Management of Noonan Syndrome

A Clinical Guideline

Noonan Syndrome Guideline Development Group
Contents

Introduction 3

... to Noonan Syndrome 3

... to the Noonan Syndrome Guidelines Development project 3

... to the Noonan Syndrome Clinical Management Guidelines 3

Diagnosis and clinical features of Noonan Syndrome 4

Recommended baseline investigations in Noonan Syndrome 5

Recommendations for the Management of Noonan Syndrome 6

... in neonates & infancy 6

... in childhood 8

... in adolescence 11

... in adulthood 13

Noonan Syndrome Growth Charts 15

... Boys—Length for Age and Weight for Length: 0–36 months 15

... Girls—Length for Age and Weight for Length: 0–36 months 16

... Boys—Stature and Growth Velocity for Age: 2–20 years old 17

... Girls—Stature and Growth Velocity for Age: 2–20 years old 18

References 19

Information for Parents 29

Acknowledgements 30
Introduction...

... to Noonan Syndrome (NS)

Noonan syndrome (NS) is one of the more common genetic conditions. The incidence of NS is estimated as 1 in 1,000 to 1 in 2,500 births, so it is still a relatively rare condition. The severity of NS is the same in males and females. The main features are congenital heart defects, short stature and characteristic facial features. Early motor delay associated with hypotonia is not necessarily associated with later learning difficulty, and most adults with NS are able to lead independent autonomous lives.

... to the Noonan 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 30.

... to the Noonan 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 Noonan syndrome.

Who are they aimed at?
These guidelines are provided for people with NS to use with their primary care and specialist clinicians as many healthcare professionals will not have had personal experience of managing Noonan syndrome. As it is a multisystem disorder, people with NS may require various tests, screening, assessments, referrals and multidisciplinary interventions at different stages of their lives. These guidelines lay out these requirements in a clear format that is accessible to anybody who is involved in the care of an individual with NS.

How are they organised?
The guidelines are divided into recommendations for four age groups:

- Neonatal and Infancy—0–1 years old
- Childhood: 1–11 years old
- Adolescence: 11–18 years old
- Adulthood: 18 years old +

Page 4 contains an overview of the diagnostic criteria and clinical features of NS, and page 5 lists the suggested baseline investigations. Subsequently, the guidelines are organised into specific age groups. For each group, management issues along with any recommended tests/screenings are listed, and follow-up options depending on the outcome of the test or screening are indicated.

NB. ABNL= Abnormal

A full list of references starts on page 19, organised by body system, which can be used as a signpost to further information on specific aspects of NS for healthcare professionals.
Additionally, there is a list of useful contacts for parents and families affected by NS, on page 29.
**Diagnosis and clinical features of Noonan Syndrome**

**Diagnostic features of NS (van der Burgt 1997)**

<table>
<thead>
<tr>
<th>Feature</th>
<th>A = Major</th>
<th>B = Minor</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Facial</td>
<td>Typical face (Facial features of NS vary over time and may have only subtle differences. Expert assessment is therefore required. See Allanson 1987—full reference p.19).</td>
<td>Suggestive face</td>
</tr>
<tr>
<td>2. Cardiac</td>
<td>Pulmonary valve stenosis and/or hypertrophic cardiomyopathy (HCM)</td>
<td>Other cardiac defect</td>
</tr>
<tr>
<td>3. Height</td>
<td>&lt; 3rd centile</td>
<td>&lt; 10th centile</td>
</tr>
<tr>
<td>4. Chest wall</td>
<td>Pectus carinatum/excavatum</td>
<td>Broad thorax</td>
</tr>
<tr>
<td>5. Family History</td>
<td>First degree relative with definite NS</td>
<td>First degree relative suggestive of NS</td>
</tr>
<tr>
<td>6. Other</td>
<td>Mild developmental delay, cryptorchidism and lymphatic dysplasia</td>
<td>Mild developmental delay, cryptorchidism, OR lymphatic dysplasia</td>
</tr>
</tbody>
</table>

