

6. Down syndrome

Contents

6.1 Key points	2
What is Down syndrome?	2
What causes Down syndrome?	2
Important management issues	2
Risk of Down syndrome in pregnancy	2
Testing for Down syndrome in pregnancy.....	2
6.2 Background	3
What is Down syndrome?	3
How do I determine if a baby has Down syndrome?	3
What types of Down syndrome are there?	3
What medical conditions are associated with Down syndrome?	4
Management	5
Who is at increased risk?	9
Testing for Down syndrome during pregnancy	9
6.3 Patient and further information	10
6.4 Where to refer	11
6.5 References	12

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6.1 Key points

What is Down syndrome?

- Down syndrome is the most common identifiable cause of intellectual disability.
- It causes a range of physical characteristics and medical complications. These characteristics vary in type and severity between individuals.
- People with Down syndrome express the full range of human personality traits.

What causes Down syndrome?

- Down syndrome is a chromosomal condition.
- The majority (>90%) of people with Down syndrome have standard trisomy 21; that is, they have an extra complete copy of chromosome 21 in all cells (Gardner & Sutherland 1996).
- Down syndrome is rarely inherited (~1%) (Gardner & Sutherland 1996).

Important management issues

- All babies suspected of Down syndrome should have a chromosome analysis.
- Parental chromosome analysis is not necessary if the child has standard trisomy 21.
- If Down syndrome is not due to standard trisomy 21, referral to a genetics service should be made to determine if it is an inherited form of Down syndrome.
- Most medical interactions between people with Down syndrome and their GP will be for everyday medical problems unrelated to the syndrome.
- Investigations for specific medical issues related to the syndrome are recommended in addition to routine health checks.

Risk of Down syndrome in pregnancy

- The overall prevalence of Down syndrome is 1 in 525 (Riley & Halliday 2000). This represents the number of pregnancies and births diagnosed with Down syndrome. The live birth rate is lower due to spontaneous miscarriage, still birth and termination of pregnancy.
- Of babies born with Down syndrome, a significant number are born to mothers under 35 years (Riley & Halliday 2000).
- **The risk of Down syndrome is increased:**
 - ✦ As maternal age increases (see Figure 1).
 - ✦ For women with a previous pregnancy with Down syndrome.
 - ✦ For women with a positive (high-risk) prenatal screening test (see Part 5 Testing during pregnancy).
 - ✦ For a parent carrying a translocation involving chromosome 21.

Testing for Down syndrome in pregnancy

See Part 5 *Testing during pregnancy* for detailed information regarding screening tests and diagnostic tests.

All women should be given information regarding screening tests for Down syndrome.

Parents should be referred to a variety of reliable sources for information relating to Down syndrome that is correct, up to date and unbiased, to enable them to make an informed decision as to the path they wish to follow concerning their pregnancy.

Women at increased risk of having a baby with Down syndrome should be given information about their risk, diagnostic tests and screening tests. Women should be aware that counselling is available.

6.2 Background

What is Down syndrome?

Approximately 50 to 60 babies with Down syndrome are born in Victoria each year (Riley & Halliday 2000).

Down syndrome is due to the presence of additional chromosome 21 material. This is usually in the form of an extra, complete copy of chromosome 21 in every cell of the body (standard trisomy 21). Rare forms of Down syndrome include mosaic Down syndrome, where an extra chromosome 21 is present in only some cells, and Down syndrome caused by chromosome translocations, which in some cases may be inherited.

How do I determine if a baby has Down syndrome?

Features present in neonates include:

- Hypotonia.
- Facial characteristics.
- Physical malformations, particularly cardiac and/or gastrointestinal.
- Brachycephaly and prominent parietal eminences.

Older babies may present with developmental delay.

Referral to a paediatrician is recommended if a baby is suspected to have Down syndrome.

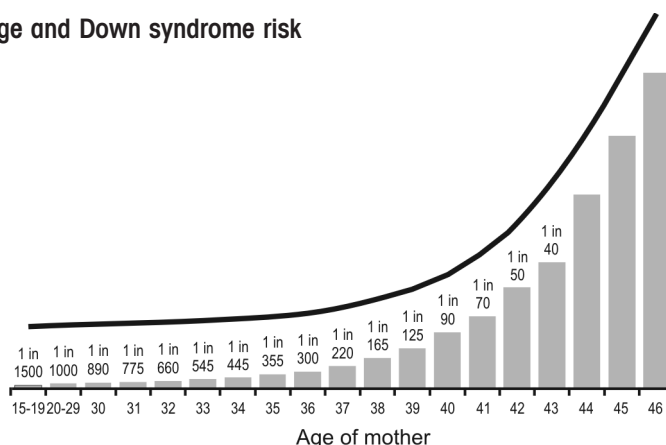
Chromosome analysis by blood test confirms the diagnosis and identifies the nature of the chromosome abnormality.

