

# Fragile X Syndrome

## Health Watch Table

### 1. Head, eyes, ears, nose, throat

Considerations	Recommendations
<p><i>Children:</i></p> <ul style="list-style-type: none"> <li>▶ <i>Vision:</i> strabismus, refractive errors are common</li> <li>▶ <i>Hearing:</i> recurrent otitis media is common</li> <li>▶ <i>Nose:</i> sinusitis is common</li> </ul> <p><i>Adults:</i></p> <ul style="list-style-type: none"> <li>▶ strabismus and refractive errors are common</li> </ul>	<ul style="list-style-type: none"> <li>▶ Undertake newborn vision and hearing screening and an auditory brainstem response (ABR)</li> <li>▶ Refer for a comprehensive ophthalmologic examination by 4 years of age</li> <li>▶ Visualize tympanic membranes at each visit</li> <li>▶ Undertake hearing and vision screening at each visit with particular attention to myopia and hearing loss</li> </ul>

### 2. Dental

Considerations	Recommendations
<p><i>Children and Adults:</i></p> <ul style="list-style-type: none"> <li>▶ High arched palate and dental malocclusion are common</li> </ul>	<ul style="list-style-type: none"> <li>▶ Refer to a dentist for a semi-annual exam</li> </ul>

### 3. Cardiovascular

Considerations	Recommendations
<p><i>Children:</i></p> <ul style="list-style-type: none"> <li>▶ Mitral valve prolapse (MVP) is less common in children (~10%) but may develop during adolescence</li> </ul> <p><i>Adults:</i></p> <ul style="list-style-type: none"> <li>▶ MVP is common (~ 80%).</li> <li>▶ Aortic root dilation usually is not progressive</li> <li>▶ Hypertension is common and exacerbated by anxiety</li> </ul>	<ul style="list-style-type: none"> <li>▶ Auscultate for murmurs or clicks at each visit. If present, do an ECG and echocardiogram; refer to cardiologist, if indicated</li> <li>▶ Undertake an annual clinical exam. Based on findings, obtain an ECG and echocardiogram. Refer to cardiologist, as appropriate</li> <li>▶ Measure BP at each visit and at least annually</li> <li>▶ Treat hypertension when present</li> </ul>

### 4. Sleep

Considerations	Recommendations
<p><i>Children and Adults:</i></p> <ul style="list-style-type: none"> <li>▶ Obstructive sleep apnea (OSA) may be due to enlarged adenoids, hypotonia or connective tissue dysplasia</li> <li>▶ Sleep apnea is more common in individuals with Fragile X-associated tremor/ataxia syndrome</li> <li>▶ <i>Children and Adults:</i> Sleep-onset or sleep-maintenance insomnia is common</li> </ul>	<ul style="list-style-type: none"> <li>▶ Ascertain a sleep history, examining bedtime, waketime, time needed to fall asleep and possible waking throughout the night</li> <li>▶ Assess for evidence of OSA</li> <li>▶ Refer to a sleep specialist, as appropriate</li> <li>▶ Behavioral sleep interventions or supplemental melatonin may be helpful</li> </ul>

## 5. Gastrointestinal

### Considerations

#### *Children:*

- ▶ In infants, feeding problems are common with recurrent emesis associated with Gastroesophageal Reflux Disease (GERD) in ~ 30% of infants

### Recommendations

- ▶ Refer for assessment of GERD. Thickened liquids and upright positioning may be sufficient to manage GERD

## 6. Genitourinary

### Considerations

#### *Children and Adults:*

- ▶ Inguinal hernias are relatively common in males
- ▶ Macroorchidism generally develops in late childhood and early adolescence and persists
- ▶ Ureteral reflux may persist into adulthood

### Recommendations

- ▶ Assess for inguinal hernia annually beginning at age 1 year
- ▶ Reassure patients and caregivers that macroorchidism does not require treatment
- ▶ Monitor for signs of urinary tract infections (UTI), screen with urinalysis.
- ▶ Evaluate recurring UTIs with cystourethrogram and renal ultrasound. Refer to a nephrologist.
- ▶ Consider and assess for a renal etiology, such as scarring, as the basis for persistent hypertension

## 7. Sexual function

### Considerations

#### *Adults:*

- ▶ Males and females are fertile

### Recommendations

- ▶ Consider discussion of recurrence risk and reproductive options as a basis for referral to a geneticist. Make such a referral even if Fragile X is only suspected so that molecular testing can be undertaken in the person concerned and relevant family members

## 8. Musculoskeletal (MSK)

### Considerations

#### *Children & Adults:*

- ▶ Hyperextensible joints and pes planus are common. Scoliosis, clubfeet, joint dislocations (particularly congenital hip) may also occur

### Recommendations

- ▶ Undertake an MSK exam at birth, then at each regularly scheduled checkup
- ▶ Elicit a history of possible dislocations
- ▶ Refer to an orthopedic surgeon as dictated by clinical findings
- ▶ Consider referral to a physical therapist (PT) or an occupational therapist (OT) to improve specific aspects of gross or fine motor skills if joint laxity or hypotonia interferes with function
- ▶ Consider referring to a physiotherapist and podiatrist for orthotics

