Angelman Syndrome Clinical Management Guidelines

Management of Angelman Syndrome

A Clinical Guideline

Angelman Syndrome Guideline Development Group

A network of centres of expertise
dyscerne
for dysmorphology

nowgen
A Centre for Genetics in Healthcare

Contents

Introduction…

… to Angelman Syndrome (AS)

Angelman syndrome is a neurodevelopmental disorder that occurs in 1 in 20-40,000 births. It is characterised by severe learning difficulties, ataxia, a seizure disorder with a characteristic EEG, subtle dysmorphic facial features, and a happy, sociable disposition. Most children present with delay in developmental milestones and slowing of head growth during the first year of life. In the majority of cases speech does not develop. Patients with AS have a characteristic behavioural phenotype with jerky movements, frequent and sometimes inappropriate laughter, a love of water, and sleep disorder. The facial features are subtle and include a wide, smiling mouth, prominent chin, and deep set eyes. It is caused by a variety of genetic abnormalities involving the chromosome 15q11-13 region, which is subject to genomic imprinting. These include maternal deletion, paternal uniparental disomy, imprinting defects, and point mutations or small deletions within the UBE3A gene, which lies within this region (see Appendix: Genetic Mechanisms in AS, p. 24 for more information).

… to the Angelman Syndrome Guideline Development Project

The guidelines have been developed using a robust methodology based on the one utilised by the Scottish Intercollegiate Guidelines Network (SIGN). The method has been adapted to suit rare conditions where the evidence base is limited, and where expert consensus plays a greater role. The members of the guideline development group are listed on page 25.

… to the Angelman Syndrome Clinical Management Guidelines

What are the aims of the guidelines?

The guidelines aim to provide clear and wherever possible, evidence-based recommendations for the management of patients with Angelman Syndrome.

Who are they aimed at?

As AS is rare, it is unlikely that many of the healthcare professionals usually responsible for managing and co-ordinating the care of people with the condition will have had much prior experience of the syndrome. As AS is a multisystem disorder, people with AS may require various diagnostic and screening tests, assessments, referrals and multidisciplinary interventions at different stages of their lives. These guidelines lay out these requirements in a clear format that is easily accessible to anybody involved in the care of an individual with AS. Though much of the information is relevant to all with AS, we have in the main used information relevant to a European audience. Though these guidelines have been prepared principally for professionals, they will also be of interest to the parents of Angelman syndrome children. If you are reading these guidelines as a parent we would emphasise that your child may not be affected by all the complications mentioned herein as every child is an individual. We would recommend that you discuss any terminology or information which may concern you with your child's doctor.

How are they organised?

The first pages contain information on the diagnosis of Angelman syndrome. Thereafter, the guidelines have been organised into sections depending on the different body systems. Within each system, different age groups are considered where relevant.

Key references are provided at the bottom of the page if more in-depth information is needed. At the end of the guideline document we list useful resources.

Clinical Diagnosis of Angelman Syndrome

Making a clinical diagnosis of Angelman Syndrome can be difficult because the signs and symptoms evolve with age and overlap with those of other disorders. Consensus clinical criteria have been developed to help with making a clinical diagnosis. Below is a summary of these criteria. It is important to note that although the diagnostic criteria can be used as a guide, there will be exceptional patients who do not fulfil these. Fulfilling the clinical criteria for AS is not absolute proof of diagnosis and once a clinical diagnosis of AS has been made it should be confirmed by genetic testing (see page 5).

Consensus Diagnostic Criteria For Angelman Syndrome (Williams et al 2006)

Consistent Clinical Features (seen in 100%)
Severe developmental delay
Movement Disorder (ataxia/tremor)
Behavioural uniqueness (frequent laughter, excitable, hypermotoric)
Speech impairment (minimal or no words)