What types of Down syndrome are there?

Standard trisomy 21

- Most cases of Down syndrome have an extra, whole chromosome 21 in all cells and tissues.
- Usually, the extra chromosome 21 is acquired during germ cell formation, most commonly in the egg, and is therefore present at conception.
- It is not necessary to test parental chromosomes, as this form of Down syndrome is not inherited.
- The only known risk factors for trisomy 21 are maternal age (see Figure 1) and a previous affected pregnancy.
- Parents of a previously affected pregnancy have a recurrence risk of approximately one in 100 or, where the mother is >37 years at EDD, approximately the maternal age risk (Gardner & Sutherland 1996).
- An individual with Down syndrome has, in theory, a 50% risk of having a child with trisomy 21; however, the rates of fertility are low.
- Siblings and other family members have essentially the same risk as other women the same age.

Figure 1. Maternal age and Down syndrome risk



Mosaic trisomy 21

- People with mosaic Down syndrome have a mix of normal cells and cells with trisomy 21.
- The proportion of normal cells varies and influences the degree to which features associated with Down syndrome are present, so an individual with fewer trisomy 21 cells is likely to be less affected.
- Mosaic trisomy 21 is uncommon.
- The majority of mosaic trisomy 21 occurs as a result of a failure of the chromosome 21 pair to separate during cell division after conception (mitotic non-dysjunction). Analysis of parental chromosomes is not necessary and the theoretical risk of recurrence is less than 1% (Gardner & Sutherland 1996).

Translocations

- Chromosome rearrangements (translocations) involving chromosome 21 can result in the presence of an extra part of chromosome 21.
- Translocations are responsible for approximately 5% of cases (Gardner & Sutherland 1996).
- Approximately one-third of people with a translocation have inherited the translocation from one parent. The risk of recurrence in these cases is between 1% and 15%, depending on which parent is transmitting the translocation (Gardner & Sutherland 1996).
- Where the translocation is not inherited, parents have less than a 1% risk of recurrence (Gardner & Sutherland 1996) and other family members are not at increased risk.
- Referral to a genetics service is recommended.
- Parental chromosomes should be analysed.
- Usually, there is no difference clinically between children with translocation Down syndrome and standard trisomy 21.

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What medical conditions are associated with Down syndrome?

An individual who has Down syndrome has far more normal characteristics than abnormal characteristics. While there are many physical characteristics that can be found in people who have Down syndrome, no individual with Down syndrome will have all the characteristics. The number of physical characteristics present does not have any relationship to intellectual ability or vice versa.

Conditions that occur more commonly in people with Down syndrome include:

- *Intellectual disability*: There is a wide spectrum of intellectual disability, ranging from mild to moderate and occasionally severe (American Academy of Pediatrics 2001).
- *Cardiac malformations*: Cardiac malformations are very common in people with Down syndrome. Approximately half of those with malformations will require surgery, which is usually successful. An echocardiograph and cardiology consultation is recommended for all babies with Down syndrome (American Academy of Pediatrics 2001).
- *Gastrointestinal malformations*: Gastrointestinal conditions are very common in the neonatal period. Approximately 12% of babies with Down syndrome have malformations such as duodenal atresia or stenosis, imperforate anus and Hirschsprung disease and require surgery (American Academy of Pediatrics 2001). Constipation, resulting in part from low muscle tone, is extremely common. Breast-feeding may also be difficult and appropriate support from a lactation consultant may be required. Coeliac disease is increasingly being recognised and may be present in 4 to 14% of people with Down syndrome (Gale et al. 1997). In the presence of symptoms, serological screening or duodenal biopsy should be considered.

