SIU CARBONDALE Southern Illinois University

TRIS project online module Trisomy 13: Overview of the syndrome, care and management, parent experiences and resources

Deborah A. Bruns, Ph.D.

Southern Illinois University Carbondale

Carbondale, IL

TRIS project
Mission statement

The Tracking Rare Incidence Syndromes (TRIS) project seeks to increase the knowledge base on rare incidence trisomy conditions, and to make this information available to families and interested educational, medical and therapeutic professionals. Related outcomes will be the development of appropriate services, advance treatment options, and supports during the prenatal, newborn and subsequent developmental periods. Children affected by trisomy 18, trisomy 13, and other rare syndromes possess unique needs requiring education of those involved in their daily, educational and medical care.

Continuing Education (CE) information

This module will provide a historical review and current perspective on cases diagnosed with trisomy 13 (full trisomy 13 is the focus). Information includes prevalence and incidence, overview of the literature, phenotypic characteristics, common medical issues and their treatment as well as ongoing management and care. Developmental outcomes will also be shared. A list of resources and a glossary of terms are also provided.

Nora
DOB 2/19/13

Module overview

This module will provide results from the medical literature along with findings from the TRIS project, materials from rare trisomy focused organizations such as the Support Organization for Trisomy 18, 13 and related disorders (SOFT), media reports (e.g., newspaper articles) and parent experiences. Photos are also provided to illustrate phenotypic features and highlight long-term survivors with this genetic condition.

Taken together, this module offers a synthesis of care and management for cases diagnosed with trisomy 13 within a context of professional recommendations and those involved in day-to-day care.

Trisomy 13
Patau syndrome

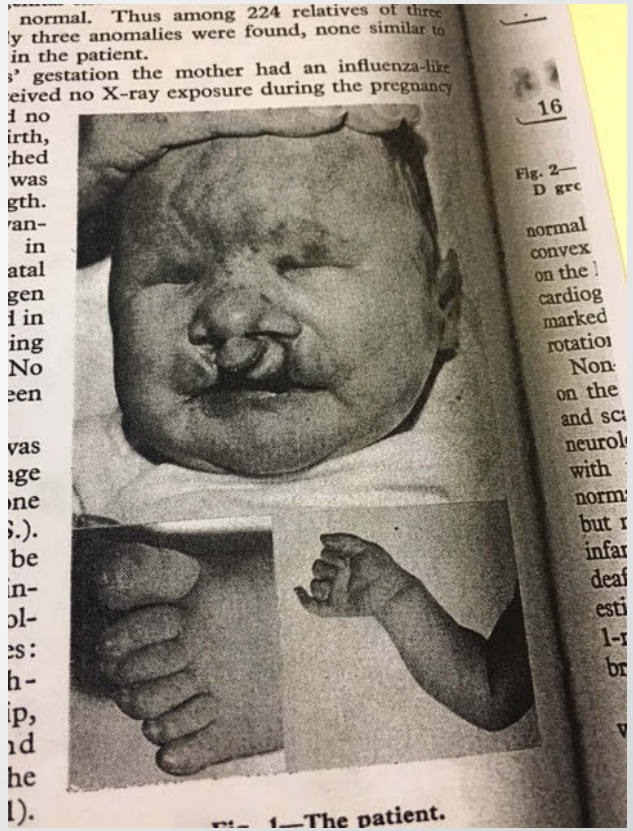
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Fig. 1—The patient.

The first published account was by Patau and colleagues in 1960.

The authors described the infant as follows:

"The patient, a full-term female infant, was born in January 1959, and is still alive (February 1960)…At birth, the patient weighed 6 lb 5 oz and was 19 in in length…apparent anophthalmia, hare lip, cleft palate, and polydactyly of the left foot…Pulmonary vascularity was increased…The clinical impression was a rotational anomaly with intraventricular septal defect…She was considered to be deaf… Since the age of 3 months she has had frequent brief seizures of myoclonic type."

Patau K, Smith DW, Therman D, & Inhorn SL. (1960). Multiple congenital anomaly caused by an extra autosome. The Lancet, 275(7128), 790-792.