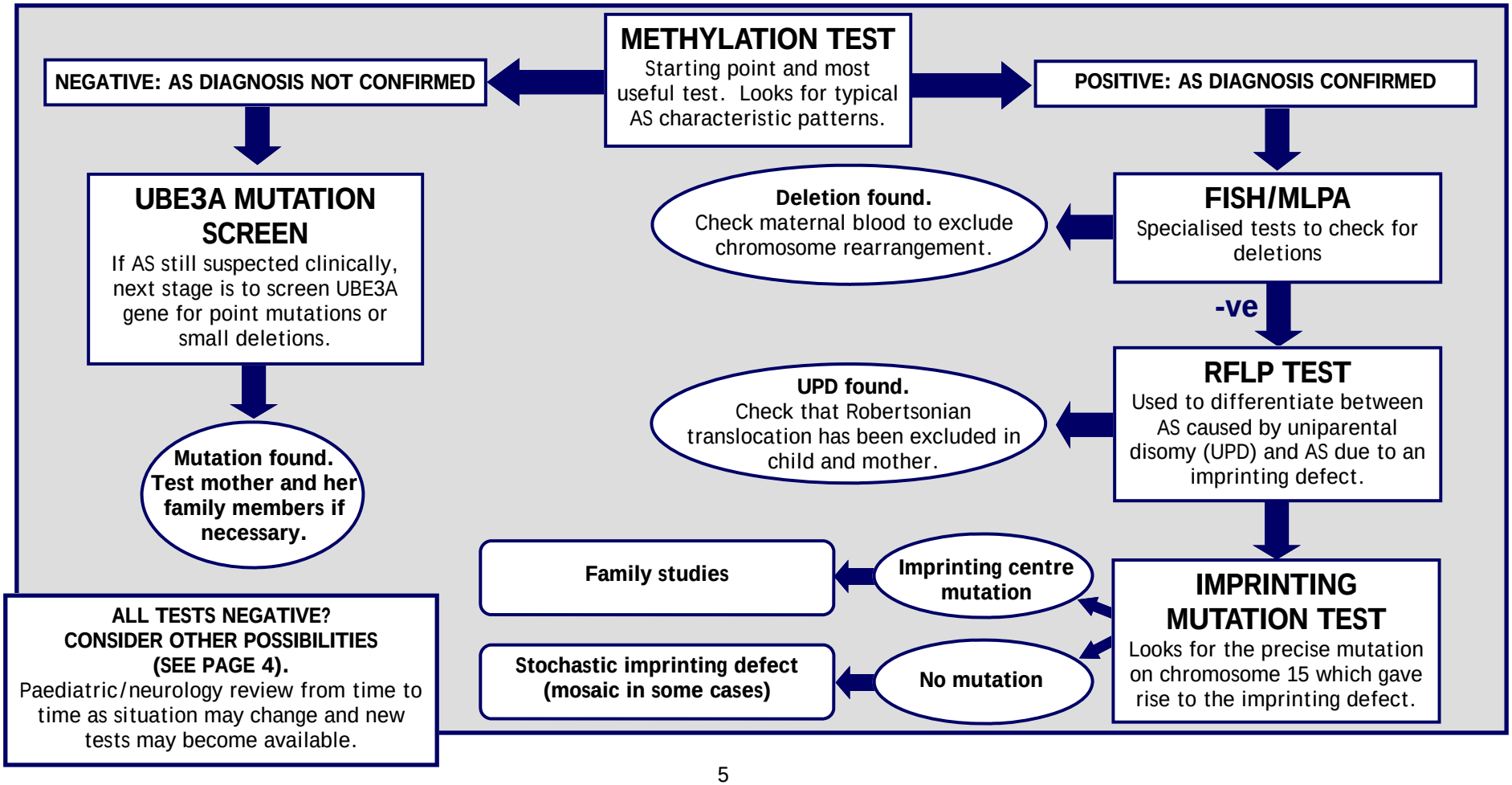
Frequent features (seen in 80%)
Impaired head growth with microcephaly/disproportionate head circumference
Seizures (onset usually <3 years)
Characteristic EEG (not associated with seizures)

Associated features (20-80%)
Flat occiput with occipital groove
Protruding tongue
Tongue thrusting
Poor suck and swallowing disorder
Feeding difficulties in infancy/truncal hypotonia
Prominent chin
Drooling, excessive chewing, mouthing
Wide mouth, wide-spaced teeth
Strabismus
Hypopigmentation
Increased deep tendon reflexes
Up-lifted, flexed position of arms on walking
Wide-based gait with feet pronated or valgus position
Increased sensitivity to heat
Abnormal sleep pattern
Fascination with water
Abnormal food-related behaviours (eating non-food items/apparent increased appetite/increased behavioural orientation towards food)
Obesity
Scoliosis
Constipation