**Definitive NS:**

<table>
<thead>
<tr>
<th>Criterion 1A +</th>
<th>Criterion 1B +</th>
</tr>
</thead>
<tbody>
<tr>
<td>One of 2A—6A</td>
<td>Two of 2B—6B</td>
</tr>
<tr>
<td>Two of 2A—6A</td>
<td>Three of 2B—6B</td>
</tr>
</tbody>
</table>

*Currently, mutation testing will prove a diagnosis of Noonan Syndrome in 70% of cases; in 30% the responsible gene remains unknown. The diagnosis of NS should be considered in parents when a child is diagnosed with the syndrome. Given the number of different genes where mutations can cause NS, the appropriateness and sequence of gene testing should be decided by a clinical geneticist.

**Differential diagnoses:**

- Cardio-facio-cutaneous syndrome (CFC)
- Costello syndrome
- LEOPARD syndrome
- King-Denborough Syndrome (phenotypically distinct. Malignant hyperthermia is not described in NS)

NB—Neurofibromatosis-Noonan syndrome formed part of the differential diagnosis in the past; it is now known that some patients with either of these conditions will have overlapping clinical features, due to the causative mutations occurring in the same biological pathway.
### Clinical Features of Noonan Syndrome

- Congenital heart defects (e.g. pulmonary stenosis, hypertrophic cardiomyopathy, atrial septal defect)
- Failure to thrive/slow growth rate/feeding problems
- Short stature
- Developmental delay and neuropsychological/behavioural issues
- Minor renal anomalies
- Bleeding disorders
- Visual problems (e.g. posterior segment ocular changes and anterior segment ocular abnormalities)

### Baseline investigations

- Full cardiac evaluation at diagnosis.
- Monitor and plot growth on appropriate NS and age-based growth chart.
- Refer patient in second half of first year or at diagnosis for formal developmental assessment.
- Baseline neuropsychological assessment at primary school entry.
- Refer for renal ultrasound at diagnosis.
- Carry out baseline coagulation screening in patients aged 5+, or earlier if major procedure to be undertaken. (Prothrombin Time (PT) Activated Partial Thromboplastin Time (aPPT) and FXI assay.)
- Refer for specialist ophthalmology assessment at the point of diagnosis.

(where an investigation is not indicated for a specific clinical feature, please refer to the relevant age group-specific page for management recommendations)
### Recommendations for the management of Noonan Syndrome

#### in neonates & infancy (1)

<table>
<thead>
<tr>
<th>Recommended Testing/Screening</th>
<th>Clinical Management Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Feeding assessment</strong></td>
<td>Refer for dietary assessment and evaluation of swallowing if needed.</td>
</tr>
<tr>
<td></td>
<td>Refer to speech therapist for management if necessary.</td>
</tr>
<tr>
<td><strong>Full cardiac evaluation</strong></td>
<td>Frequent vomiting should prompt investigation for gastro-oesophageal reflux and malrotation.</td>
</tr>
<tr>
<td></td>
<td>Treat with anti-reflux measures. Persistent vomiting or food refusal may require tube feeding (although this is rare).</td>
</tr>
<tr>
<td><strong>Growth monitoring</strong></td>
<td>At diagnosis.</td>
</tr>
<tr>
<td><strong>Neuropsychological and Behavioural Issues</strong></td>
<td>If hypertrophic cardiomyopathy (HCM) is found, follow up carefully.</td>
</tr>
<tr>
<td></td>
<td>Management of congenital heart disease is as per the general population, however a dysplastic valve is more likely and therefore surgery may be more likely to be necessary.</td>
</tr>
<tr>
<td><strong>Renal ultrasound</strong></td>
<td>Measure height, weight and occipitofrontal circumference (OFC) at birth and 1-3 monthly.</td>
</tr>
<tr>
<td></td>
<td>Plot on NS-specific growth charts.</td>
</tr>
<tr>
<td></td>
<td>Routine paediatric investigations for failure to thrive and reduced growth velocity.</td>
</tr>
<tr>
<td></td>
<td>Refer for formal developmental assessment in 2nd half of first year.</td>
</tr>
<tr>
<td><strong>Neurology</strong>—potential complications in NS include seizures, craniosynostosis, hydrocephalus and Arnold Chiari Malformation.</td>
<td>Developmental delay caused by hypotonia will improve with occupational and physiotherapy. Management of developmental delay will be as per the general population.</td>
</tr>
</tbody>
</table>
### Recommended Testing/Screening