- **Auditory deficits:** up to 75% have significant hearing loss, usually of the conductive type (American Academy of Pediatrics 2001). All babies with Down syndrome should be screened with brainstem auditory evoked response (BAER) testing in the first few months of life and standard audiometry regularly throughout the preschool years from the age of 12 months. Alertness to the possibility of fluctuating hearing loss from otitis media with effusion is important and if there are suspicions of possible hearing loss, appropriate audiology is recommended.
- **Visual deficits:** Cataracts may occur in 15% of children with Down syndrome (American Academy of Pediatrics 2001). Congenital cataracts need to be diagnosed early to prevent blindness from amblyopia. If there is doubt about the presence of the red reflex, refer to an ophthalmologist. Vision problems such as near or far sightedness are common and regular vision assessments are recommended from about 12 months. These need to be appropriate to the developmental age of the individual.
- **Hypothyroidism:** Hypothyroidism is more common in people with Down syndrome and may be either congenital or acquired. Yearly screening for hypothyroidism is recommended (American Academy of Pediatrics 2001).
- **Epilepsy:** Five to 10% of people with Down syndrome will have epilepsy. There appear to be two peaks of age of onset: in the first two years of life, and in the third decade of life (Pueschel & McKnight 1991).
- **Atlantoaxial instability:** Ten to 30% of adolescents with Down syndrome may have asymptomatic atlantoaxial instability, 1 to 2% will be symptomatic. Testing for atlantoaxial instability is extremely controversial. Regular clinical surveillance may be appropriate. Warning signs of symptomatic atlantoaxial instability include deteriorating gait and incontinence (American Academy of Pediatrics 2001).
- **Respiratory problems:** People with Down syndrome are prone to respiratory tract infections. Obstructive sleep apnoea affects up to 75% of those with Down syndrome (American Academy of Pediatrics 2001). If there is a clinical suspicion of significant obstructive sleep apnoea, this can be clarified with polysomnography.
- **Dementia of the Alzheimer's type:** A number of adults with Down syndrome may develop Alzheimer disease, with a mean age of onset in the sixth decade. Clinicians should be watchful for signs of dementia beyond the age of 40.
- **Immunodeficiency:** People with Down syndrome are more prone to infections and the infections tend to be more severe.
- **Leukemia:** People with Down syndrome have approximately a 1% risk of leukemia.

Management

Medical care

General practitioners can expect to be involved in the medical care of people with Down syndrome from the time of first diagnosis through to old age. The average life expectancy is into the sixth decade.

Most interactions between people with Down syndrome and their general practitioner will be for everyday medical problems unrelated to the syndrome.

People with Down syndrome should have the same health checks as those without. Down syndrome-related medical issues require additional checks (Table 1).

Intervention strategies

Current research shows that benefits can result from stimulation, play and general encouragement given from the time of birth. Early intervention can assist parents to provide developmentally appropriate activities. Intervention services (including physiotherapy, occupational and speech therapies) integrate multiple health professionals, the parents and carers. Most people with Down syndrome can learn to read, write, handle money, do simple maths, use a calculator and become competent and independent.

Referral is strongly recommended

The Down Syndrome Association of Victoria and Paediatric Services (see Where to refer) are sources of information regarding early intervention and therapeutic services.

Useful contacts

- Community workers or social workers can provide support for families and assist in access to services.
- Support groups, for support and information regarding services.
- Counselling services; for example, grief counselling, genetic counselling.
- Centrelink for application forms for the Carer's Allowance, other allowances and, in some cases, carers pension.
- The Association for Children with a Disability can provide information and advocacy for parents. The guide to services Through the maze is available from the association.
- Regional Department of Human Services for government assistance available (including early intervention).
- Family planning services, adult disability services and/or support groups may be useful during adolescence, especially regarding issues relating to sexuality.
- Respite care through Department of Human Services, regional Carer Links, local council and regional Interchange.
- Noah's Ark Toy Library.