Important Differential Diagnoses of AS
Rett Syndrome;
Important differential in girls.
History of regression
Hand-wringing movements
Hyperventilation
Mowat-Wilson Syndrome
Associated with agenesis of corpus callosum
Hirschsprung's or constipation
Congenital heart defect
Uplifted ear lobes
Pitt Hopkins Syndrome
Coarse facial features, prominent lips
Agenesis corpus callosum
Hyperventilation from mid-childhood
ATRX Syndrome
Consider in boys.
X-linked disorder
Severe hypotonia in infancy
Genital abnormalities
Anteverted nares, tented upper lip
SLC9A6 associated X-linked disorder
"X-linked Angelman syndrome"
Dystonia
Fast EEG rhythm
MTHFR Deficiency
Raised urine homocysteine
Slim build, stereotypic movements
Chromosome abnormalities
Cri-du-chat/microdeletions—consider microarray analysis
CDKL5 mutation
Early seizure onset Rett phenotype
Seizures before 6 months, hand stereotypies

Genetic Investigation of Angelman Syndrome

A clinical diagnosis of AS should be confirmed by genetic investigation. This is particularly important if parents are considering having further children as an accurate assessment of recurrence risk is dependent upon the underlying genetic mechanism involved.
AS arises due to a variety of genetic abnormalities which interfere with the normal expression of the UBE3A gene at 15q11-13. The majority (75%) have a deletion of 15q11-13, 2-3% have uniparental disomy of chromosome 15, 3-5% have impaired imprinting of the maternal copy of 15q11-13 and 5-10% have a point mutation or small deletion of the UBE3A gene. Though there are subtle clinical differences between these groups, with the deletion group showing more of the characteristic features and the UPD group being most able, overall there is a great deal of overlap between the groups, all of them having typical clinical characteristics. A group of patients exists, however, who are mosaic for a 15q11-13 imprinting defect and these individuals may show milder features, and often have more speech.
* See Appendix: Genetic Mechanisms in AS, p. 24 for more information.
A suggested strategy for genetic testing in AS is shown below. In those individuals where deletions are identified, it is also important to exclude a chromosome 15 rearrangement in the mother, as this would have a high recurrence risk in future pregnancies. When a diagnosis of AS is made, parents should be offered referral to their local genetic clinic for further discussion, as there may be implications for future pregnancies and other family members.



Recommendations for the management of Angelman Syndrome:

~ Feeding & Diet ~

Infancy and Childhood	
Feeding difficulties: seen in the majority of infants. Suck ineffective and breast feeding may be problematic.	Monitor weight gain carefully. Refer to specialised team to advise and train on feeding..
Gastro-oesophageal reflux	Administer an anti-reflux medication e.g. Gaviscon, Ranitidine, to patient in upright position. In severe cases, surgery (fundoplication) may be needed.
Constipation: often caused by inadequate fluid intake.	Encourage fluid intake. Jelly is an alternative and often more acceptable source of fluid.
Diet	Encourage healthy eating habits from an early age (including varied tastes and textures). Advise caution that children aren't chewing/swallowing toxic, corrosive or other dangerous items.

Adolescence and Adulthood	
Obesity: often caused by excessive appetite.	Check weight and BMI on an annual basis. Involve dietician if overweight. Encourage a regular exercise programme with age-appropriate activities.
Gastro-oesophageal reflux	Often returns and is problematic in older AS individuals. Suspect if an AS person becomes inexplicably distressed, appears miserable or behaviour deteriorates. Treat with anti-reflux medication.