Historical view

An early large scale study described 27 cases highlighted the following:

- - Incidence of 1 in 7,602 births
- - Very few survived to six months of age (mean = 89.2 days)
- - Low set ears, short neck, ocular hypertelorism, polydactyly, and micrognathia in majority of cases
- - Feeding difficulties were also noted
- - Most cases diagnosed with congenital heart disease and microcephaly

Taylor AI. (1968). Autosomal trisomy syndromes: A detailed study of 27 cases of Edwards' syndrome and 27 cases of Patau's syndrome. J Med Genet, 5(3), 227-252.

Historical overview continued

A study published in 1981 discussed 13 cases living up to 82 days and two, additional long-term survivors in upstate New York . The latter two were described with microcephaly, microphthalmia, rocker bottom feet, and polydactyly. Cases with translocations were not included in the analyses.

Redheendran R, Neu R, Bannerman RL, RM. 1981. Long survival in trisomy-13-syndrome: 21 cases including prolonged survival in two patients 11 and 19 years old. Am J Med Genet Part A, 8, 167–172.

Approximately 10 years later, Baty and colleagues presented 32 cases. At one year, 12 (38%) were living and 5 years, four (13%). At 10 years, one (3%) case was living. Close to 60% was diagnosed with a cardiac defect. Seizures were noted in about half the group and 48% with cleft palate. Approximately 25% of cases had a surgery during the neonatal period including correction of omphalocele and removal of extra digits.

Baty BJ, Blackburn BL, Carey JC. 1994. Natural history of trisomy 18 and trisomy 13: I. Growth, physical assessment, medical histories, survival, and recurrence risk. Am J Med Genet Part A, 49, 175–188.

Historical overview continued: Case studies focusing on trisomy 13

Authors describe a 16 year old with "classic features" of trisomy 13. Developmental skills were evident in activities of daily living (e.g., dressing) as well as walking and using sign language to communicate. On the last point, progressive hearing impairment is discussed. [*Based on description, possible case was mosaic trisomy 13; "…provisional diagnosis was made at birth…chromosomal analysis at age six*."]

Coburn KL, Campbell K C, Kuhn MJ, & Moreno MA. (1996). Electrophysiological and structural abnormalities in a long-term survivor of trisomy 13 (Patau's syndrome). Amer J Audiol, 5(1), 35-43.

Parents agreed to palliative care for their infant with trisomy 13. There were prolonged periods of apnea beginning in the fifth week of life. Infant received oxygen, feedings by nasogastric tube, caffeine and vitamins. Some bottle and breastfeeding was also tolerated. Infant passed at 10 weeks of age.

Stafford CO. (2015). A case study of trisomy 13: Balancing hope and reality. Adv Neonatal Care, 15(4), 285-289.

Current thoughts on trisomy 13

In a 2017 publication addressing care for infants with a prenatal diagnosis, the authors say arguments for withholding treatment are no longer valid as studies and anecdotal reports point to positive outcomes (e.g., cardiac surgery).

The authors also describe patient-centered care as guided by dignity and respect, information sharing, participation, and collaboration and focusing on the parent and child's best interest. This is echoed by Brosco and Feudtner.

Haug S, Goldstein M, Cummins D, Fayard E, & Merritt TA. (2017). Using patient-centered care after a prenatal diagnosis of trisomy 18 or trisomy 13: A review. JAMA Pediatrics, 171(4), 382-387.

Brosco JP, & Feudtner C. (2017). Shared decision making for children with trisomy 13 and 18. JAMA Pediatrics, 171(4), 324-325.

Current thoughts on trisomy 13 continued

Although mortality was the most common outcome, approximately 13% of cases survived to 10 years of age (n=174 live born between 1991 and 2012 in Ontario, Canada). Among children who underwent surgical interventions (n=41, 23.6%; ranging from minor procedures to cardiac repair at mean age of 205.5 days), survival at one year post-surgery approached 70%. Most frequent type of surgery was related to "implant[ing] medical devices" (n=16). A total of six surgical interventions were to resolve a cardiac issue.

Nelson KE, Rosella LC, Mahant S, & Guttmann A. (2016). Survival and surgical interventions for children with trisomy 13 and 18. JAMA, 316(4), 420-428.