Table 1. Medical care for individuals with Down syndrome

Age	Medical Issues	Recommendations
Neonatal 0–6 weeks	Cardiac malformation Cataract Feeding difficulties Constipation Other	Echocardiograph and cardiology referral Check red reflexes. Early diagnosis prevents irreversible visual loss from amblyopia. If any doubt refer to ophthalmologist Liaison with trained lactation consultant or paediatrician Simple constipation is common, consider Hirschsprung disease Early, comprehensive paediatric review. Consider genetics referral
Infancy 6 weeks to 1 year	Hypothyroidism Auditory deficit Immunisations Growth	Check result of newborn screening test, repeat at 6 months then annual biochemical screening Auditory brainstem evoked response or oto-acoustic emissions within first 6 months. Examine ears at each visit for otitis media with effusion Immunisation with usual doses of vaccines at the usual intervals Ensure normal growth using Down syndrome growth charts (American Academy of Pediatrics 2001)
Preschool 1–5 years	Auditory Deficit Visual Deficit Hypothyroidism Dental problems and periodontal disease Atlantoaxial instability	Annual hearing tests (standard) Tympanometry Annual ophthalmological examination Continue hypothyroidism screening Regular dental checks Discuss risk with parents. Surveillance for symptoms of spinal cord compression; for example, weakness, spasticity or loss of previously acquired continence Immunisation with usual doses of vaccines at the usual intervals
Primary school 5–11 years	Hypothyroidism Auditory and visual deficit Sleep apnoea	Annual thyroid function screening Biannual screening Annual otoscopic examinations Monitoring for symptoms of obstructive sleep apnoea. Refer for polysomnography if suspicious Immunisation with usual doses of vaccines at the usual intervals

Age	Medical Issues	Recommendations
Secondary school	Atlantoaxial instability Obesity predisposition Sleep apnoea	Surveillance for neurological symptoms Establish good diet and exercise habits. Plot growth on Down syndrome growth charts (American Academy of Pediatrics 2001) As above
Adulthood	Hypothyroidism Mitral Valve prolapse Epilepsy	Annual thyroid function screening Annual cardiovascular examination and, if clinical uncertainty exists, echocardiograph Usual blood pressure monitoring Usual cholesterol screening Usual breast or testes examination Usual cervical cytology Track weight throughout life using height and weight charts normalised for Down syndrome If skills decline in early adulthood, suspect depression Electroencephalogram if clinically indicated Monitor skills as part of a routine check and assess for Alzheimer disease if there is significant decline
Aged care	Dementia and Alzheimer disease	Exclude depression, situational crisis, hypothyroidism, menopause, diabetes, visual & hearing impairment, cerebrovascular accident, adverse effects of medication, occult infection, carcinoma Immunisation with usual doses of vaccines at the usual intervals

Who is at increased risk?

Women at increased risk of having a baby with Down syndrome include:

- Those who have had a *previous pregnancy* with Down syndrome or other trisomy.
- Those *aged 37 or over at EDD*.
- Those with an *increased risk result* on a **prenatal** screening test.
- Carrier, or partner of a carrier, of a chromosome translocation involving chromosome 21.

Testing for Down syndrome during pregnancy

- Two types of tests are available during pregnancy: screening and diagnostic tests.
- Knowledge that a baby has, or is at increased risk of, Down syndrome gives parents the opportunity to make decisions regarding the pregnancy or to plan for the future.
- All pregnant women or women contemplating a pregnancy should be given information about screening for Down syndrome.
- Women over 37 years and those at high risk should be offered a choice of screening or diagnostic testing.
- Some women and couples choose not to have testing during pregnancy.

Prenatal screening tests

- Identify pregnancies at increased risk of Down syndrome
- Include nuchal translucency determined by ultrasonography in the first trimester, and blood tests in the first or second trimester.

Women with positive antenatal screening tests are offered diagnostic tests to determine fetal karyotype.

Diagnostic tests

- Identify pregnancies with Down syndrome by chromosome analysis.
- Are performed after fetal sampling by either chorionic villus sampling (CVS) and amniocentesis.

See Part 5 *Testing during pregnancy* for further details.

If a pregnancy is affected by Down syndrome, it is important that the parents are referred to a variety of reliable sources for information which is correct, up to date and unbiased, to enable them to make an informed decision as to the best path for their pregnancy.

6.3 Patient and further information

Support groups

Down Syndrome Association Victoria
495 High Street, Northcote 3070
Call: (03) 9486 2377
Fax: (03) 9486 2435
Email: dsavic@netspace.net.au
Website: <http://www.dsav.asn.au>

Association for Children with a Disability
590 Orrong Road, Armadale 3143
Call: (03) 9500 1232
Fax: (03) 9500 1240
Email: mail@acd.org.au
Website: <http://www.acd.org.au>

Other

Noah's Ark Family Resource and Toy Library
28 The Avenue, Windsor, 3181
Call: (03) 9529 1466

1 Altona Street, Heidelberg West 3081
Call: (03) 9458 4133

Websites

Health Channel:

<http://www.betterhealth.vic.gov.au>

Relevant topics:

- Amniocentesis
- Birth defects involving chromosomes – trisomy disorders
- Down syndrome – the school experience
- Down syndrome and Alzheimer's
- Down syndrome and health
- Down syndrome and your family
- Down syndrome is a common genetic condition
- Maternal serum screening

American Academy of Pediatrics:

<http://www.aap.org/policy/re0016.pdf>

Includes growth charts for Down syndrome

Books

Cunningham, C 1988, *Down's syndrome: an introduction for parents*, Souvenir Press, Great Britain.