<table>
<thead>
<tr>
<th>Recommended Testing/Screening</th>
<th>Clinical Management Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coagulation screening</td>
<td>To be carried out before any major surgery in neonates/infants, and at least once during childhood.</td>
</tr>
<tr>
<td>Check for cryptorchidism</td>
<td>Manage in the standard way at the appropriate time.</td>
</tr>
<tr>
<td>Skin problems: Keratosis Pilaris/Ulerythema</td>
<td>Avoid skin dryness, which can be worsened by long hot baths, perfumed soaps and dry atmospheres. Manage using emollients, keratolytic agents e.g. salicylic acid in urea cream, if tolerated, or short courses of topical steroids if necessary (especially if erythematous). Within a specialist dermatology setting, it should be noted that retinoids may not be a first choice treatment as they have been shown not to work in some NS patients.</td>
</tr>
<tr>
<td>Genetic mutation screening</td>
<td>Should be considered in the context of genetic management—which genes are tested for should be decided by a clinical geneticist.</td>
</tr>
<tr>
<td>Vision screening: squint, posterior segment ocular changes and anterior segment ocular abnormalities have been described in NS.</td>
<td>Refer for baseline evaluation at point of diagnosis.</td>
</tr>
<tr>
<td>Hearing assessment</td>
<td>Ophthalmic follow up/management as deemed appropriate by the ophthalmologist.</td>
</tr>
<tr>
<td>! Anaesthesia</td>
<td>Refer for baseline evaluation in 2nd half of first year.</td>
</tr>
<tr>
<td></td>
<td>Management in standard way.</td>
</tr>
</tbody>
</table>

---

**NS can cause coagulation difficulties that should be evaluated prior to surgical procedures so that care, including anaesthesia, can be planned accordingly.**

**Patients with NS and haemodynamically significant cardiac involvement such as severe hypertrophic cardiomyopathy need to treated according to the usual principles for patients with such cardiovascular risk factors.**

**Patients with NS may have craniofacial and/or vertebral anomalies that could affect intubation or the administration of spinal anaesthesia.**
## Recommendations for the management of Noonan Syndrome

### ~ in childhood (1) ~

<table>
<thead>
<tr>
<th>Recommended Testing/Screening</th>
<th>Clinical Management Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Echocardiogram (ECHO)</strong></td>
<td>Annually until the age of 3 and then at 5 and 10 years old, to assess for onset of HCM.</td>
</tr>
<tr>
<td></td>
<td>If results indicate HCM, follow-up regularly.</td>
</tr>
<tr>
<td></td>
<td>Management of congenital heart disease is as per the general population, however a dysplastic valve is more likely and surgery may be more likely to be necessary.</td>
</tr>
<tr>
<td></td>
<td>If ECHO results are normal at the age of 10 years old and older, cardiac follow up remains necessary due to the ongoing increased risk of cardiomyopathy.</td>
</tr>
<tr>
<td><strong>Growth assessment</strong></td>
<td>Nearly half of children with NS will reach a height within the normal range without growth hormone (GH) intervention.</td>
</tr>
<tr>
<td></td>
<td>Modest response to growth hormone therapy (GHT) has been documented but some NS patients will continue to grow into their late teens/early twenties (because of late puberty) and thereby reach normal range.</td>
</tr>
<tr>
<td></td>
<td>Final height may also be influenced by parental height.</td>
</tr>
<tr>
<td></td>
<td>Plot growth on NS growth charts.</td>
</tr>
<tr>
<td>Growth hormone (GH) axis evaluation</td>
<td>All children with a height below the mean for NS should be referred to a paediatric endocrinologist for assessment.</td>
</tr>
<tr>
<td>GH &amp; hypertrophic cardiomyopathy (HCM)</td>
<td>If height is below 2.5 standard deviations (SD) from the mean on standard childhood charts, GHT may be considered without evaluation of the GH axis.</td>
</tr>
<tr>
<td></td>
<td>If IGF-1 levels are low, testing of the GH axis should be considered to show growth hormone deficiency (GHD).</td>
</tr>
<tr>
<td><strong>Coagulation screening</strong></td>
<td>Should be carried out at least once during mid/late childhood (5—11 years old), and before major surgery.</td>
</tr>
<tr>
<td></td>
<td>Aspirin should be withheld before any surgical interventions, as per standard practice.</td>
</tr>
</tbody>
</table>