Recommendations for the management of Angelman Syndrome:

~ Development ~

Childhood	
General developmental delay	An early, active and individualised intervention programme should be coordinated. Use appropriate scales to assess development—Bayley scales are best.
Gross motor skills	Refer for physiotherapy assessment to advise on balance, posture and management of contractures. Refer for orthotics if needed for flat feet, ankle support. Consider botulinum toxin or surgery for muscle groups with increased tone/musculo-skeletal deformities.
Fine motor skills	Occupational therapy (OT) assessment.
Education	Ensure that strengths and needs are fully assessed and appropriate support identified, including consideration of most appropriate school placement.
Communication	Early intervention by speech and language therapist (see page 12.)
Self-help skills	Standard toilet training regimes have been found to be successful in children with learning disabilities. Daytime continence can be achieved in over 50% of AS children, but in less than 20% at night.
Adolescence	
Transition from paediatric to adult care	Contact with multi-disciplinary transition team (UK statutory requirement from Year 9—age 14). See SEN Toolkit published by the Department for Education and Skills (p.20).
Adulthood	
Gross motor skills	Regular physiotherapy assessment with attention to posture and prevention of contractures. Regular exercise programme.
Communication	Pursue speech and language therapy as concentration improves with age with potential to develop language skills further.
Behaviour	Concentrate on developing functional skills to aid daily living. Refer for OT assessment. Encourage independence with nights away from home, respite, move to alternative accommodation when ready.

Recommendations for the management of Angelman Syndrome

~ Seizures and CNS ~

Seizures occur in around 90% of patients and onset is commonly in the second year of life.

Seizure Types—the following are typical of AS:

Atypical absences
Atypical absence seizures are characterised as staring spells, during which the patient is not, or only minimally, responsive.
Eye blinking or slight jerking movements of the lips may occur.
It may be difficult to distinguish an atypical absence seizure from an individual's usual behaviour.

Myoclonic jerks
Myocolnic seizures are brief jerks of a muscle or group of muscles, e.g. face or hands.
The twitches are caused by sudden muscle contractions, or more rarely by brief lapses of concentration.
Myoclonic jerks can be a manifestation of epilepsy, but can also be due to other causes that may not require treatment.

Non-convulsive status epilepticus (NCSE)
Whereas convulsive status epilepticus refers to an extremely prolonged and obvious (usually tonic-clonic) seizure and is life threatening, NCSE causes more subtle epileptic activity and an individual may appear not to be their 'usual selves', with further impairment of cognition or behaviour. This may manifest as transient regression which, while reversible, may interfere with learning and quality of life.

* Diagnosis can be facilitated by short video-clips of episodes.

Treatment

* Therapy must be balanced with quality of life and side effects.

Follow standard treatment regimens for generalised epilepsy.	→	Valproate and benzodiazepines are most commonly used and are often effective. Lamotrigine, levetiracetam and topiramate may also be effective. Some drugs (carbamazepine, oxcarbazepine, vigabatrin) have been associated with worsening of seizures in some cases but are not absolutely contra-indicated if other drugs are ineffective.
Type-specific treatments: Cortical myoclonus	→	Piracetam is a recommended treatment.
Atypical absences	→	Ethosuximide has proven effective in a small study.
NCSE	→	Leviteracetam & benzodiazepines both used.
Refractory epilepsy	→	Steroids used with success in small study.
Other treatments	→	Ketogenic diet & vagal nerve stimulation both used.
Discontinuing treatment	→	Re-evaluate medication at each visit. Consider discontinuation of treatment after 2 seizure free years—joint decision between parents & neurologist.

Recommendations for the management of Angelman Syndrome

~ *Sleep* ~

Sleep disturbance is common in Angelman Syndrome. Several studies have mentioned that AS children have a decreased need for sleep. However many children do not show the usual signs of sleep deprivation that are seen in adults but may instead become more active and demonstrate more challenging behaviour. In one study of a child with AS with a very short amount of daily sleep, improving the length of sleep had a positive impact on activity levels and behaviour, and a maintenance of more expected total sleep amounts.
Improving sleep is also of significant benefit to parents and other family members.