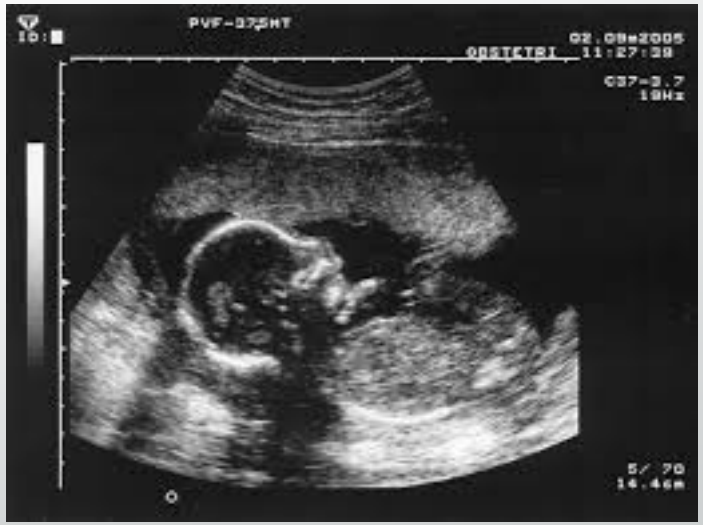
An additional study focused on 693 children with trisomy 13 from nine states in the United States (part of a larger study of 12 states). Approximately 60% were female. Five year survival was 9.7%. Gestational age was "the strongest independent determinant of survival" with those closer to full term correlated with longer survival.

Meyer R E, Liu G, Gilboa SM, Ethen MK, Aylsworth AS, Powell CM, … & Canfield MA. (2016). Survival of children with trisomy 13 and trisomy 18: A multi-state population-based study. Amer J Med Genet Part A, 170(4), 825–837.

Prenatal markers

Although some conditions may resolve prior to birth, the following are considered "**major**" prenatal markers for trisomy 13:

- One or more cardiac defects (most common are VSD and ASD; more severe include hypoplastic left heart syndrome, and double outlet right ventricle)
- Holoprosencephaly
- Ventriculomegaly
- Cystic hygroma
- Omphalocele
- Diaphragmatic hernia
- Renal cystic dysplasia
- Polycystic kidneys
- Ureteral obstruction
- Intrauterine growth restriction (small for gestational age)



Prenatal markers

The following are considered "**minor**" prenatal markers for trisomy 13 and primarily related to phenotype (physical characteristics):

- Abnormal head shape (e.g., "strawberry")
- Cleft lip and/or palate
- Nuchal edema
- Hypoplastic or absent nasal bone
- Micrognathia
- Clenched hands
- Overlapping digits or contractures
- Prominent calcaneus
- Rocker-bottom feet

Prenatal testing and diagnostics

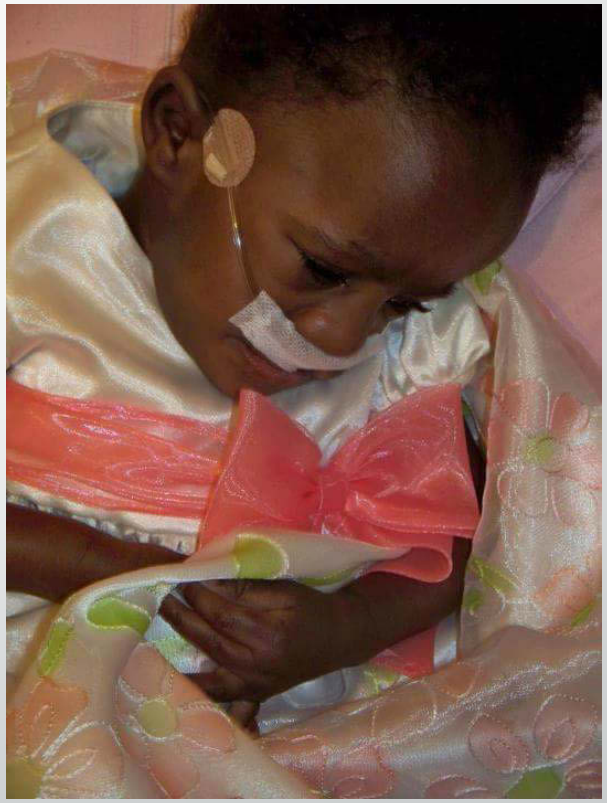
- It is critical to fully explain results of non-invasive prenatal testing (NIPT; also termed Cell Free DNA Screening) to prospective parents including the occurrence of false positives and results are not definitive as this testing only screens for possible genetic issues.
- Testing can begin as early as 10 weeks gestation.
- Parents with NIPT results can use the Predictive Value Calculator to view the risk of trisomy chromosome conditions by maternal age at https://www.perinatalquality.org/Vendors/NSGC/NIPT/
  This is one option for measuring risk of a chromosomal condition, there are others. Important to note that prevalence defaults may not be the best estimates of an individual patient's prior risk for a chromosome condition. Also, sensitivity of the screening test contributes to determining the risk percentile.

