimore: The Johns Hopkins University Press. 3-109. 2002.

如果我被診斷為FXS攜帶者怎麼辦？

前突變攜帶者存在將該前突變等位基因遺傳給後代的風險，及其它健康問題，應進行遺傳諮詢。孕婦為攜帶者可能需產前診斷。我科可提供產前診斷和遺傳諮詢服務。

若想知道更多資料，可向您的專科醫生查詢詳情
或 歡迎致電 2632-4219 預約或查詢
https://www.fetalmedicine.hk/en/Fragile_X/leaflet.pdf