NB. While many consider existing HCM or malignancy as relative contraindications to GHT, there are no data to support this claim. Additionally, there is no evidence of an increased risk of HCM or malignancy developing in people with NS undertaking GHT.
Recommendations for the management of Noonan Syndrome
~ in childhood (2) ~

**Recommended Testing/Screening**

- Neuropsychological and Behavioural Issues: hypotonia and motor delay are common in NS and can cause developmental delay.

- Neurology—potential complications in NS include seizures, craniosynostosis, hydrocephalus and Arnold Chiari Malformation.

- Musculoskeletal

- Feeding assessment: if necessary—most feeding issues will have resolved by 18 months.

- Check for cryptorchidism

- Lymphoedema: There is an increased risk of developing lymphoedema in NS, throughout childhood and later life.

**Clinical Management Recommendations**

Screening for developmental delay and full neuropsychological assessment at primary (to include speech acquisition) and secondary school entry, and if/when symptomatic.

Assess intellectual/cognitive abilities with special attention for learning difficulties as a result of motor delay, executive dysfunctions and inattention.

Developmental delay caused by hypotonia will improve with occupational and physiotherapy.

Referral for speech therapy if acquisition is delayed.

Management of developmental delay will be as per the general population.

Ongoing review and support of learning and development with further assessment of special educational needs as required.

Low threshold for investigation of neurological symptoms e.g. consider Arnold-Chiari malformation and hydrocephalus if patient presents with headache or other neurological symptoms, and refer for MRI if suspected.

Monitor for scoliosis. Be aware that it can worsen with GHT.

Talipes occurs in 5 % of NS patients and should be managed as per the general population.

Refer for occupational therapy for management of hypermobility.

Refer for dietary assessment and evaluation of swallowing if needed.

Refer to speech therapist for management if necessary.

Frequent vomiting should prompt investigation for gastro-oesophageal reflux and malrotation.

Treat with anti-reflux measures. Persistent vomiting or food refusal may require tube feeding (although this is rare).

Manage in the standard way at the appropriate time.

Management should be the same as for general population.
Recommendations for the management of Noonan Syndrome
~ in childhood (3) ~

**Recommended Testing/Screening**

- **Skin problems:** Keratosis Pilaris/Ulerythema
- **Vision screening:** squint, posterior segment ocular changes and anterior segment ocular abnormalities are frequent in NS.
- **Hearing assessments:** NS patients have an increased risk of conductive hearing loss. Sensorineural hearing loss is rare but has been described.
- **Dental screening**
  - Giant cell lesions of the jaw