Prenatal testing and diagnostics continued

- Diagnostic testing is required for a definitive diagnosis. These tests are more invasive than NIPT and there is a nominal risk to the fetus.
- If trisomy 13 is confirmed prior to approximately 24 weeks gestation, termination of the pregnancy may be recommended. Prospective parents should also be assisted to plan for a live birth including development of a birth plan and active care options. Many hospitals offer a perinatal palliative care program for this purpose. An end of life plan may also be developed.
- AND parents and family members are increasingly turning to social media including Facebook groups and blogs to ask questions and gather recommendations (e.g., "trisomy friendly" hospitals and physicians, details about identified anomalies, care options at birth, perinatal course).

Incidence of trisomy 13

- Based on available data, best overall estimate is 1 in 10,000 live births (Haug, Goldstein, Cummins, Fayard, & Merritt, 2017)
- Limited data on prevalence by sex at birth and beyond; tend to be more female survivors
- 5-10% survive to one year of age; could be higher



Bruns DA, & Campbell E. (2014). Nine children over the age of one year with full trisomy 13: A case series describing medical conditions. Am J Med Genet Part A, 164(12), 2987-2995.

Naiyah
9/1/09-11/10/12

Phenotype

Facial features including:

- Microphthalmia
- Colobama of iris
- Cleft lip (60-80%)
- Cleft palate
- Low-set ears
- Shallow supraorbital ridges
- Upslanting palprebral fissures
- Absent philtrum

Jones KL, Jones MC, & Del Campo M. (2013). *Smith's recognizable patterns of human malformation*. Elsevier Health Sciences.