All Ages

Improve Sleep Hygiene	Ensure correct room temperature and amount of bedding. Avoid caffeine. Avoid stimulatory activities before bed—no TV in bedroom. Maintain the same bed time and getting up time each day. Follow the same bedtime routine which should not be too prolonged. Use blackout curtains.
Restless Sleep	Restless sleep is common in children with AS. It is multifactorial. Management is mainly behavioural though medication remains to be evaluated. Check for medical causes: Pain e.g. from teeth, ears or constipation. Gastro-oesophageal reflux. Obstructive sleep apnoea – more common in AS.
Sleep routine: underpins sleep management.	Encourage parents to keep a sleep diary. Design an individualised behavioural programme. A home visit to assess individual home circumstances can be useful.
Melatonin: baseline levels in AS are usually normal but treatment improves endogenous secretion and benefits many (but not all) patients.	Use a prescription-only medication, not health food prep. and ensure properly monitored by a doctor. Start on low dose 0.5-2mg, increase up to 10mg if needed—it has been suggested that smaller children need higher doses in comparison to their body weight. Side effects are usually minimal but monitor for any changes e.g. for seizure frequency (may improve on melatonin).
Other hypnotics	Only use benzodiazepines on a short-term basis because of the risk of dependence and inability of AS individuals to communicate about side effects.

Recommendations for the management of Angelman Syndrome

~ Vision & Hearing ~

Most children with Angelman Syndrome will have normal vision and hearing, but like any other child with learning disability they should be kept under regular review. The problems below can be seen at a higher frequency in Angelman Syndrome.

Vision	
General screening	At pre-school and school medical check ups as per local protocol with a low threshold for additional checks if any concerns.
Strabismus	Common in younger children, especially if hypopigmented. If suspected refer to orthopic/ophthalmology service—may require surgical correction.
Retinal hypopigmentation/Oculo-cutaneaous albinism: mainly in individuals with 15q11-13 deletions who may have signs of Type II oculucutaneous albinism due to deletion of one copy of Type II OCA gene plus mutation on other allele.	Look for iris transillumination (at slit lamp, before pupil dilation). Dilate pupils to examine fundus—assess hypopigmentation (particularly macula). If OCA is suspected VEPs are helpful—look for electrodiagnostic signs of aberrant decussation of fibres at optic chiasm which affects binocular vision and visual acuity.
Keratoconus: increased curvature of the cornea.	May be associated with visual impairment. Has been reported in some older patients. Can result from frequent eye-rubbing which should be discouraged. Severe keratoconus may require corneal transplant.
Hearing	
Otitis media	Occurs at an increased frequency in young children, most likely to be due to altered middle ear drainage because of angle of Eustachian tube. Examine ears if there is unexplained distress or fever and treat appropriately.

Recommendations for the management of Angelman Syndrome

~ Behaviour ~

One of the main diagnostic features of Angelman Syndrome is a characteristic pattern of behaviour with easily provoked laughter, "exuberance", movement disorder with ataxia, and wide-based, stiff-legged gait with arms upheld. The problem behaviours below may, however be encountered. The key to behaviour management is **CONSISTENCY** and involving everyone at home, school, respite and leisure activities.

All Ages

Mouthing and chewing	Try a behavioural approach using distraction. Splints are usually not helpful long term.
Hyperactivity/impulsive behaviour: characteristic of the syndrome	If severe, can be treated with low dose Risperidone or with amitryptiline. ***NB**—Risperidone can cause weight gain or sedation. (Psychostimulants such as methylphenidate are not usually used because they are known to have caused side effect of extreme lethargy in a reported AS patient.)
Aggressive behaviour: e.g. pulling, grabbing, hair-pulling. This can be stressful for AS individuals **and** parents/carers so should be addressed.	Difficult or challenging behaviour may be caused by upset or boredom and providing entertainment/activities may help. It may occur when a child doesn't want to do something e.g. sit in car seat. **Check first** for pain or discomfort e.g. toothache, earache, reflux, constipation. Analyse what leads to the behaviour and try to address cause e.g. if used as communication suggest introducing communication aid. Refer for expert help with behaviour modification. Explain to parents why problem behaviour occurs. Challenging behaviour should not be reinforced or rewarded by attention (especially eye contact) from others, or by "giving in".
Fascination with water	Advise supervision near water as accidental drowning has occurred. Useful to use water-based activities as re-inforcers for good behaviour and as part of educational programmes.
Self injury	If head-banging occurs look particularly for signs of otitis media. If hitting themselves check if they are hitting a source of pain.
Autistic behaviour	Refer for assessment and educational approaches/intervention used in autism.