Selikowitz, M 1990, *Down syndrome: the facts*, Oxford University Press.

Stray-Gundersen, K (ed.) 1995, *Babies with Down syndrome: a new parent's guide*, Woodbine House, Bethesda, MD.

For professionals

Lennox, N & Diggins, J (eds) 1999, *Management guidelines: people with developmental and intellectual disabilities*, Therapeutic Guidelines Limited.

Information folder for health professionals, from the Down Syndrome Association Victoria.

6.4 Where to refer

Assessment of children with developmental delay

Child Development and Rehabilitation Department
Royal Children's Hospital
Flemington Road, Parkville 3052
Call: (03) 9345 5898

Developmental Disability Clinic
Department of Paediatrics
Level 4, Monash Medical Centre
Clayton Road, Clayton 3168
Call: (03) 9594 6666
For appointments, fax letter to Dr Philip Graves:
(03) 9594 6925

Early childhood intervention services

For information regarding local intervention services contact:

Disability Services
Department of Human Services
Level 2, 555 Collins Street, Melbourne 3000
Call: (03) 9616 8654
Fax: (03) 9616 7403
TTY: 1300 131 525 during business hours, for people who are deaf or have a hearing, speech or communication impairment (for the cost of a local call)

Down Syndrome Association Victoria
495 High Street, Northcote 3070
Call: (03) 9486 2377
Fax: (03) 9486 2435
Email: dsavic@netspace.net.au
Website: <http://www.dsav.asn.au>

Assessment of adults with developmental delay

Centre for Developmental Disability Health Victoria
Suite 202, 3 Chester Street, Oakleigh 3166
Clinics are held at a number of locations
For appointments, call (03) 9564 7511

Genetic counselling services

Royal Children's Hospital
Genetic Health Services Victoria
Flemington Road, Parkville 3052
Call: (03) 8341 6270
Fax: (03) 8341 6390

Monash Medical Centre
Clinical Genetics/Genetic Health Services Victoria
Clayton Road, Clayton 3168
Call: (03) 9594 2026
Fax: (03) 9594 2022

Non-metropolitan services

(Ballarat, Bendigo, Frankston, Geelong, Mildura, Sale, Shepparton, Traralgon, Warragul, Warrnambool)

Genetic Health Services Victoria
Call: (03) 8341 6270
Fax: (03) 8341 6390

Albury/Wodonga Genetics Clinic
Genetic Health Services Victoria
78 Vermont Street, Wodonga 3690
Call/Fax: (02) 6056 0451

Royal Women's Hospital
Genetic Health Services Victoria
Grattan Street, Carlton 3053
Call: (03) 9344 2121
Fax: (03) 9344 2066

Mercy Hospital for Women
Genetics Department
Clarendon Street, East Melbourne 3002
Call: (03) 9270 2394
Fax: (03) 9270 2498

6.5 References

American Academy of Pediatrics 2001, 'Health supervision for children with Down syndrome', *Pediatrics*, 107:442–49 or at <http://www.aap.org/policy/re0016.pdf>

Gale, L, Wimalaratna, H, Brotodiharjo, A & Duggan JM 1997, 'Down's syndrome is strongly associated with coeliac disease', *Gut*, 40:492–96.

Gardner, RJ & Sutherland GR 1996, *Chromosome abnormalities and genetic counselling*, Oxford University Press.

Pueschel, SM, Louis, S & McKnight, P 1991, 'Seizure disorders in Down syndrome', *Archives of Neurology*, 48:318–20.

Riley, M & Halliday, J 2000, *Birth defects in Victoria (1983–1998)*, Perinatal Data Collection Unit, Department of Human Services Victoria.

⁷ Chromosome mosaicism is the presence of mixture of cells with normal and abnormal karyotype. Where mosaicism is found on CVS,