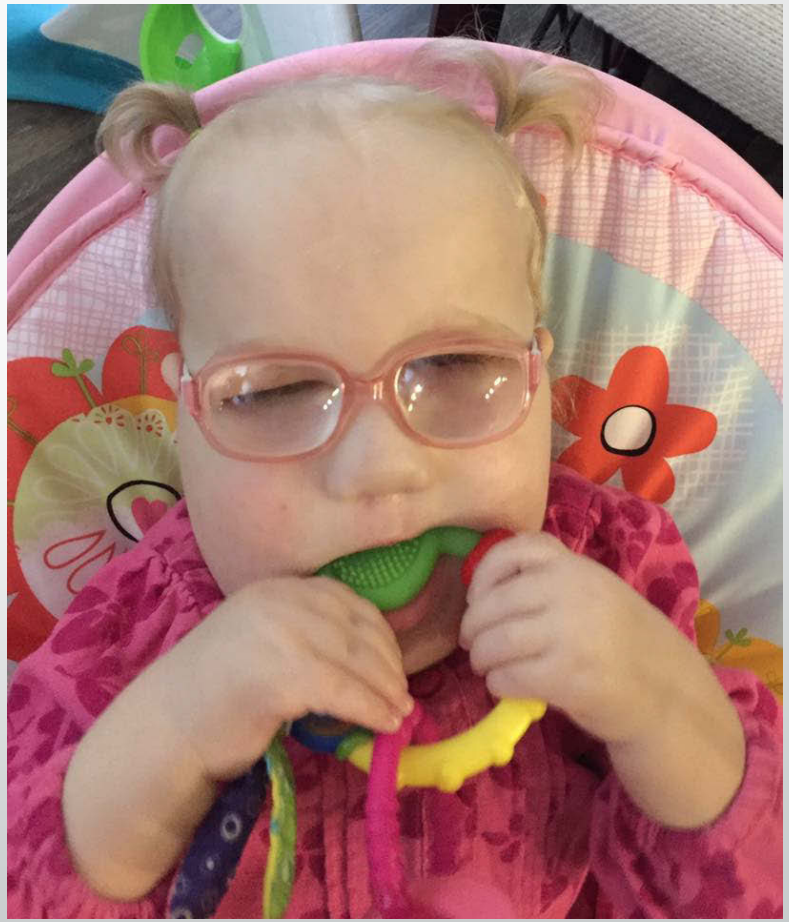
Zion
5/2/01-2/16/10

Phenotype

Other features including:

- Ulnar deviation at wrist
- Radial aplasia
- Syndactyly
- Hypoplasia of pelvis
- Posterior prominence of heels

Jones KL, Jones MC, & Del Campo M. (2013). *Smith's recognizable patterns of human malformation*. Elsevier Health Sciences.



Sofie
DOB 1/24/14

Key medical information

- Common cardiac conditions include ventricular septal defect, patent ductus arteriosus, and atrial septal defect. Less frequently diagnosed anomalies include pulmonary stenosis, hypoplastic aorta, bicuspid aortic valve, and mitral valve atresia.
- Medication may be prescribed. Palliative and corrective surgeries are options with the latter being increasingly shown as effective.

Janvier A, Farlow B, & Barrington K. (2016). Cardiac surgery for children with trisomies 13 and 18: Where are we now? Semin Perinatol, 40(4), 254-260.

Key medical information continued

- A common respiratory condition is apnea. There are two types (central and obstructive) and may be difficult to determine which is causing breathing difficulties. Some infants may experience both; termed mixed apnea. Supplemental oxygen or greater mechanical support may be necessary (e.g., tracheotomy).
- Renal conditions may include include horseshoe-shaped kidney, hydronephrosis, duplicated ureters, and polycystic kidney.
- Omphalocele may occur as well as Meckel's diverticulum and incomplete rotation of colon.
- Defects to male and female genitalia is possible.

Key medical information continued

- Variety of feeding difficulties due to anatomical anomalies such as cleft palate, low muscle tone and/or impaired ability to coordinate suck, swallow and breathing in neonates and infants.
- Concerns about aspiration and reflux affecting oral intake, weight gain and overall health. Often need supplemental nutrition or fully tube fed to intake concerns and address medical or anatomical conditions.
- Tube feeding can be blended diets and/or commercially available formula (e.g., Pediasure, Compleat). Should have a feeding team including a dietitian.

Key medical information continued

- Neurological conditions may be present including holoprosencephaly (may be fatal depending on type), microcephaly, and absence of corpus callosum.
- Seizures are possible as well as infantile spasms in neonates.
- Potential for vision and/or hearing issues with greater likelihood of the former due to eye defects (e.g., types of colobama, microphthalmia). Treatment will depend on type of defect and presence of additional conditions that may impact interventions.

Seminal articles

Baty BJ, Jorde LB, Blackburn BL, Carey JC. (1994). Natural history of trisomy 18 and trisomy 13: I. Growth, physical assessment, medical histories, survival,and recurrence risk. Am J Med Genet, 49, 175-188.

Carey J. (2012). Perspectives on the care and management of infants with trisomy 18 and trisomy 13: Striving for balance. Curr Opin Pediatr, 24, 672–678.

Pont S, Robbins J, Bird TM, Gibson J, Cleves M, Tilford J. (2006). Congenital malformations among live born newborns with trisomies 18 and 13. Amer J Med Genet Part A, 140, 1749–1756.

Additional information

Acharya K, Leuthne, S, Clark R, Nghiem-Rao TH, Spitzer A, & Lagatta J. (2017). Major anomalies and birth-weight influence NICU interventions and mortality in infants with trisomy 13 or 18. J Perinatol, 37(4), 420-426.