**Clinical Management Recommendations**

- Avoid skin dryness, which can be worsened by long hot baths, perfumed soaps and dry atmospheres.
  - Manage using emollients, keratolytic agents e.g. salicylic acid in urea cream, if tolerated, or short courses of topical steroids if necessary (especially if erythematous).
  - Within a specialist dermatology setting, it should be noted that retinoids may not be a first choice treatment as they have been shown not to work in some NS patients.
- **Anaesthesia**
  - NS can cause coagulation difficulties that should be evaluated prior to surgical procedures so that care, including anaesthesia, can be planned accordingly.
  - Patients with NS and haemodynamically significant cardiac involvement such as severe hypertrophic cardiomyopathy need to be treated according to the usual principles for patients with such cardiovascular risk factors.
  - Patients with NS may have craniofacial and/or vertebral anomalies that could affect intubation or the administration of spinal anaesthesia.
- **Recommended Testing/Screening**
  - **Vision screening:** squint, posterior segment ocular changes and anterior segment ocular abnormalities are frequent in NS.
  - **Hearing assessments:** NS patients have an increased risk of conductive hearing loss. Sensorineural hearing loss is rare but has been described.
  - **Dental screening**
    - Giant cell lesions of the jaw
  - **Skin problems:** Keratosis Pilaris/Ulerythema
  - **Anaesthesia**
    - NS can cause coagulation difficulties that should be evaluated prior to surgical procedures so that care, including anaesthesia, can be planned accordingly.
    - Patients with NS and haemodynamically significant cardiac involvement such as severe hypertrophic cardiomyopathy need to be treated according to the usual principles for patients with such cardiovascular risk factors.
    - Patients with NS may have craniofacial and/or vertebral anomalies that could affect intubation or the administration of spinal anaesthesia.
- **Clinical Management Recommendations**
  - **Skin problems:** Keratosis Pilaris/Ulerythema
  - **Vision screening:** squint, posterior segment ocular changes and anterior segment ocular abnormalities are frequent in NS.
  - **Hearing assessments:** NS patients have an increased risk of conductive hearing loss. Sensorineural hearing loss is rare but has been described.
  - **Dental screening**
    - Giant cell lesions of the jaw
  - **Anaesthesia**
    - NS can cause coagulation difficulties that should be evaluated prior to surgical procedures so that care, including anaesthesia, can be planned accordingly.
    - Patients with NS and haemodynamically significant cardiac involvement such as severe hypertrophic cardiomyopathy need to be treated according to the usual principles for patients with such cardiovascular risk factors.
    - Patients with NS may have craniofacial and/or vertebral anomalies that could affect intubation or the administration of spinal anaesthesia.
### Recommendations for the management of Noonan Syndrome ~ in adolescence (1) ~

<table>
<thead>
<tr>
<th>Recommended Testing/Screening</th>
<th>Clinical Management Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Echocardiogram (ECHO)</strong></td>
<td>An ECHO in adolescence is recommended as this is when familial HCM may first be identified.</td>
</tr>
<tr>
<td></td>
<td>Continued cardiac follow up throughout adolescence is important.</td>
</tr>
<tr>
<td><strong>Puberty</strong></td>
<td>The likelihood of delayed puberty should be anticipated, and appropriate education and counselling provided around this issue.</td>
</tr>
<tr>
<td><strong>Neuropsychological and Behavioural Issues</strong></td>
<td>Access to social skills training, and programmes to teach basic self help and daily living skills, if required.</td>
</tr>
<tr>
<td></td>
<td>Screen for mood and anxiety disorders if suspected.</td>
</tr>
<tr>
<td><strong>Neurology</strong>—potential complications in NS include seizures, craniosynostosis, hydrocephalus and Arnold Chiari malformation)</td>
<td>No routine screening is recommended, however there should be a low threshold for investigation of neurological symptoms e.g. consider Arnold-Chiari malformation and hydrocephalus if patient presents with headache or other neurological symptoms, and refer for MRI if suspected.</td>
</tr>
<tr>
<td></td>
<td>Management of specific complications, including epilepsy, will be as per the general population.</td>
</tr>
<tr>
<td><strong>Coagulation screening</strong></td>
<td>Screen before any surgical intervention, and withhold aspirin prior to surgery, as per standard practice.</td>
</tr>
<tr>
<td><strong>Musculoskeletal</strong></td>
<td>Monitor for scoliosis.</td>
</tr>
<tr>
<td></td>
<td>Be aware that scoliosis can worsen with GHT and in adolescence.</td>
</tr>
<tr>
<td><strong>Thyroid screening</strong></td>
<td>Screen blood for thyroid abnormalities every 3—5 years in older children and adults.</td>
</tr>
<tr>
<td></td>
<td>Manage anomalies as in general population.</td>
</tr>
<tr>
<td><strong>Lymphoedema</strong></td>
<td>There is an increased risk of developing lymphoedema in NS, throughout childhood and later life.</td>
</tr>
<tr>
<td></td>
<td>Management should be the same as for general population.</td>
</tr>
</tbody>
</table>
### Recommended Testing/Screening