## 9. Neurology

### Considerations

#### *Children & Adults:*

- ▶ ~ 20% have epilepsy (may include generalized tonic-clonic seizures, staring spells, partial motor seizures, and temporal lobe seizures)
- ▶ Hypotonia is common, in addition to fine and gross motor delays
- ▶ Epilepsy occasionally persists into adulthood

### Recommendations

- ▶ Ascertain a history of seizures, which usually present in early childhood
- ▶ Assess for atypical seizures in adulthood if suspicious findings occur or if intellectual function decreases
- ▶ Arrange an EEG if epilepsy is suspected from the history
- ▶ Refer to a neurologist as dictated by clinical findings

## 10. Behavioral/mental health

### Considerations

#### *Children:*

- ▶ 70% - 80% are hyperactive; ~ 30% have autism
- ▶ Autistic-like features are common and may indicate concurrent autism spectrum disorder
- ▶ Anxiety and mood disorders can also be present
- ▶ Some features of autism, tantrums and aggression as well as anxiety and mood disorders may be treated with specific pharmacological agents
- ▶ Sensory defensiveness is common and may trigger problem behaviors

#### *Adults:*

- ▶ Aggressive behavior, sensory defensiveness, attention deficit hyperactivity disorder (ADHD), mood instability, and anxiety are common in adolescence and adulthood

### Recommendations

- ▶ Make an early referral to a clinical psychologist for essential parental teaching of appropriate behavior modification techniques following diagnosis
- ▶ Hyperactivity may be managed using stimulant medications after age 5 years
- ▶ Refer to an intensive behavioral intervention autism treatment program if autism spectrum disorder is present
- ▶ Consider a referral to a psychiatrist for possible mental health disorders
- ▶ Refer to a speech and language therapist following diagnosis
- ▶ Consider referral to a psychiatrist or psychologist to assess and manage possible mental health disorders
- ▶ Violent outbursts may occur, especially in males, and may respond to behavioral and/or pharmacological measures (as for children)

## 11. Endocrine

### Considerations

#### *Children:*

- ▶ Precocious puberty may occur

#### *Adults:*

- ▶ Premenstrual symptoms (PMS) may be severe

### Recommendations

- ▶ Include attention in clinical examination to signs of precocious puberty in females.
- ▶ Refer to an endocrinologist for consideration of use of a gonadotropin agonist to manage precocious puberty
- ▶ Ascertain history of PMS with attention to menstruation, anxiety, depression, and mood lability. Consider an selective serotonin re-uptake inhibitor (SSRI) to stabilize mood if PMS symptoms are severe enough

## 12. Other

Considerations	Recommendations
<ul style="list-style-type: none"><li>▶ Occasionally presents as Prader-Willi syndrome-like phenotype</li><li>▶ <b>Premutation Carriers:</b></li><li>▶ A late onset tremor/ataxia syndrome has been reported in ~ 40% – 50% of male and ~ 8% of female Fragile X premutation carriers</li><li>▶ Premature ovarian failure by age 45 has been reported in ~ 20% – 40% of female Fragile X premutation carriers</li><li>▶ Psychiatric problems (e.g., mood and anxiety disorders) seem likely to occur in both male and female Fragile X premutation carriers 1, 2</li></ul>	<ul style="list-style-type: none"><li>▶ For management of obesity and hyperphagia, consider approaches recommended for persons with Prader-Willi syndrome</li><li>▶ Refer to appropriate specialists (e.g., neurologist, endocrinologist, psychiatrist) as indicated to assist in managing Prader-Willi syndrome-like symptoms</li><li>▶ If premutation is suspected but not yet identified, order Fragile X DNA testing or refer to a genetics clinic</li><li>▶ To manage depression or anxiety in premutation carriers, SSRIs, regular exercise and counseling have been helpful</li></ul>

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### Expert Clinician Reviewers

*Thanks to the following clinicians for the review and helpful suggestions.*

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Modified with permission of Surrey Place Centre. This tool was reviewed and adapted for U.S. use by physicians on the Toolkit's Advisory Committee; for list, view [here](#).

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## Resources

- ▶ 8 published Fragile X syndrome health care guidelines reviewed and compared (For full list of references, see [http://ddprimarycare.surreyplace.ca/wp-content/uploads/2018/03/HWT\\_Fragile-X.pdf](http://ddprimarycare.surreyplace.ca/wp-content/uploads/2018/03/HWT_Fragile-X.pdf)) Accessed March 2025.
- ▶ Fragile X syndrome websites that may be helpful for families and caregivers
  - FRAXA Research Foundation, [www.fraxa.org](http://www.fraxa.org). Accessed March 2025.
  - The National Fragile X Foundation, [www.fragilex.org](http://www.fragilex.org). Accessed March 2025.
  - Fragile X Research Foundation of Canada, [www.fragilexcanada.ca](http://www.fragilexcanada.ca). Accessed March 2025.

## References

1. Amiri K, Hagerman RJ, Hagerman PJ. Fragile X-associated tremor/ataxia syndrome: an aging face of the fragile X gene. *Arch Neurol* 2008 Jan;65(1):19-25.
2. Bourgeois JA, Coffey SM, Rivera SM, Hessel D, Gane LW, Tassone F, et al. A review of fragile X premutation disorders: expanding the psychiatric perspective. *J Clin Psychiatry* 2009 Jun;70(6):852-62.