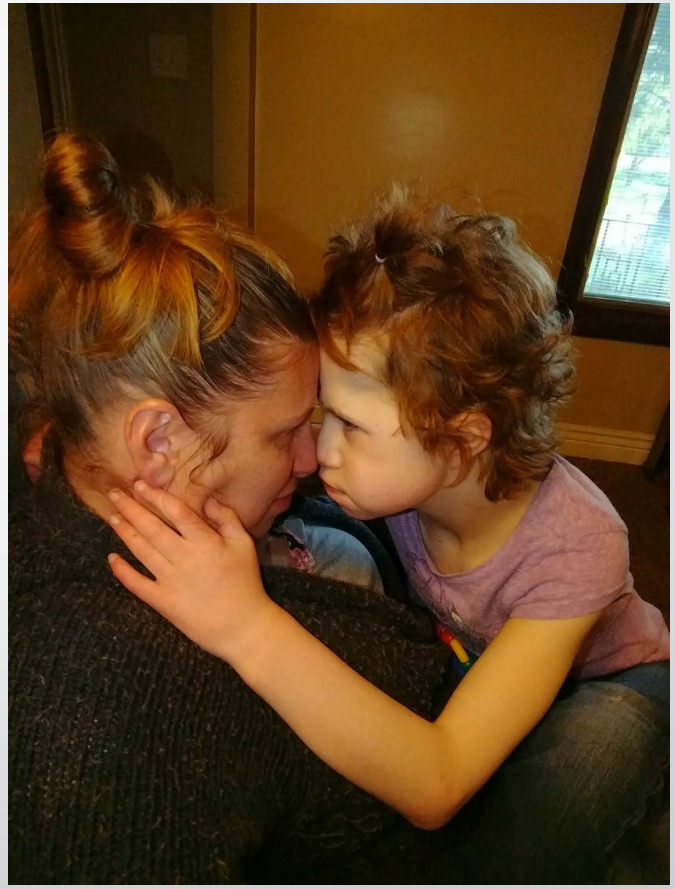
Bruns D. (2011). Birth history, physical characteristics, and medical conditions in long-term survivors with full trisomy 13. Amer J Med Genet Part A, 155(11), 2634-2640.

Oka N, Inoue T, Shibata M, Yoshii T, Nakamura Y, Araki H, ... & Kitamura T. (2016). Norwood Procedure performed on a patient with trisomy 13. Int Heart J, 57(1), 121-122.

Developmental milestones

A recent article described developmental milestones; some key findings:

- Language and communication skills including vocalizing to indicate needs and producing open vowel sounds or consonant-vowel combinations
- Social-emotional skills such as showing preferences for parents, and other family members and caregivers, and engaging in social play
- Fine motor skills include exploration of objects with hands
- Motor skills including sitting without support for several minutes and rolling



Bruns DA. (2015). Developmental status of 22 cases with trisomy 18 and eight cases with trisomy 13: Implications and recommendations. Am J Med Genet Part A, 167, 1807–1815.

Arianna
DOB 6/19/06

Care and management: Special issue of American Journal of Medical Genetics Part C

Carey, JC & Kosho, T. (Editors) (September 2016). Perspectives on the care and advances in the management of children with trisomy 13 and 18, 172(3), 247–308.

Topics include:

- Shared decision making in pre and postnatal management
- Medical interventions and survival by gender
- Treatment of epilepsy
- Treatment of Wilms tumor

All children at right are enrolled in the TRIS project

Care and management

- Monitor cardiac conditions and determine treatment when/if needed. Some research studies note positive outcomes for palliative and more intensive care.
- Work with medical team to provide treatment for apnea such as continuous positive airway pressure (CPAP) or bi-level positive airway pressure (BiPAP). Sleep study may be necessary.
- Consider positioning options and use of a “Shake vest” to loosen mucus and secretions. These options can assist to decrease the likelihood of pneumonia.

Jillian
DOB 4/4/12

Care and management continued

- Ongoing monitoring of growth; refer to trisomy 13 growth charts at http://trisomy.org/?page_id=4203 or review the SOFT Care Book located for download at http://trisomy.org/wp-content/uploads/2014/08/Carebook-updated-8-15-14.pdf
- Monitor feeding for reflux and dysphagia. There are several tests to determine these conditions such as a videoflouroscopy or upper GI series. Testing may need to be repeated if intake changes.
- Work with child's team to maintain oral feeds, if appropriate, and determine amount and type of tube feeding (blended diet, commercially available formula).