- **Skin problems:** Keratosis Pilaris/Ulerythema
- **Vision screening:** squint, posterior segment ocular changes and anterior segment ocular abnormalities have been described in NS.
- **Dental screening:** Giant cell lesions of the jaw
- **Genetic counselling**

### Clinical Management Recommendations

- Avoid skin dryness, which can be worsened by long hot baths, perfumed soaps and dry atmospheres.
- Manage using emollients, keratolytic agents e.g. salicylic acid in urea cream, if tolerated, or short courses of topical steroids if necessary (especially if erythematous).
- Within a specialist dermatology setting, it should be noted that retinoids may not be a first choice treatment as they have been shown not to work in some NS patients.
- Unless already under ophthalmic management, NS patients should be referred to an ophthalmologist for assessment if/as appropriate.
- Published evidence on the management of routine dental problems in NS is limited. Routine follow up and regular dental examinations by a family dentist or local community dental services are essential.
- Missing teeth/malocclusion/other dental anomalies: refer to a consultant in paediatric dentistry for multidisciplinary management.
- Refer to Oral/Maxillofacial/Head & Neck Surgeon or expert dental care centre.
- Refer for genetic counselling, mutation testing and discussion of risks to children and options in pregnancy, at an appropriate time.

### Anaesthesia

NS can cause coagulation difficulties that should be evaluated prior to surgical procedures so that care, including anaesthesia, can be planned accordingly.

Patients with NS and haemodynamically significant cardiac involvement such as severe hypertrophic cardiomyopathy need to treated according to the usual principles for patients with such cardiovascular risk factors.

Patients with NS may have craniofacial and/or vertebral anomalies that could affect intubation or the administration of spinal anaesthesia.
### Recommendations for the management of Noonan Syndrome ~ in adulthood (1) ~

<table>
<thead>
<tr>
<th>Recommended Testing/Screening</th>
<th>Clinical Management Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Genetic counselling</td>
<td>Refer for genetic counselling, mutation testing and discussion of risks to children and options in pregnancy.</td>
</tr>
<tr>
<td>• Fertility issues</td>
<td>Care providers should be made aware of the increased risk of infertility in males with NS, and not just in those with cryptorchidism. Refer to a fertility clinic or endocrinologist if necessary.</td>
</tr>
<tr>
<td>• In pregnancy</td>
<td>Prenatal features include; polyhydramnios, increased nuchal translucency, hydrops fetalis and cystic hygroma, with or without associated ascites, pleural effusion, renal abnormalities and congenital heart defects. Chorionic villus sampling (CVS) or amniocentesis is possible—referral to a clinical genetics service preconceptually is ideal—if parental mutation is known and couple wish for a prenatal diagnosis. Ultrasounds at 12—14 and 20 weeks and undertake mutation analysis if parental mutation known and clinical features are suggestive, if required. Potential difficulties, for example those arising from coagulation defects during childbirth, should be considered and planned for as appropriate.</td>
</tr>
<tr>
<td>Fetal considerations</td>
<td>Repeat neuropsychological assessment if patient is symptomatic of mood/anxiety disorder(s), or if cognitive impairments are suspected. Pay extra attention to the evaluation of social cognition and social embedding. Consider the risk of under-diagnosing because of problems in expressing emotions. If necessary, consider pharmacological management. Facilitate access to support for employment, self help and independent living. Social skills intervention as needed.</td>
</tr>
<tr>
<td>Maternal considerations</td>
<td>Low threshold for investigation of neurological symptoms e.g. consider Arnold-Chiari malformation and hydrocephalus if patient presents with headache or other neurological symptoms, and refer for MRI if suspected. Management of specific complications, including epilepsy, will be as per the general population.</td>
</tr>
<tr>
<td>• Neuropsychological and Behavioural Issues</td>
<td>Screen before any surgical intervention, and withhold aspirin prior to surgery, as per standard practice. Newly diagnosed adults: full cardiac evaluation including ECHO. Previously diagnosed adults: regular cardiac assessment of existing heart disease, or cardiac evaluation incase aortic disease missed previously. Follow up for pulmonary valve insufficiency.</td>
</tr>
<tr>
<td>• Neurology—potential complications in NS include seizures, craniosynostosis, hydrocephalus and Arnold Chiari malformation</td>
<td></td>
</tr>
</tbody>
</table>
Recommendations for the management of Noonan Syndrome ~ in adulthood (2) ~

