

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"> ▶ Vision: strabismus, refractive errors are common ▶ Hearing: recurrent otitis media is common ▶ Nose: sinusitis is common 	<ul style="list-style-type: none"> ▶ Undertake newborn vision and hearing screening and an auditory brainstem response (ABR) ▶ Refer for a comprehensive ophthalmologic examination by 4 years of age ▶ Visualize tympanic membranes at each visit
<p><i>Adults:</i></p> <ul style="list-style-type: none"> ▶ strabismus and refractive errors are common 	<ul style="list-style-type: none"> ▶ Undertake hearing and vision screening at each visit with particular attention to myopia and hearing loss
2. Dental	
Considerations	Recommendations
<p><i>Children and Adults:</i></p> <ul style="list-style-type: none"> ▶ High arched palate and dental malocclusion are common 	<ul style="list-style-type: none"> ▶ Refer to a dentist for a semi-annual exam
3. Cardiovascular	
Considerations	Recommendations
<p><i>Children:</i></p> <ul style="list-style-type: none"> ▶ Mitral valve prolapse (MVP) is less common in children (~10%) but may develop during adolescence <p><i>Adults:</i></p> <ul style="list-style-type: none"> ▶ MVP is common (~ 80%). ▶ Aortic root dilation usually is not progressive ▶ Hypertension is common and exacerbated by anxiety 	<ul style="list-style-type: none"> ▶ Auscultate for murmurs or clicks at each visit. If present, do an ECG and echocardiogram; refer to cardiologist, if indicated ▶ Undertake an annual clinical exam. Based on findings, obtain an ECG and echocardiogram. Refer to cardiologist, as appropriate ▶ Measure BP at each visit and at least annually ▶ Treat hypertension when present
4. Sleep	
Considerations	Recommendations
<p><i>Children and Adults:</i></p> <ul style="list-style-type: none"> ▶ Obstructive sleep apnea (OSA) may be due to enlarged adenoids, hypotonia or connective tissue dysplasia ▶ Sleep apnea is more common in individuals with Fragile X-associated tremor/ataxia syndrome ▶ Children and Adults: Sleep-onset or sleep-maintenance insomnia is common 	<ul style="list-style-type: none"> ▶ Ascertain a sleep history, examining bedtime, waketime, time needed to fall asleep and possible waking throughout the night ▶ Assess for evidence of OSA ▶ Refer to a sleep specialist, as appropriate ▶ Behavioral sleep interventions or supplemental melatonin may be helpful

5. Gastrointestinal

Considerations	Recommendations
<p><i>Children:</i></p> <ul style="list-style-type: none">In infants, feeding problems are common with recurrent emesis associated with Gastroesophageal Reflux Disease (GERD) in ~ 30% of infants	<ul style="list-style-type: none">Refer for assessment of GERD. Thickened liquids and upright positioning may be sufficient to manage GERD

6. Genitourinary

Considerations	Recommendations
<p><i>Children and Adults:</i></p> <ul style="list-style-type: none">Inguinal hernias are relatively common in malesMacroorchidism generally develops in late childhood and early adolescence and persistsUreteral reflux may persist into adulthood	<ul style="list-style-type: none">Assess for inguinal hernia annually beginning at age 1 yearReassure patients and caregivers that macroorchidism does not require treatmentMonitor 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	Recommendations
<p><i>Adults:</i></p> <ul style="list-style-type: none">Males and females are fertile	<ul style="list-style-type: none">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	Recommendations
<p><i>Children & Adults:</i></p> <ul style="list-style-type: none">Hyperextensible joints and pes planus are common. Scoliosis, clubfeet, joint dislocations (particularly congenital hip) may also occur	<ul style="list-style-type: none">Undertake an MSK exam at birth, then at each regularly scheduled checkupElicit a history of possible dislocationsRefer to an orthopedic surgeon as dictated by clinical findingsConsider 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 functionConsider referring to a physiotherapist and podiatrist for orthotics

9. Neurology

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

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

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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) Accessed March 2025.
- ▶ Fragile X syndrome websites that may be helpful for families and caregivers
 - FRAXA Research Foundation, www.fraxa.org. Accessed March 2025.
 - The National Fragile X Foundation, www.fragilex.org. Accessed March 2025.
 - Fragile X Research Foundation of Canada, 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, Hessl 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.