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Down Syndrome

Clinical guidance

OFFICIAL

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**Key messages**

* Down syndrome is the most common chromosomal condition with approximately 30 babies born with Down syndrome in Victoria each year. Whilst many are known or anticipated to have the condition before birth, some are not.
* Down syndrome is caused by an additional full or partial copy of chromosome 21 and so is also known as Trisomy 21.
* Early recognition and diagnosis, knowledge of potentially associated health problems and necessary screening are important to allow prompt treatment if necessary and optimise health.
* Knowledge of the appropriate use of language, supports available in the immediate and longer term and parental counselling are imperative when making or discussing the diagnosis.
* Chromosomal analysis should be performed whenever the diagnosis of Down syndrome is suspected. Initial genetic testing can be performed urgently with a result usually available within 24 to 48 hours.

**Acknowledgement**

This guidance may use the terms ‘woman’ and ‘mother,’ which are intended to be inclusive of anyone who may use other self-identifying terms and aims to encompass all for whom this guidance is relevant.

**Consumer Engagement Statement**

All interactions between health care staff with consumers (women, mothers, patients, carers and families) should be undertaken with respect, dignity, empathy, honesty and compassion.

Health care staff should actively seek and support consumer participation and collaboration to empower them as equal partners in their care.

**Definitions/Abbreviations**

|  |  |
| --- | --- |
| CVS | Chorionic villus sampling |
| DNA | Deoxyribonucleic acid |
| DSV | Down Syndrome Victoria |
| ECG | Electrocardiogram |
| FISH | Fluorescent in-situ hybridisation |
| NIPS | Non-invasive pre-natal screening |
| PPV | Positive predictive values |
| RCH | Royal Children’s Hospital |
| TAM | Transient abnormal myelopoiesis |
| TFT’s | Thyroid Function Tests |
| VCGS | Victorian Clinical Genetics Service |

**Introduction**

Down syndrome is also known at Trisomy 21. Human cells each contain 46 chromosomes – 22 pairs of autosomes numbered 1-22, and one pair of sex chromosomes. Down syndrome results when all, or most cells, have three copies of chromosome 21 instead of two.

Down syndrome is the most common single chromosome condition with approximately 30 babies born each year in Victoria. Whilst a woman’s individual chance of having a baby with Down syndrome increases with age, many babies with Down syndrome are born to younger mothers.

In Victoria women are offered screening tests for a number of conditions including Down syndrome early in their pregnancy. This can be by either first trimester combined screening – maternal serum screening between 9 and 13 weeks of pregnancy alongside ultrasound for nuchal translucency at 11-13 weeks or by non-invasive pre-natal screening (NIPT) to detect cell-free fetal DNA (genetic material) in maternal serum from 10 weeks' gestation. Both screening methods will determine a numerical chance that the fetus has Down syndrome1. They are screening tests and cannot make a definitive diagnosis.

Neither test has a 100% accuracy in either confirming or excluding Down syndrome (and other conditions screened for) in a pregnancy. There are a number of different providers of NIPT with varying positive predictive values (PPV) – that is, the probability that, following a positive screening result, the fetus actually has the condition.

The PPV also varies based on several factors including maternal age, maternal weight, and the prevalence of Down syndrome in the general population. It is important that health care providers are able to accurately communicate the significance of PPV to prospective parents or have referral pathways to appropriate counselling in place.1,2

Further information on antenatal genetic screening and testing can be found [on the VCGS website](https://www.vcgs.org.au/health-professionals-landing/).

If a pregnancy is determined to have a high chance of being affected by Down syndrome, some women elect to receive a definitive diagnosis during pregnancy by sampling either the placenta (chorionic villus sampling/CVS) or the amniotic fluid (amniocentesis). This testing is invasive and carries some risk to the pregnancy and so appropriate counselling to assist in making this decision is essential. Some parents will opt to wait until birth to confirm the diagnosis.

If Down syndrome is diagnosed antenatally, some women may choose to not continue with their pregnancy, and some parents may use the diagnosis to better prepare for their baby’s arrival.

