**Health Watch Table — Angelman Syndrome (AS)**  
*Forster-Gibson, Berg and Korossy 2015*

**About Angelman syndrome:**  
Neurogenetic disorder due to lack of expression of a gene on the maternally inherited chromosome 15q11-q13. Physical features include delayed motor milestones, movement or balance disorders and ataxic gait, severe intellectual developmental delay, limited or absent speech, seizures, sleep disturbances, characteristic facial features and distinctive EEG pattern. Behaviour characteristics, include apparent bouts of excessive, often inappropriate laughter (contributing to an impression of happy demeanor), easy excitability, repetitive or stereotyped behaviours (such as hand flapping and mouthing) and hypermotoric behaviour 1-3

**Video** overview of AS produced by Angelman Foundation (the Netherlands), in Dutch. For English subtitles, place cursor on ‘cc’ on menu bar below screen and select “on”:  
www.youtube.com/watch?feature=player_detailpage&v=RHastPSc9XQ

**Note:** This health watch table (HWT) was developed for use with the *Primary care of adults with developmental disabilities: Canadian consensus guidelines* 4 and associated set of tools 5 which focus on health care specific to individuals with developmental disabilities. The guideline number will be referenced in the table if applicable to individuals with AS.

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### CONSIDERATIONS

<table>
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<tr>
<th>1. HEENT (HEAD, EYES, EARS, NOSE, THROAT)</th>
<th>RECOMMENDATIONS</th>
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</table>
| **Children & Adults:**  
Strabismus and refractive errors (hyperopia, astigmatism and myopia) are common 6  
Keratoconus, leading to visual distortion, associated with frequent eye-rubbing, can present in adulthood 7  
Otitis media is relatively common in young children, and can manifest as head banging or other self-injurious behaviour  
High rates of swallowing/ choking/ aspiration episodes, associated with eating, and gagging, unrelated to eating, have been reported 8  | ☐ Arrange ophthalmology assessment at diagnosis, then every 2 years.  
☐ Explore underlying cause for eye rubbing if present. Behavioural therapy may be helpful to discourage eye rubbing if there is concern about damage to the eye. 9  
☐ Screen for otitis media, especially in childhood and in the presence of recent-onset self-injurious behaviour.  
☐ Consider referral for a swallowing study, or, if not feasible, alert caregivers to possible occurrence of pneumonia due to aspiration risk. |

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<th>2. DENTAL</th>
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| **Children & Adults:**  
Dental related problems (e.g., widely-spaced teeth, drooling, teeth grinding, excessive chewing/mouthing [possibly associated with GERD – see GI below] are common.  | ☐ Ensure adherence to good oral hygiene and regular preventive dental evaluation and treatment practices.  
☐ Consider medications (carefully administered) and surgical intervention for excessive drooling, each of which has been associated with variable degrees of success. |

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<th>3. GASTROINTESTINAL</th>
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| **Children:**  
Feeding problems – typically, sucking and swallowing difficulties, due to hypotonia, are common in infants  
Constipation (often due to reduced fluid intake) and GERD are common  
Obesity, with onset typically in | ☐ Evaluate feeding problems and monitor weight gain carefully. Refer for feeding and nutritional management if underweight. Consider including possibly beneficial occupational therapy in management strategy to improve fine motor and oral motor control.  
☐ Ensure adequate fluid and fiber intake and consider management strategies, especially PEG 3350, recently recognized as an effective and well-tolerated medication choice for constipation. 10; evaluate and treat GERD as per *DD guidelines* (#15)4; |
### Health Watch Table – Angelman Syndrome

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<td><strong>adolescence, may occur, often due to overeating [possibly associated with limited sense of fullness] and lack of exercise, particularly in children with AS caused by paternal uniparental disomy (pUPD) (see section 11 – Other, below)</strong></td>
<td>□ Consider referral to dietician, if overweight.</td>
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<tr>
<td><em>Adults</em>: GERD and constipation are common. Obesity may occur</td>
<td>□ Evaluate and treat as described for children above.</td>
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### 4. ENDOCRINE & SEXUALITY

**Children**  
Puberty and development of secondary sexual characteristics, while normal, may be delayed from 1 to 3 years.

**Adults**:  
Both genders are presumed to be fertile.

Women are vulnerable to sexual abuse, sexually transmitted disease and unwanted pregnancy (see DD guidelines #6).

Individuals of both genders may engage in masturbation.

□ Ascertain status and discuss menstrual management.

□ Recommend genetic counseling for family members. (Also see #11 – Other, below.)

□ While contraception may be requested to avoid unwanted pregnancy, it may increase the potential for sexual abuse.

□ Recommend behaviour therapy to deal with masturbation.

### 5. MUSCULOSKELETAL

**Children & Adults**:  
All have some degree of movement or balance disorder, most characteristically jerky movements, ataxic, wide-based, stiff-legged gait with arms flexed; ~10% may never walk.

Hypotonia in ~50% during infancy may persist in ~20%; ~30% develop hypertonia.

Ankles may sublux or pronate.

Contractures may develop.

Scoliosis is common, occurring in ~20% of children and over 50% of adults.

Cardiorespiratory compromise may occur and should be considered in individuals who develop severe scoliosis.

Osteopenia/osteoporosis may develop in early adulthood due to reduced mobility and chronic antiepileptic treatment (see #6 below and DD guidelines #17).

