

## Difficulties in Diagnosing AS

Non-specific developmental problems at birth or in infancy make AS difficult to recognize.

- Normal prenatal and birth history with normal head circumference; absence of major birth defects
- Developmental delay evident by 6-12 months of age
- Delayed but forward progression of development (no loss of skills)
- Normal metabolic, hematologic and chemical laboratory profiles
- Structurally normal brain using MRI or CT (may have mild cortical atrophy or dysmyelination)

Thanks to increased awareness and improved genetic testing, many cases of AS that may have gone undiagnosed or misdiagnosed for many years are now being caught much earlier. Early diagnosis and intervention are extremely beneficial for individuals with Angelman Syndrome.

As children with Angelman Syndrome are studied, there is much being learned about educational and behavioral interventions that are effective in the areas of schooling, communication, sleep disturbances, and behaviors. Various traditional therapies such as physical, occupational, speech, and language have proven beneficial, as well as newer therapies such as music, and hippotherapy (horseback riding).



## Angelman Syndrome Websites

Pacific Northwest Angelman Syndrome Foundation

- [www.pnwasf.org](http://www.pnwasf.org)

Angelman Syndrome Foundation

- [www.angelman.org](http://www.angelman.org)

International Angelman Syndrome Foundation

- [www.international.angelmansyndrome.org](http://www.international.angelmansyndrome.org)

The Angelman Project

- [www.angelmanproject.org](http://www.angelmanproject.org)

## Help for Families

Initial diagnosis of Angelman Syndrome may be an overwhelming experience. Along with the specific medical information that can be provided by the doctors and specialists, parents may have practical questions about living with someone affected by Angelman Syndrome. Talking with other families who have gone through similar experiences can be very beneficial. We have a number of parents within our group, with children of varying ages and abilities, who are available to answer questions and share their experiences. Parents interested in contacting families in their area can find that information at:

[www.pnwasf.org/parentoparent.html](http://www.pnwasf.org/parentoparent.html)



Pacific Northwest Angelman Syndrome Foundation  
12932 SE Kent-Kangley Road, #375  
Kent, WA 98031

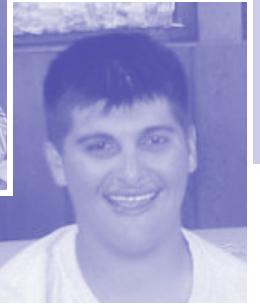
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ANGELMAN  
Pacific Northwest Angelman Syndrome Foundation



The Facts About Angelman Syndrome

## What is it?

Angelman Syndrome (AS) is a genetic disorder caused by abnormal function of the gene UBE3A, located within a small region (q11-q13) on chromosome #15. It has confounded and confused both families and the medical community for hundreds of years.

In 1965, Dr. Harry Angelman, an English physician, first described three children with the characteristics now known to be Angelman Syndrome. The first cases in North America were recognized in the early 1980's and the number of diagnosed cases continues to rise.

Once thought to be extremely rare, we now know that Angelman Syndrome affects males, females, and all racial/ethnic groups equally. Although the exact incidence of Angelman Syndrome is not known, it is thought to be about 1 in 15,000.

## Characteristics

### Consistent (100%)

- Developmental delay, functionally severe
- Speech impairment, minimal or no use of words; receptive and non-verbal communication skills higher than verbal ones
- Movement or balance disorder, usually ataxia of gait and/or tremulous movement of limbs
- Behavioral uniqueness: any combination of frequent laughter and or smiling; apparent happy demeanor; easily excitable personality, often with hand flapping movements; hypermotoric behavior; short attention span

### Frequent (more than 80%)

- Delayed, disproportionate growth in head circumference, usually resulting in microcephaly (absolute or relative) by age 2
- Seizures, onset usually before 3 years of age
- Abnormal EEG, characteristic pattern with large amplitude slow-spike waves



### Associated (20-80%)

- Strabismus
- Sleep disturbance
- Excessive chewing/mouthing behaviors
- Attraction to/fascination with water
- Uplifted, flexed arm position especially during ambulation
- Feeding problems during infancy
- Wide mouth, wide-spaced teeth
- Hyperactive lower limb deep tendon reflexes
- Flat occiput
- Hypopigmented skin and eyes (compared to family), only in deletion cases
- Frequent drooling, protruding tongue
- Tongue thrusting; suck/swallowing disorders
- Prognathia
- Increased sensitivity to heat

## Classes of AS

### Deletion positive - (70-80%)

- UBE3A gene on chromosome #15 is deleted from the maternally derived chromosome
- Typical deletion is about 4 million base pairs in length
- Usually the most severe form of AS
- Recurrence risk is very minimal, <1%

### UBE3A mutation - (5-7%)

- Mutation in the UBE3A gene inherited from the mother.
- Area can be as small as one base pair in size
- Individuals usually higher functioning than deletion positive AS
- Possible recurrence risk of up to 50%

### Uniparental disomy (UPD) - (2-3%)

- Two copies of chromosome #15 from the father.
- No mutation or deletion
- Risk of recurrence <1%
- Typically it is the highest functioning form of AS

### Imprinting Defect - (3-5%)

- Mother's copy of chromosome #15 acts like the father's inactive copy.
- May have small deletions in the imprinting center
- Possible recurrence in more than one member of a family

### Clinical - (15%)

- All known genetic tests come back normal
- Many of the typical Angelman Syndrome characteristics are present
- Cause not known, therefore recurrence rates also not known

## Testing

Angelman Syndrome can be caused by a variety of different genetic abnormalities, therefore a variety of different genetic tests must be used to screen for Angelman Syndrome

### Methylation Test

- Most useful diagnostic test
- "Positive" test confirms Angelman Syndrome
- Further testing to determine the class of Angelman Syndrome

### FISH Test

- Specialized chromosome analysis
- Detects abnormalities normally invisible on routine examination
- Way to check for a deletion
- "Positive" test confirms deletion positive Angelman Syndrome

### RFLP analysis

- DNA test to check that a chromosome #15 has been inherited from each parent
- Used to differentiate between AS due to uniparental disomy and from imprinting defect
- RFLP can confirm Angelman Syndrome due to uniparental disomy

### Search for imprinting center mutations

- Used as a means of providing accurate genetic counseling
- Looks for the precise "mutation" on chromosome #15.
- Very few labs offer this testing

### UBE3A Screening

- All other tests negative
- AS still strongly suspected
- Looks for tiny changes within the gene
- Important for genetic counseling