

# Noonan Syndrome

## Introduction

This syndrome was first described in 1963. The classical features include a typical facial appearance, valvular pulmonary stenosis, short stature and mild intellectual disability. However there is considerable variation in expression and the phenotype does change with age.

## Aetiology

The pattern of transmission in families suggests autosomal dominant inheritance although a significant proportion of cases are sporadic. PTPN11 gene mutations are identifiable in approximately 50% of cases.

## Prevalence

The epidemiology of Noonan syndrome is not yet defined. It has been estimated that Noonan syndrome with intellectual disability accounts for less than one per 10,000 births. However, as Noonan syndrome is associated with an intellectual disability in only one third of cases, the true incidence of this syndrome would be much greater.

## Diagnosis

Diagnosis is based on clinical findings and is usually made by a clinical geneticist. History should address the possibility of maternal abuse of alcohol or use of teratogens during pregnancy. Chromosomes should be normal. The differential diagnosis of Noonan syndrome includes Williams syndrome, foetal alcohol syndrome and Aarskog syndrome.

## Characteristics

### Facial Features

Facial features include hypertelorism (widely spaced eyes), ptosis, and downslanting palpebral fissures. Strabismus and refractive errors are common. The ears tend to be lowset and posteriorly rotated. There is a high arched palate, flattened nasal bridge and micrognathia. Although wispy in the infant, the hair tends to become more curly or woolly in the older child. The contour of the face also becomes more triangular with age. There is a low posterior hairline and excess nuchal skin may be noted in the newborn. Webbing of the neck again becomes more obvious in older children.

### Growth

In infancy there may be failure to thrive. Short stature is present in 80%. The majority of females are fertile but puberty may be normal or delayed in both sexes. In over half the males one or both testes is undescended and there may be inadequate secondary sexual development associated with deficient spermatogenesis.

### Medical Problems

Congenital heart defects are present in about two thirds of cases with the commonest defect, accounting for about half, being pulmonary valvular stenosis. Less common are atrial septal defect, asymmetrical septal hypertrophy, ventricular septal defect and persistent ductus arteriosus. There is a typical electrocardiographic pattern.

A chest deformity such as pectus carinatum or pectus excavatum is found in 90% of cases. Cubitus valgus and hand anomalies are also common. Scoliosis and talipes equinovarus may occur.

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Abnormalities of clotting factors and platelet dysfunction occur in a proportion of individuals and unexplained hepatosplenomegaly in about one quarter. Abnormalities of the lymphatic channels may give rise to general or peripheral lymphoedema in some cases.

There is some overlap between the phenotypes of Noonan and neurofibromatosis and cafe au lait patches and pigmented naevi commonly occur in this condition.

## **Cognitive, Behavioural and Neurological Problems**

About one third of individuals with Noonan syndrome have a mild intellectual disability with an average IQ 10 points below that of unaffected family members. The learning disability appears to be associated with specific visual-constructional problems. The language delay may be secondary to perceptual motor disabilities, mild hearing loss or articulation problems. Using a behavioural phenotype questionnaire, children with Noonan syndrome were found to be clumsy, stubborn and irritable, and psychiatric problems and communication difficulties were reported. Hypotonia is common. Seizures and vision and hearing impairments have also been reported in children.

## **Key Recommendations for Management**

- Referral to geneticist for diagnosis and genetic counselling.
- Management of congenital heart disease and periodic cardiac evaluation.
- Management of cryptorchidism.
- Screening for clotting abnormalities.
- Behavioural management.
- Monitoring of vision and hearing, ophthalmological examination and audiology.
- Management of seizures, if present.

## **Support Association**

Information is available from the Noonan Syndrome Association. (phone 02 9804 6762)

The material in this sheet has been adapted from the Therapeutic Guidelines book 'Management Guidelines for People with Developmental and Intellectual Disabilities' and updated from the 2005 version, Management Guidelines – Developmental Disability' which can be consulted for more detailed information.

Sheet revised: June 2005