Tetrasomy 18p
Treatment and Surveillance
ICD-10 =Q93.2

These recommendations are inclusive of the entire population of people with Tetrasomy 18p. It should be noted that there is a great deal of variation among individuals with Tetrasomy 18p. Not all complications or concerns will be listed in this document. However, the recommendations contained here should be used as a baseline for monitoring and the health of individuals with Tetrasomy 18p.

Potential conditions in a neonate:
- **Structural**
  - Palatal anomalies - 80%
  - Heart abnormalities – 47% by ECG
  - Congenital orthopedic abnormalities – 45%
  - Hernias – 12%
  - Myelomeningocele – 7%
- **Functional**
  - Feeding problems – 83%
  - Respiratory distress – 31%
- **Biochemical**
  - Jaundice – 57%

Initial evaluations after diagnosis:
- **Ophthalmology**
  - Strabismus – 45%
  - Refractive errors – 34%
- **Audiology / otolaryngology**
  - Hearing loss - 32%
  - Recurrent otitis media – 35%
- **Genitourinary**
  - Cryptorchidism – 39%
  - Hypospadias – 4%
  - Urinary tract anomalies – 8%

Immediate Referrals to:
- Appropriate subspecialist as indicated by initial evaluations
- Genetics follow-up if not previous to diagnosis
- Early intervention/developmental services
- The Chromosome 18 Registry & Research Society
- The Chromosome 18 Clinical Research Center

Closely monitor, manage, and refer appropriately:
- **Failure to thrive/ growth failure**
  - Underweight (<3rd percentile)
- **Endocrinology**
  - Short stature (<25th percentile)
  - Growth hormone deficiency
- **Otorhinolaryngology**
  - Recurrent otitis media
  - Hearing loss
- **Gastroenterology**
  - Constipation
  - GE reflux
  - Hernias
  - Eosinophilic esophagitis
- **Immunology/Rheumatology**
  - Atopic disorders
  - IgA deficiency
  - Eosinophilic esophagitis
- **Orthopedics**
  - Congenital hip dysplasia
  - Foot abnormalities
  - Decreased bone mineral density
- **Development**
  - Milestones
  - School performance
- **Neurology**
  - Seizures
  - Hypotonia
- **Behavioral/ mood changes**
- **Dental**

Annual Screenings:
- Vision
- Hearing

Updated 2016
Potential conditions in a neonate:

- **Structural**
  - Palatal anomalies - 80%
  - High, arched or narrow
  - Cardiac abnormalities – 47% by ECG
    - PDA, PFO, ASD, and VSD most common. All but one closed spontaneously
    - Other cardiac anomalies have included: hypoplastic transverse aortic arch; right ventricular hypertrophy; pulmonic stenosis; and valve abnormalities
  - Congenital orthopedic abnormalities – 45%
    - Club foot – 14%
    - Vertical talus – 5%
    - Metatarsus adductus – 5%
    - Rockerbottom feet – 5%
    - Hip dysplasia – 17%
    - Hernias (inguinal, umbilical) – 12%
    - Myelomeningocele – 7%
- **Functional**
  - Feeding problems – 83%
    - Due to hypotonia, high arched palate or gastroesophageal reflux
  - Respiratory distress – 31%
- **Biochemical**
  - Jaundice – 57%

Initial evaluations after diagnosis:

- **Ophthalmology**
  - Strabismus – 75%
  - Esotropia – 17%
    - Accommodative – 30%
    - Infantile – 21%
    - Acquired non-accommodative – 8%
    - Intermittent – 8%
  - Esophoria – 4%
  - Intermittent exotropia – 4%
  - Refractive errors – 71%
    - Myopia – 17%
    - Hyperopia – 33%
    - Astigmatism – 25%
  - Anisometropia – 17%
- **Audiology / Otorhinolaryngology**
  - Hearing loss - 12%
    - Conductive, sensorineural, and mixed hearing loss have all been reported
  - Recurrent otitis media – 57%
  - Small or narrow ear canals – 32%
• **Genitourinary**
  - Cryptorchidism – 63%
  - Hypospadias – 4%
  - Urinary tract anomalies – 8%
    - horseshoe kidneys and bladder diverticuli
    - The actual incidence of kidney abnormalities may be higher than reported in the literature as abdominal ultrasounds have not performed on all individuals

**Immediate Referrals to:**

**Genetics**
- Referral to genetics is appropriate to review the condition, its management, and implications for other family members.
- A minority of parents of children with tetrasomy 18p have a chromosome abnormality. There have been case reports of parents with mosaicism or with some type of chromosome rearrangement.

**Early intervention/developmental services**
- All children with chromosome 18 abnormalities have a significant risk for developmental delay and intellectual disabilities. Prompt referral to a program that includes physical, occupational, and speech therapy is important in order to maximize their development.
  - 100% with tetrasomy 18p have developmental delay
  - 100% have muscle tone abnormalities that may benefit from physical therapy
  - 100% have intellectual disability, though the degree of severity varies.

