

What Do We Know *Now* About Trisomy 18?

Trisomy 18 syndrome (Edwards syndrome) is a disorder of human chromosomes which occurs in approximately 1 in 7,000 live born infants. Trisomy refers to three copies of a chromosome instead of the normal two and in trisomy 18 there is a presence of an extra #18 chromosome. Over 90% of infants with Trisomy 18 syndrome will have a full trisomy in all body cells while the remainder will have a trisomy due to a rearrangement of part or all of one chromosome (attached to another chromosome), called a translocation, or have mosaicism (two different cell lines such as some normal cells and some trisomy cells).

Most often a diagnosis of Trisomy 18 is suspected by results of maternal blood screening and fetal ultrasound findings. **Optional invasive testing**, amniocentesis or chorionic villus sampling, is needed **to confirm a diagnosis** but carry a small risk to the fetus. A prenatal diagnosis of Trisomy 18, before 24 weeks, is often followed with an option to terminate; a decision made by 75% in the USA and 90% in Europe. A diagnosis can also affect the care provided to those continuing pregnancy, their birthing options, and the care of their infant.

The new non-invasive prenatal test (NIPT) is increasing in use. A Positive Predictive Value (PPV) calculator is a tool used to determine accuracy of a NIPT *positive* result.

Infants born with Trisomy 18 usually are small in size at birth. There is a recognizable pattern of physical features that often allows the health professional to make the diagnosis of the syndrome. These physical findings are not medically significant but provide clues. They include: prominence to the back part of the head, short eyelid fissures, small mouth and jaw, external ear variations, clenched fist with index finger overlapping the third, and 5th finger overlapping the 4th, small fingernails, underdeveloped or altered thumbs, short sternum (breastbone), club feet and redundant skin at the back of the neck.

The major impact of Trisomy 18 is a predisposition to congenital malformations (birth defects), a high incidence of infant mortality, and developmental and motor disability in older infants and children.

Birth Defects

The congenital malformations involve the medically significant findings mentioned above as well as the presence of some internal or external birth defects. The most common and important is a defect of the heart. Over 90% of children with Trisomy 18 will have a congenital heart malformation; these include:

- **Ventricular septal defect (VSD)**, an opening between the lower chambers of the heart which prevents the heart from pumping blood correctly (a heart murmur is generally heard from this finding);
- **Atrial septal defect (ASD)**, an opening between the two upper chambers of the heart making it difficult for the heart to pump sufficient oxygen-rich blood to body tissues (a heart murmur is often heard);
- **Patent ductus arteriosis (PDA)**, a heart defect involving the lack of closure of the channel that usually closes near the time of birth and thus is a persistence of the opening of this channel.

In addition, children with Trisomy 18 usually have an alteration of one of the four heart valves. This combination is referred to as a ventricular septal defect with polyvalvular dysplasia. The majority of heart lesions are usually not those that cause death in the neonatal period but about 10% of children with Trisomy 18 will have a life-threatening heart defect noted before or soon after birth. These include a double outlet right ventricle and hypoplastic left heart.

The increased occurrence of infant mortality is related to a combination of factors but most importantly *central apnea*, where the brain does not give the message to breathe. Other complicating factors include upper airway problems, difficulty feeding with aspiration, and a predisposition to *aspiration pneumonia*, and underdevelopment of the lungs. The *heart defects* can play some role in this but are usually not the only cause of this increased mortality.

Important and common birth defects in Trisomy 18

Congenital heart defects 90%
Multiple joint contractures (including club foot) >50%
Meningomyelocele (a form of Spina bifida) <10%
Hearing loss >50%
Radial aplasia (underdevelopment or missing radial bone of forearm) 5-10%
Cleft lip or palate or both 10-20%
Birth defects of the eye <10%

Common Disorders and Illnesses in Trisomy 18

Feeding difficulties
Gastroesophageal reflux
Slow postnatal growth
Apnea (central, obstructive, or both)
Seizures
Kidney defects
Urinary tract infections
Developmental disability
Scoliosis (curvature of the spine, primarily seen in older child)
Frequent pneumonia
Urinary tract infection
Chronic constipation
Development of pulmonary hypertension

Often reported surgeries for Trisomy 18

Gastrostomy tube placement
Fundoplication
Cardiac surgery
Tracheostomy
Tumor (Wilms/Liver)
Spinal fusion
Strabismus
Cleft lip and/or palate
Gastrointestinal, various procedures

Survival in Trisomy 18

High risk of fetal loss early in pregnancy decreases as pregnancy progresses but during labor risk of loss is higher than for an unaffected fetus

5-8% survive past 1 year **without** extraordinary measures. Recent studies report increased survival in Trisomy 18 **with** medical interventions; *respiratory, nutritional, cardiac, and surgery* when appropriate.

Largest Trisomy 18/13 survival study in the USA reported Trisomy 18 survival of 13.5% at 1 year, and 12.3% at 5 years. [Meyer et al., 2016]

Largest Trisomy 18/13 cardiac surgery study in the USA-Trisomy 18 outcomes: In-hospital mortality 13%
Median survival post discharge 16.2 years [Peterson et al., 2017]

Routine follow-up of infants with Trisomy 18

- Routine child care/anticipatory guidance
- Cardiac evaluation
- Eye evaluation
- Hearing test
- Infant/pre-school program early intervention
- Ongoing Support
- Routine ultrasound for Wilms and liver tumor
- Routine immunization
- Referral for feeding clinic if appropriate
- Scoliosis check

Survey of >350 parents of children with Trisomy 13 or 18 : Most chose comfort care for their infant; 30% lived >1 year. Of infants who received interventions, 50% lived >1 year. Half said care of a disabled child is/was harder than expected. 89% reported a positive enriching experience regardless of lifespan. [Janvier et al., 2012]

Resources: John C. Carey, MD, MPH, Medical Advisor for SOFT, Professor of Pediatrics and Genetics, University of Utah
Janvier A, Farlow B, Wilfond BS. 2012. [The Experience of Families With Children With Trisomy 13 and 18 in Social Networks](#) .Am Academy of Pediatrics, doi:10.1542/peds.2012-0151

Meyer RE, et al., for the National Birth Defects Prevention Network. 2016. Survival of children with trisomy 13 and trisomy 18: A multi-state population-based study. Am J Med Genet Part A 9999A:825–837. <http://onlinelibrary.wiley.com/doi/10.1002/ajmg.a.37495/full>

Peterson, JK, Kochilas LK, Catton KG, Moller JH, Setty SP. [Long-term Outcomes of Children with Trisomy 13 and 18 After Congenital Heart Disease Interventions](#). *Ann Thorac Surg*. 2017 Apr 26. pii: S0003-4975(17)30375-2. doi: 10.1016/j.athoracsur.2017.02.068.

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