**Recommended Testing/Screening**
- **Thyroid screening**
  - Screen blood for thyroid abnormalities every 3—5 years.
  - Manage anomalies as in general population.
- **Lymphoedema**
  - There is an increased risk of developing lymphoedema in NS, throughout adulthood.
  - Management should be the same as for general population.
- **Skin problems:**
  - **Keratosis Pilaris/Ulerythema**
    - Avoid skin dryness, which can be worsened by long hot baths, perfumed soaps and dry atmospheres.
    - Manage using emollients, keratolytic agents e.g. salicylic acid in urea cream, if tolerated, or short courses of topical steroids if necessary (especially if erythematous).
    - Within a specialist dermatology setting, it should be noted that retinoids may not be a first choice treatment as they have been shown not to work in some NS patients.
- **Vision screening:**
  - Squint, posterior segment ocular changes and anterior segment ocular abnormalities have been described in NS.
  - Unless already under ophthalmic management, NS patients should be referred to an ophthalmologist for assessment if/as appropriate.
- **Dental screening**
  - Published evidence on the management of routine dental problems in NS is limited.
  - Routine follow up and regular dental examinations by a family dentist or local community dental services are essential.
  - Missing teeth/malocclusion/other dental anomalies: refer to a consultant in dentistry for multidisciplinary management.
  - Refer to Oral/Maxillofacial/Head & Neck Surgeon or expert dental care centre.

**Clinical Management Recommendations**
- **Giant cell lesions of the jaw**
  - NS can cause coagulation difficulties that should be evaluated prior to surgical procedures so that care, including anaesthesia, can be planned accordingly.
  - Patients with NS and haemodynamically significant cardiac involvement such as severe hypertrophic cardiomyopathy need to be treated according to the usual principles for patients with such cardiovascular risk factors.
  - Patients with NS may have craniofacial and/or vertebral anomalies that could affect intubation or the administration of spinal anaesthesia.
### Noonan Syndrome Clinical Management Guidelines

#### NOONAN SYNDROME BOYS

Birth to 36 Months
Length for Age and Weight for Length

<table>
<thead>
<tr>
<th>Name:</th>
<th>DOB:</th>
<th>ID:</th>
</tr>
</thead>
</table>

#### Mother’s Stature:  
Father’s Stature:  
Gestational Age:  weeks

<table>
<thead>
<tr>
<th>Date</th>
<th>Length</th>
<th>Weight for Length</th>
<th>Head Circ.</th>
<th>Comment</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Length (cm)</th>
<th>3</th>
<th>6</th>
<th>9</th>
<th>12</th>
<th>15</th>
<th>18</th>
</tr>
</thead>
<tbody>
<tr>
<td>cm</td>
<td>35</td>
<td>38</td>
<td>41</td>
<td>44</td>
<td>47</td>
<td>50</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Weight (lb)</th>
<th>3</th>
<th>6</th>
<th>9</th>
<th>12</th>
<th>15</th>
<th>18</th>
</tr>
</thead>
<tbody>
<tr>
<td>in</td>
<td>45</td>
<td>50</td>
<td>55</td>
<td>60</td>
<td>65</td>
<td>70</td>
</tr>
</tbody>
</table>

---

**Legend:**
- Entire Male Population
- SD = standard deviation
- % = population percentile

---

**References:**
- Noonan Syndrome Database: [www.noonan.org](http://www.noonan.org)

---

**Copyright:**
© 2007 Novo Nordisk Inc.  
132541A June 2007 Printed in the U.S.A.
Table: Growth Chart for Noonan Syndrome Girls (Birth to 36 Months)