**Referral to Chromosome 18 Registry & Research Society**
- The Chromosome 18 Registry is a parent support organization that provides family members with the opportunity to meet and learn from those who have gone before them. These are complex conditions to manage even in the least affected children, making the establishment of a network of support a crucial component for maximizing the affected child’s potential. The Registry has annual national and international conferences, regional get-togethers, and social media outlets, all with programs for parents, siblings, and affected adults. The Registry works closely with and financially supports the Chromosome 18 Clinical Research Center. (www.chromosome18.org)

**Referral to the Chromosome 18 Clinical Research Center**
- The goal of the Chromosome 18 Clinical Research Center is to make the chromosome 18 abnormalities the first treatable chromosome abnormalities. Anyone with any chromosome 18 abnormality is eligible to enroll and encouraged to enroll. Once enrolled, participants have the opportunity to be involved in longitudinal studies of developmental progress, and when available, other studies that could include surveys or treatment trials. Families enrolled in the Research Center will also be the first to know new information about the conditions when it becomes available. Enrollment is a key part of proactive clinical management (www.pediatrics.uthscsa.edu/centers/chromosome18)
Closely monitor and manage:

- **Failure to thrive/ growth failure**
  - Underweight (<3rd%) – 19%
  - Weight gain
    Due to their hypotonia, feeding may be more difficult for an infant with Tetrasomy 18p. In addition, many affected children have gastroesophageal reflux, which increases not only their risk for aspiration, but also for pain, discomfort or emesis after feeding. Children <3 years who are failing to meet expected rates of weight gain should be evaluated for reflux and potentially for placement of a feeding tube. In addition, there have been a handful of individuals with Tetrasomy 18p that have been diagnosed with eosinophilic esophagitis.

- **Endocrinology**
  - Short stature (<25%) – 52%
  - Failed two growth hormone provocative tests - 19%
  - IGF1 and IGFBP3 are not definitive tests for GH deficiency in these children
  - Children that are failing to grow linearly (length or height) at expected rates for age and sex should be tested using growth hormone stimulation (provocative) testing. This testing is typical performed by a pediatric endocrinologist.
  - Thyroid and gonadotropin testing was normal in all participants

- **Otorhinolaryngology**
  - Recurrent otitis media – 35%
    - It is important to monitor hearing and treat ear infections quickly to avoid hearing loss and delayed speech development.
  - Hearing loss – 32%
    - Conductive, sensorineural, and mixed hearing loss have all been reported in individuals with Tetrasomy 18p

- **Gastroenterology**
  - Chronic constipation - 81%
  - GE reflux – 36%
  - Hernias - 8%
  - Eosinophilic esophagitis – only a few individuals have been definitively diagnosed by endoscopy, however a significant proportion have some symptomology.

- **Immunology/Rheumatology**
  - Atopic disorders
    - Food allergies – 33%
    - Asthma – 9%
    - Hay fever – 45%
    - Eczema – 21%
  - Celiac disease in one patient
  - Eosinophilic esophagitis – only a few have been definitively diagnosed by endoscopy, however a significant proportion have some symptomology.
• **Orthopedics**
  - Orthopedic abnormalities – 69%
    - Scoliosis or kyphosis - 53%
    - Pes planus and pes cavus – 37%
  - Low BMD (this is a new finding under investigation – so far 100% of those assessed down to the age of 4 years have low bone mineral density.)

• **Development**
  - The average full scale IQ score is 48
  - Cognitive abilities vary significantly;
    - 37% in the mild range
    - 37% moderate
    - 26% in the severe to profound range
  - Developmental milestones are delayed compare to a typical population (see O’Donnell et al., 2015).

• **Neurology**
  - Although some variants have been identified on brain MRI, such as a thin corpus callosum or enlarged ventricles, a screening MRI is not recommended for individuals with Tetrasomy 18p
  - Abnormal muscle tone – 98%
    - Hypotonia – 50%
    - Hypertonia – 19%
    - Mixed tone – 28%
  - Seizures - 24%
  - Febrile seizures – 17%

• **Behavioral/ mood changes**
  - Autistic characteristics are common (see O’Donnell et al., 2015).
  - For those individuals with mild cognitive deficits, the main behavioral concerns involve limited social and metacognitive skill development and behavior regulation problems.

• **Dental**
  - Dental crowding – 19%

• **Early death**
  - In general, individuals with Tetrasomy 18p are not medically fragile. In our cohort of 70 individuals with Tetrasomy 18p, only one participant has died. Although the cohort is relatively young with an average age of about 14 years. The oldest participant is 50 years old. The one death was presumed to be from sudden cardiac arrest at age 13 years.
  - There is no reason to think that they are at increased risk for surgical or anesthesia complications although they may need increased monitoring due to hypotonia.
References