Despite the existence of screening during pregnancy some babies are found to have Down syndrome only after birth due to a mother not having screening (intentionally or otherwise) or falsely low-chance results on screening.

**Diagnosis**

A diagnosis of Down syndrome may be clinically suspected in a term newborn based on a combination of distinctive physical features, known collectively as the Down syndrome phenotype.

These features, which can be present in any combination include:

* hypotonia
* up slanting palpebral fissures
* broad epicanthic folds
* flat facial profile
* low set ears and narrow ear canals
* protruding tongue
* single palmar crease
* sandal gap with increased space between first and second toes
* brachycephaly – flattening of the back of the head with relative increase in width of the skull.

It can be more difficult to identify the features of Down syndrome in preterm babies and in some ethnicities.

There is no single physical feature that is 100% specific for Down syndrome and genetic testing is needed to confirm the diagnosis. If there is reasonable clinical suspicion of Down Syndrome, this should be performed early but always after discussion with the parents. If antenatal diagnostic testing has been performed, repeating this after birth is not necessary unless the result has shown a possibility of mosaicism.

Those with mosaic Down syndrome (where only some cells have trisomy 21) may have no or very subtle physical features and initially go unrecognised. Mosaic Down syndrome accounts for only 2–4% of cases of Down syndrome.

**Family discussion**

The most experienced clinician available should discuss with the parents the clinical suspicion of Down syndrome and proposed plan for testing at the earliest opportunity, and the same clinician (if possible) should speak with the parents again once the diagnosis is confirmed. It is recommended to have a nurse and/or social worker also present to provide additional support if needed. Parents should also be given the opportunity to have any support persons they wish present.

All families will react in their own way to hearing unexpected news and this will direct how the conversation proceeds and what follow-up discussions are needed and when. It is important to ensure the parents feel supported and able to ask questions and are given time to process a lot of new information. If the baby has a feature of Down syndrome (or any other medical condition) necessitating urgent transfer to another hospital for medical or surgical management it will be necessary to convey this information in a more urgent manner and revisit the discussion later, or to ensure colleagues at the receiving hospital will do so.

It is important to use appropriate language when disclosing a suspected or confirmed diagnosis of Down syndrome in their newborn baby to parents. Examples of preferred language when discussing disability is provided [here.](https://www.afdo.org.au/news/language-guide/)4

**Investigations**

**Investigations for Down syndrome**

* Chromosomal analysis is required for diagnosis.
* Fluorescent in-situ hybridisation (FISH) using a probe specific for the Down syndrome critical region can be processed in around 48 hours when an urgent result is required. 0.5-1mL of blood in lithium heparin tube should be sent. Direct communication with the scientists at the cytogenetics service utilised by the birth hospital is necessary to facilitate this. Many, but not all, Victoria healthcare providers use the Victorian Clinical Genetics Service (VCGS) for cytogenetic testing. They can be contacted on 1300 118 247. Similarly, the RCH (Royal Children s Hospital) on-call genetics Fellow can be contacted for advice via the RCH switchboard on 0393455522.
* A full karyotype will also be performed on cultured lymphocytes from the same blood sample. This assesses for any other genetic anomalies such as translocations and for mosaicism. It usually takes 3-6 weeks, although can be done within 5-7 days if urgent and discussed with the laboratory.
* Buccal swab microarray is another means of obtaining a sample for karyotype that is less invasive than taking blood and becoming widely used, however FISH cannot be performed on this sample and a result usually takes 2-4 weeks and so is not recommended for urgent results.

**Screening for associated health conditions**

Many babies with Down syndrome are healthy and well, but there can be associated health problems that should be screened for and treated if detected.

Some babies with Down syndrome have hypotonia that can affect feeding and so may need additional support from Speech and Language Therapists or a temporary naso-gastric tube until tone improves.