Recommendations for the management of Angelman Syndrome

~ *Speech and Communication* ~

One of the key characteristics of Angelman Syndrome is a lack of speech development. Verbal comprehension is also impaired, but is better than expressive speech. There is a limited ability to make speech sounds and to vary voice tone and quality. Despite this, very few children with AS cannot communicate in some way and speech and language therapy is an important part of their management. Recommended interventions are listed below. Individuals without deletions appear to have slightly better communication skills.

Childhood

Speech and language assessment	This should be carried out by an expert at an early stage to plan effective intervention.
Interventions	Tailor to the individual child. Try different approaches e.g. signing/PECS, as different children will work better with different modes of communication. Use the same system at home, school and in all other networks. Concentrate on communication which is *functional* i.e. to communicate needs and express choices rather than just naming. Utilise IT to aid communication: making a "gesture dictionary" with photos of gestures used and meanings and taking photos of daily activities downloaded onto a digital photo frame can aid communication. Video diaries are also useful as method of sharing information. Introduce augmentative communication aids e.g. Dynavox early.

Adolescence and Adulthood

Speech and language assessment	Receptive language improves with age so speech and language therapy should be continued into adulthood and be part of an AS person's life-long learning.
Impact on behaviour	Ensuring adults have some means of non-verbal communication is essential so that they can initiate, maintain and terminate social interactions. Having an effective means of communication can curb problem behaviours.

Recommendations for the management of Angelman Syndrome

~ Dental & Drooling ~

All Ages

Drooling: caused by pooling of saliva at front of open mouth.
Common in young children. May decrease with age but persistent in some.

Parents should encourage closure of the mouth either verbally or by gently closing the mouth.
Be consistent.

Treatment

Anticholinergics: Use anticholinergics e.g. scopolamine patches, glycopyrrolate.
Watch for side effects e.g. constipation, thick lung secretions.
With scopolamine patches start with low dose e.g. quarter or half a patch and titrate up as needed.

Botulinum toxin: Injecting botulinum toxin into salivary glands can reduce saliva flow for up to four months.

Surgery: Refer for surgery if behavioural and medical treatments are not successful.
The two approaches used are to ligate salivary ducts or to re-direct them. The latter leaves more residual saliva and is preferable.

Mouthing/Chewing

Use a behavioural approach with distraction rather than splints (see page 11).
Look to see if mouthing/chewing are being caused by stress, or boredom.
Do not allow sharp or toxic objects near mouth.

Dental Care

Parents should emphasise importance of good dental hygiene and supervise and assist with any tooth brushing carried out by patient.
A curved (Collis Curve) toothbrush may be effective.
Regular visits to local dentist for preventative care.

Invasive dental treatment usually requires general anaesthetic (see page 14). Refer to paediatric dentist.

*** METICULOUS DENTAL HYGIENE IS IMPERATIVE WHEN ANY TREATMENT WHICH DECREASES SALIVA PRODUCTION IS USED.**

Recommendations for the management of Angelman Syndrome

~ General health & Anaesthesia ~

General health	
Growth	Monitor height and weight annually and check BMI.
Cardiorespiratory	Cardiorespiratory compromise may occur and should be considered in individuals who develop severe scoliosis. Rarely, outbursts of laughter may provoke syncope. If this happens, refer for 24 hour ECG monitoring. Avoid medications which increase vagal tone.
Gastro-oesophageal reflux: be aware of GOR at all ages but especially in infants. In adults suspect if there is unexplained distress, reluctance to eat, misery.	Treat with anti-reflux medication.
Immunisation: no contra-indication to normal childhood immunisations.	AS individuals should be offered seasonal flu immunisation.
Temperature Control: may be poor with a tendency to overheat.	Avoid overdressing and increase fluids in hot climates. Treat fever promptly with paracetamol but note that giving paracetamol prophylactically with immunisations is not recommended as it may impair immune response.
Hypopigmentation	Use high factor sunscreen with sun exposure.

Anaesthesia	
Anaesthesia: Few reports of problems with anaesthesia in NS.	Refer for rigorous pre-operative assessment and ensure careful choice of anaesthetic agents. Monitor perioperatively for bradycardias (due to high vagal tone). Ensure anaesthetist aware of reflux risk and treats appropriately. All regular medication to be taken as normal. Increased vigilance post-op—risk of delayed recovery if there is muscle wasting. Epilepsy is not a contra-indication to anaesthesia but seizures may occur. Anecdotal reports of high pain threshold in AS patients.