<table>
<thead>
<tr>
<th>Age (Months)</th>
<th>Mother's Stature</th>
<th>Father's Stature</th>
<th>Gestational Age (weeks)</th>
<th>Date</th>
<th>Age</th>
<th>Weight for Length</th>
<th>Head Circ.</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>21</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>24</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>27</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>33</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>36</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


www.noonansyndrome.com
www.noonansyndrome.org
www.noonansyndromeinternational.org

% = population percentile
SD = standard deviation
References 1

General papers & Guidelines

Anaesthesia

Behaviour, Developmental Delay & Communication
Bleeding


Cancer & Tumours

References 3

Cancer and tumours continued...


Cardiac

References 4

Cardiac continued...

References 5

Dental

Diagnosis

Gastrointestinal & Feeding
References 6

Growth & Stature, Endocrine & Cryptorchidism

Noonan Syndrome Clinical Management Guidelines

References 7

Growth & Stature, Endocrine & Cryptorchidism continued...


Hearing


Immune


Lymph


Miscellaneous

References

Neurology


Orthopaedic

## References 9

### Prenatal

### Renal

### Skin
Vision

Information for Parents

Sources of Information and Support

Support for parents and other family members is cited in the literature as being an important provision for families affected by NS. The groups listed below are useful sources of support and information.

- **The Noonan Syndrome Support Group, Inc. (www.noonansyndrome.org)**
  The Noonan Syndrome Support Group is an international organisation, based in the US, that aims to support families affected by NS all over the world.
  They offer information, support, and networking opportunities, and aim to improve awareness of NS and fund research into various aspects of the condition.
  They regularly broadcast webchats with medical experts in NS, and run a well-used discussion forum.
  For more information, or to join the Support Group, visit their website.

- **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 Williams Syndrome, and lists specialised clinics, diagnostic tests, patient organisations, research projects, clinical trials and patient registries relating specifically to Noonan 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.
Acknowledgements

• The Noonan Syndrome Guideline Development Group
  Bronwyn Kerr (Condition Lead) St Mary’s Hospital, Manchester, UK
  Ineke van der Burgt (Condition Lead) Radboud University, Nijmegen Medical Centre, Nijmegen, the Netherlands
  Sus Biswas Manchester Royal Eye Hospital, UK
  Jill Clayton-Smith St Mary’s Hospital, Manchester, UK
  Jovanna Dahlgren Queen Silvia Children’s Hospital, Gothenburg, Sweden
  Bruce Gelb Mount Sinai School of Medicine, New York City, USA
  Malgorzata Krajewska-Walasek Instytut Pomniki-Centrum Zdrowia Dziecka, Warsaw, Poland
  Jacqueline Noonan University of Kentucky, USA
  Cees Noordam Radboud University, Nijmegen Medical Centre, Nijmegen, the Netherlands
  Nick Plant Royal Manchester Children’s Hospital, UK
  Adam Shaw Institute of Child Health, London, UK
  Nalin Thakker University of Manchester, UK
  Brad Williamson Salford Royal Hospital, UK
  Ellen Wingbermuhle Vincent van Gogh Institute for Psychiatry, Venray, the Netherlands
  Rob Wynn Royal Manchester Children’s Hospital, UK

• The Noonan Syndrome Guideline Development Team
  Kate Strong, University of Manchester
  Pam Griffiths, University of Manchester
  Caroline Harrison, University of Manchester

• DYSCERNE: A Network of Centres of Expertise in Dysmorphology (www.dyscerne.org)

• Nowgen—A Centre for Genetics in Healthcare (www.nowgen.org.uk)

• Novo Nordisk Inc. for the use of NS growth charts

These guidelines were produced thanks to funding from DYSCERNE: A Network of Centre of Expertise for Dysmorphology (funded by the European Commission Public Health Executive Agency (DG Sanco) Project: 2006122).