Care and management continued

- If present, monitor kidney conditions and treat urinary tract infections as soon as possible.
- One study identified absence of gallbladder in cases with trisomy 13 and recommends imaging to identify and evaluate this possible condition.

Rosa RF, Correia EP, Guimarães VB, Trombetta JS, Beltrão LA, Lliguin KL, ... & Zen PR. (2016). Trisomy 13 and gallbladder agenesis. Am J Med Genet Part A, 170(7), 1945-1946.

- In males, cryptorchidism (undescended testicle[s]) is possible. Treatment decided by child's medical team including parents.

Care and management continued

- May exhibit light sensitivity; provide sunglasses and/or hat for outdoor activity. There is also possibility for cataracts and glaucoma. In addition, Child may require glasses to interact with their environment.
- Monitor for ear infections and option for audiological testing to determine hearing range and acuity as both can change over time.
- Monitor neurological status; report all suspected seizure activity.

Care and management continued

- Early intervention services for infants and toddlers to encourage gains in developmental areas (in home, clinic, child care setting).
- Preschool-aged children should attend school as tolerated (e.g., one hour session, half day) for developmental activities and socialization.
- Schooling continues for children age five and older. Focus on functional skills such as choice making, sensory stimulation, and developing age appropriate interests.

Joey
DOB 3/6/07

Special considerations: Medically related

- Immunization schedule adjusted based on child's weight than chronological age as option as well as one per visit to monitor response than multiple shots at one visit per established recommendations.
- Use of blended diet via gastrostomy tube rather than prepared formulas; collaboration among parents, caregivers and child's team to meet caloric and nutritional needs. Anecdotal reports of positive outcomes. In addition, quality and quantity of oral feeds weighed against aspiration risk; importance of repeated evaluation of intake amount, swallowing, reflux etc.
- Changes at puberty (may be early onset) including start of seizures (may need to reevaluate all medications) and other symptoms including irritability.

Special considerations: Non-medical needs

- Therapy and educational goals including short and long-term outcomes related to parent and caregiver preferences and covering a range of functional skills (e.g., purposefully activate toy, ambulation in gait trainer)
- Long-term survivors may need planning in the following areas: guardianship, community and regional adult services, and application to state and national programs for adults with disabilities

Natalia
DOB 8/25/00

Parent and family experiences

Adalee
DOB 7/21/11

Parent and family experiences: Children living two months or less

- He [husband] has been very patient with all of my ups and downs, I still have ups and downs three years later and he understands.
- He [husband] supported me in wherever I was…
- I couldn't find the words to say how wonderful and supportive they [maternal grandmother and mother's sister] have been or to tell how much they love Caileigh and I.
- …my mom was always steady and stuck by my side through my pregnancy, the stillbirth of my son and the sadness that followed. She was there to talk to, cry with and just be with.
- He [husband] always showed me 100% of his support and sensitivity, we went through everything together and made every decision together, he always put my feelings and preferences first.
- She [maternal grandmother] had been through the same experience and was wonderful support.

  We [mother and husband] shared the experience as parents and supported each other.
- She's [paternal aunt] been most available to help, talk or just listen.

Parent and family experiences: Long-term survivors

- Husband helps with everything. Kids do all they are capable of helping with.
- My spouse [wife] is involved with me in every aspect of Jillian's life.
- He [husband] helps with care of t13 baby as well as other children in the house and helps to maintain the household.
- She [maternal grandmother] has helped me take care of her and has been there to help with anything I needed.
- She [maternal grandmother] really loves my son and is comfortable around him and is willing to care for him until she became physically unable.
- Her [maternal grandmother] top priority that grandson receives top care and parents receive respite.
- She [maternal grandmother] is able to help with care and is the only person other than my husband and myself that we trust watching out daughter.

Parent and family experiences: Long-term survivors continued

- She [paternal sister] gets it! She listens, offers appropriate support and does so from a great distance.
- They [maternal brother and sister-in-law] have been the most involved and helpful since diagnosis.
- She [maternal aunt] is amazing and has flown here to Tennessee several times to be with us.