Recommendations for the management of Angelman Syndrome

~ *Scoliosis & Skeletal* ~

All Ages

Skeletal	Encourage mobility to prevent development of contractures. Severe contractures may require surgical treatment. Botulinum toxin may be considered for specific tight muscles but administration may be difficult as general anaesthetic may be required.
Scoliosis: occurs in 20% children and over 50% adults with AS.	Good management of posture from an early age can prevent or alleviate scoliosis. Refer to physiotherapist and occupational therapist for advice on posture and seating from time to time, including throughout adulthood.
Surveillance	Monitor for scoliosis each visit. If in a wheelchair, take child out to examine spine. If scoliosis is suspected refer to spinal surgeon. Monitor more carefully during adolescent growth spurt when scoliosis may progress quickly. Cardiorespiratory compromise may occur and should be considered in individuals who develop severe scoliosis (see page 14).
Radiology	Scoliosis should be confirmed and measured radiologically. X-rays should be taken with child in correct position to allow accurate visualisation of spine. It may be more appropriate for X-ray to be carried out at spinal clinic visit.
Treatment	For mild scoliosis, refer for initial treatment by physiotherapist. Bracing for mild curvature. If issued with a brace which doesn't fit change it immediately. Surgery may be needed for significant degrees of scoliosis—curves >45 degrees are likely to need surgical treatment. Optimal timing of surgery to be discussed with surgeon.
Bone density: reduced with immobility and prolonged anti-epileptic drug (AED) treatment.	Encourage mobility. Ensure adequate vitamin D intake (400 IU/10 micrograms daily in diet or supplements if necessary). If a fracture occurs refer to a specialist with an interest in metabolic bone disorders for appropriate investigation. Measurement of bone density using standard techniques can be difficult in individuals with disability and especially those with treated scoliosis. Women on Depo-Provera (see page 16) should have their bone density measured every two years.

Recommendations for the management of Angelman Syndrome

~ Puberty & Sexual Health ~

Both boys and girls with Angelman Syndrome go through a normal puberty and develop normal secondary sexual characteristics. Some reports suggest that puberty may be slightly later than normal in some individuals. All aspects of a teenager's sexual health and emotional development need to be considered. The management issues below should be addressed as part of the transitional care arrangements which should be offered to all from age of 14 (DfES (2001) SEN Toolkit).

All Ages

Management of menstruation	Allow girls to progress normally through puberty before considering treatment. Consider use of combined oral contraceptive (COC) or Depo-Provera to suppress/lighten periods. In UK COC is used most often. Using one of these methods also provides effective contraception, which may influence the decision to treat in some cases. Surgical management such as endometrial ablation or hysterectomy is **not** normally recommended.
Combined Oral Contraceptive	Normal contraindications apply. Do **not** use if there is a history of thromboembolism or in patients who are very immobile. Often used continuously for 10 weeks with a break for the eleventh week. Follow up with annual review and medical checks e.g. blood pressure.
Depo-Provera injection	May also be considered, especially if contraindications to COC. Check bone density before use and every two years during treatment.
Sexual health/activity	Masturbation is a normal activity in both sexes and should not be prevented. Behavioural approaches can be used to guide AS adolescents and adults and encourage them only to masturbate in appropriate places e.g. privately in their own room. AS adults have formed relationships with those of the opposite sex but these are usually platonic and low libido has been suggested. Contraception should be considered if situation arises and if women are considered vulnerable.
Fertility: Both males and females with AS are fertile. There is a significant risk to offspring if a parent has a deletion or UBE3A mutation.	Social and ethical issues of becoming pregnant/fathering children should be discussed fully.

Recommendations for the management of Angelman Syndrome

~ *Alternative therapies* ~

Many families report that alternative therapies for children and adults with Angelman syndrome have a positive effect on well-being. The vignettes below introduce just a few of the therapies that parents have found to be beneficial.
It must be noted that there is no strong scientific evidence to support the use of these therapies in AS.

Cranial osteopathy
A technique in which the bones of the skull are manipulated. No scientific studies which prove the benefit of this technique in AS. Some parents have reported that it reduces hyperactivity and improves sleep.