It is recommended that all neonates with confirmed (or expected, awaiting confirmation) Down syndrome have the following screening investigations:5

* Growth parameters plotted on a Down syndrome specific growth chart.
* ECG (pre-discharge) and echocardiogram arranged – this may be done as an early outpatient appointment if the neonate has no murmurs on auscultation and passes oxygen saturation screening.
  + Congenital heart disease is present in 40-50% of neonates with Down syndrome, the most common findings being atrioventricular septal defect and Tetralogy of Fallot.6,7 Some cardiac conditions will require surgery in the early months of life, others can be monitored.
* Full blood count to assess white blood and other cell lines to assess for transient abnormal myelopoiesis (TAM)
  + TAM is a usually benign and self-limiting increase in circulating blast cells which, if present, requires close monitoring and Paediatric Haematology consultation; treatment with chemotherapy may sometimes be required.
* Thyroid function tests (TFTs)
  + Thyroid dysfunction spectrum is present in between 4 to 8% of neonates with Down syndrome. Full TFTs should be performed in addition to the newborn blood spot screening as congenital hypothyroidism is the only thyroid condition screened for by this method.
* Eye examination by an Ophthalmologist to assess for presence of cataracts (present in 3%). This can be performed as an outpatient early after hospital discharge. This should be repeated at six weeks of age.
* Newborn Hearing Screen – there is an increased incidence of both congenital and acquired hearing loss.

Additional information on screening and health maintenance throughout childhood for children with Down syndrome is available [here.](https://www.rch.org.au/genmed/clinical_resources/Screening_for_children_with_Down_Syndrome/)

Other associated health issues that may be present but can only be detected by means of thorough physical examination rather than specific tests are:

* Gastrointestinal – approx. 12% of neonates with Down syndrome will have one or more of:
  + oesophageal atresia
  + duodenal atresia
  + imperforate anus
  + Hirschsprung’s disease – ensure first passage of meconium occurs within 48 hours of birth.
* Developmental dysplasia of the hip – repeated examination over the newborn period is the optimal means of detection, with low threshold to perform an ultrasound.8

**Management**

Once the diagnosis is made, it is imperative that resources, information and support are provided and that the family is given the time and space to process the news and to ask questions.

As well as addressing any health issues, families will also require information and education about the psycho-social aspects of living with disability. It is therefore important that education and information is available and conducted by someone with adequate, contemporary and informed knowledge.

Parents often work through the diagnosis and its impact at different rates. Initially the reaction may be one of shock and despair as the news is unexpected. However, with the appropriate supports and information families can learn to navigate these early days with greater clarity.

Down Syndrome Victoria (DSV) offer considerable support and information for all families. A Family Support worker is available for consultation and to meet with the family, including in hospital. DSV provide resources, peer support and referral to supports and services. Most importantly DSV is able to provide an opportunity to learn and gain understanding via shared lived experience.

A [New Parent Pack](https://www.downsyndrome.org.au/vic/resources/life-stages/new-parent-resources/) containing suitable information that will address many questions and provide essential information for parents of newly diagnosed children is also available. It can be downloaded from the DSV website and should be offered to all parents of babies with Down syndrome after birth.

A referral to a general paediatrician for ongoing management and surveillance should be done before hospital discharge as well as referral to the National Disability Insurance Scheme and information about the diagnosis provided to the family’s general practitioner.

**Differential diagnosis**

Differential diagnosis for Down syndrome involves:

* Smith-Maginnis syndrome – deletion of chromosome material from chromosome 17
* Zellweger syndrome – presents in newborn period with hypotonia and feeding problems.

**More information**

**Clinical information and support services**

* [Down Syndrome Victoria](http://www.downsyndromevictoria.org.au/) – also available to provide information and training to healthcare professionals
* [Down Syndrome Victoria – Referral form](https://docs.google.com/forms/d/1a4Yw_DR8hUV1H8zCuPhR8103FCWTw5pHhQiUD-KCDOs/viewform)
* [Down Syndrome Australia](http://www.downsyndrome.org.au/)
* [Victorian Clinical Genetics Services](https://www.vcgs.org.au/)
* [Royal Children's Hospital – Screening for children with Down syndrome](http://www.rch.org.au/genmed/clinical_resources/Screening_for_children_with_Down_Syndrome/)

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