Parent and family experiences: Parent descriptions of unmet needs

Social and/or emotional support

- Desire to feel normal.
- Although support was available from extended family and friends, my spouse and I did not proactively seek out emotional support from them upon discovering Jillian's diagnosis. No one, including us, knew what to expect from Jillian and didn't quite know how to react.
- I wish that everyone would quit telling me that this happened for a reason, because I am special and having a disabled child doesn’t make your marriage closer, it’s hard on a marriage.
- I wish my family was more involved with my family but we all live in Fort Worth and since my son was born I see my extended family as much as I did when we all lived 300-400 miles away.

Parent and family experiences: Parent descriptions of unmet needs continued

Services, equipment needs etc.

- I need a night nurse…she still gets up nightly at 3 am for sometimes 2 hours.
- No ongoing respite care, no qualified individuals.
- We are financially strapped, because I stayed home in order to care for my daughter. It's been 12 years since I have worked, and now that she is gone to heaven, I have no current work experience…
- No financial help from state or other agencies to help, and would be difficult to gain full time employment due to son's disability and amount of time I need to be home with him.
- I lost my job because of her condition so we are struggling financially since I stay home to take care of her.

Trisomy 13 in the news

"Talayha [nine years old] has a condition called trisomy 13, a rare chromosomal disorder…Despite her diagnosis, our daughter's pretty healthy…We've done everything in our power to keep her that way."
(*Girl can't speak but giggles her head off on new bicycle, Orlando Sentinel, Orlando, FL, September 14, 2015*)

"…Matthew was born with trisomy 13…In the first year of his life, he spent 170 days in hospital and has had medical appointments every day…During the pregnancy …refused genetic testing because of the risk of miscarriage and say that whatever happened, it would not have changed their minds about going ahead with the pregnancy…He was sent for genetic testing when he was two days old and three weeks later the family found out he had trisomy 13…The family have just celebrated Matthew's first birthday, a milestone doctors feared he would never reach…Now Matthew has reached one…we just want to give Matthew a better quality of life."
(*The baby determined to survive: Parents' joy as boy expected to life just five days celebrates his first birthday, Daily Mail, London, UK, March 13, 2015*)

Trisomy 13 in the news continued

"They say they were treated like their children didn't matter, that their lives were not worth a fight…One family from Springfield, one family from Joplin, but the parents of both Kamry and Eden say once they received the trisomy diagnosis, some medical professionals wanted them to just give up…An ultrasound at 22 weeks and a blood test led to Kamry's diagnosis of trisomy 13…Kamry was born at a hospital in St. Louis. It was amazing to see they had teams set up for anything that they might possibly need for her…Nine days might not seem like a lot to some people, but it was the most amazing nine days…We wanted Kamry to write her own story and not have one written for her." (*Families facing trisomy diagnoses fight for life, KY3.com, Springfield, MO, June 11, 2015*)

"Tracy was told her daughter Kathleen Rose, who has trisomy 13, would not live beyond a few days. She is now eight years old…described her daughter as 'the heart of the home she's just a wee character'…families are not trying to run away from severe diagnoses, but that having incompatible with life 'tagged on her forehead' affected the level of care her daughter received…" (*I was told my daughter was incompatible with life…she's now 8, The Journal, Dublin, UK, March 9, 2015*)

Additional information: SOFT and ITA

Support Organization for Trisomy 18, 13 and Related Disorders (SOFT) provides information, support and opportunities for face-to-face meetings.

The following are links to some active SOFT groups around the world:

- SOFT USA: http://trisomy.org
- SOFT UK: http://www.soft.org.uk
- SOFT Australia: http://www.trisomyaustralia.com
- SOFT Italy: http://www.trisomia.org

The International Trisomy Alliance (ITA) offers resources for medical professionals and family members as well as booklets related to topics including preparation for delivery and supporting siblings. Booklets are available in multiple languages. Homepage is located at http://www.internationaltrisomyalliance.com

TRIS project links

TRIS project website links:

Homepage: http://tris.siu.edu

Enrolling in the project: http://tris.siu.edu/survey/form/PreEnroll.php

Publications and presentations list:
http://tris.siu.edu/publications-presentations/index.php

Case studies: http://tris.siu.edu/case-studies/index.php

TRIS project Facebook page:

https://www.facebook.com/TRIS.Trisomy.project