Hippotherapy
Therapy aided by a horse, utilising the horse's movements. Reports that posture, muscle tone, coordination, balance, sensory/motor development as well as speech and language skills can be improved by hippotherapy. No formal studies of the efficacy of hippotherapy in AS but some scientific evidence that it benefits children with cerebral palsy.

Aromatherapy
Many people with AS enjoy the sensory experience of touch and smell and this approach can aid relaxation, cooperation and listening, amongst other benefits.

Reflexology
Reflexology (massage or application of pressure to specific parts of the feet that are believed to correspond with other parts of the body) has been described as a beneficial, non-invasive approach to therapy for people with learning difficulties.

Hydrotherapy
Water-based therapies have been used successfully in managing aspects of AS, due to the common love of water in individuals with AS.

Music therapy
Music therapy has been used to help people with learning difficulties express their thoughts and feelings and communicate with others in a meaningful way.

Cycling—Static and trikes
A maintained exercise routine can be hugely beneficial, and in particular, many AS families have found carer-controlled bikes to be invaluable.

Brushing
Body brushing—a technique to stimulate nerve endings—has been used to heighten reflexes and improve CNS performance in people with learning difficulties.

Information for Parents

Sources of Information and Support

- **ASSERT—Angelman Syndrome Support Education & Research Trust (www.angelmanuk.org)**
  ASSERT is a UK-based support group , run by volunteers who have direct contact with people with AS. The organisation can offer advice and support on a wide range of problems faced by people with/affected by AS. It can also provide information to carers and professionals.
  They run a free, 24 hour telephone support line, hold local and regional meetings and fund research into AS.

- **Cerebra— For Brain Injured Children and Young People (www.cerebra.org.uk)**
  A charity set up to help improve the lives of children with both traumatic and acquired brain related conditions through research, educating and directly supporting children and their carers.

- **Contact a Family (www.cafamily.org.uk)**
  The Contact a Family website is for families who have a disabled child and whose who work with then or are interested to find out more about their needs. Contact A Family is the only UK charity providing support and advice to parents whatever the medical condition of their child, they have information on over 1,000 rare syndromes and can often put families in touch with each other.

- **Orphanet (www.orpha.net)**
  Orphanet is an online database of rare diseases and related services provided throughout Europe. It contains information on over 5,000 conditions, including Angelman Syndrome, and lists specialised clinics, diagnostic tests, patient organisations, research projects, clinical trials and patient registries relating specifically to Angelman Syndrome.

- **Department of Health—Personalisation (www.dh.gov.uk/en/SocialCare/Socialcarereform/Personalisation/index.htm)**
  This website contains information on how the delivery of social care is being ‘personalised’. This new approach uses individual budgets and direct payments to allow individuals more choice and control over the support they receive.

Genetic Counselling

Genetic counselling to assess risks to siblings and other family members is based upon knowing the mechanism involved in causing the loss of expression of this genetic region at the molecular level. Recurrence risks to parents and extended family members vary from a negligible risk of recurrence to a possible 50% risk.

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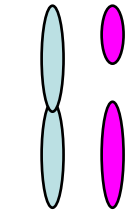
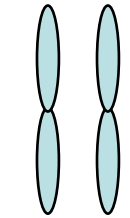
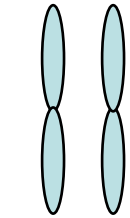
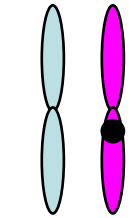
APPENDIX: Genetic Mechanisms in Angelman Syndrome

GENETIC MECHANISM:		DETECTED BY:
	Deletion of maternally inherited 15 = 75%	- Methylation test **abnormal** - FISH, MLPA, microarray
	Paternal uniparental disomy = 2-3%	- Methylation test **abnormal** - Confirmed by checking parental origin of 15s
	Imprinting defect = 5% mat 15 behaves as a pat 15	- Methylation test **abnormal** but no UPD/deletion - Pursue further studies of imprinting centre - May be mosaic (milder)
	UBE3A mutation on maternal 15 = 5-10%	- Methylation test **normal** - Confirm by UBE3A sequencing

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