□ Refer to physiotherapist and occupational therapist for advice on posture and seating from time to time, and throughout adulthood; promote lifelong physical activity (hippotherapy and swimming are frequently-mentioned preferred recreational activities) and use of adaptive devices to maintain mobility and independence.¹¹

□ Undertake regular evaluation for scoliosis in children (especially during pubertal growth spurt) and adults; refer to orthopedics for consideration of bracing or surgery.

### 6. NEUROLOGY

**Children & Adults**:  
~ 90% have history of seizures and characteristic, abnormal EEG findings (even when seizures are controlled)

Onset of seizures usually <3 years, but

□ Arrange neurology referral to ensure appropriate comprehensive initial appraisal (including MRI and EEG investigation), regular monitoring of seizure medications and periodic consideration of discontinuation after 2 seizure-free years. The latter should be a joint decision between

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¹¹ For further information, please refer to the original document or consult with a medical professional for detailed guidance.
CONSIDERATIONS

- Seizure control in some individuals (~10%) may not be achieved
- Optimal medication use has been described by Clayton-Smith
- Movement abnormalities, such as ataxia and tremors (extended and disabling tremulousness or tremor, present in teens and adults), may be mistaken for seizures, potentially leading to medication overuse
- Some anticonvulsants (carbamazepine and vigabatrin) may exacerbate seizures
- Long-term use of anti-convulsants increases risk of osteopenia and osteoporosis

RECOMMENDATIONS

- Screen early and regularly for osteopenia/osteoporosis in individuals on long-term use of anti-convulsants.
- Refer to osteoporosis specialist if situation warrants.

7. MENTAL HEALTH/BEHAVIOURAL

Children & Adults:

- Frequent laughter (often inappropriate), apparent happy demeanour, easy excitability, hyperactivity, sleep disturbance (e.g., night awakenings, obstructive sleep apnea), and aggressive behaviours such as grabbing and pulling, but not self-injury, are common

Interventions based on applied behavior analysis (ABA) are being used to teach adaptive and communication skills to improve individuals' functioning and address behaviours that challenge services

Language development is variably, though markedly impaired – majority do not develop speech; receptive language skills are always more advanced than expressive language skills and continue to improve even in adulthood

Emotional needs are often neglected in severe disability combined with limited communication

- Early and ongoing intervention by speech-language therapist is essential and should focus on nonverbal methods of communication. Use of augmentative communication aids, such as picture cards or communication boards, should be encouraged.

- “Work with the individual and family to optimize opportunities for inclusion, participation and friendship”. [see our Health Watch Table – Autism Spectrum Disorder (ASD), section 8, at www.surreyplace.on.ca/Documents/HWT_ASD.pdf]

Note: There is a divergence of opinion on the diagnosis of autism spectrum disorder (ASD) in Angelman syndrome, with some studies showing a high percentage of individuals with this condition scoring above autism cutoff on the Autism Diagnostic Observation Schedule (ADOS). Examples of behaviours in Angelman syndrome consistent with ASD diagnosis include repetitive or stereotyped movements and fascination with water. Please see our Health Watch Table – Autism Spectrum Disorder (ASD) at www.surreyplace.on.ca/Documents/HWT_ASD.pdf for details concerning diagnosis and management of ASD. Diagnosis of ASD may be important in order for individuals to gain access to specialized services.
### CONSIDERATIONS

#### 8. INFECTIOUS DISEASE/IMMUNIZATION

- Follow [DD guidelines](#20) (#20) for routine immunization.

#### 9. OTHER

**Children & Adults:**
- Genetic diagnosis can be made in 85-90% of cases.
- Four known molecular mechanisms can disrupt expression of the maternal UBE3A gene, causing Angelman syndrome:
  - Deletion 15q11-q13 region of the maternally derived #15 (70%)
  - Paternal uniparental disomy [pUPD] (2-3%)
  - Imprinting defects (3-5%)
  - Mutations in the UBE3A gene lacking the maternal methylation pattern (10%)
- These different underlying molecular mechanisms result in variability in cognitive, language, and motor features of Angelman syndrome.
- Deletion 15q11-q13 is associated with most severe and imprinting defects/UPD with less severe impairments.
- Hypopigmentation (hair, skin) occurs in individuals with deletion (sometimes encompassing the OCA2 gene) and overweight/obesity in individuals with UPD.

- If diagnosis is clinically suspected, refer to genetic centre for aetiological investigation.
- Since the recurrence risk varies with the genetic mechanism leading to disruption of UBE3A, accurate genetic testing of the individual with Angelman syndrome is imperative in order to provide accurate genetic counseling to all family members, including first and second degree relatives.
- Ensure that genetic counseling has addressed fertility and recurrence risk issues in the individual with Angelman syndrome.

The family physician can play an important advocacy role in ensuring that life-long supports, including special education in childhood and teenage years as well as close medical supervision are in place for individuals with Angelman syndrome.

### 10. CAREGIVER AND PROFESSIONAL RESOURCES


### REFERENCES CITED


**PUBLISHED HEALTH CARE GUIDELINES REVIEWED AND COMPARED**


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<th>Reference</th>
<th>Title/Description</th>
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**About this Health Watch Table**

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¹ We note with great regret that our colleague Joe Berg passed away in July 2013, during early stages of the development of the Angelman syndrome health watch table.