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Exploring the Mysteries of 22Q Deletion Syndrome

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UMKC School of Medicine

BEST CHILDREN'S HOSPITALS U.S.News

MAGNET RECOGNIZED

Objectives

- To discuss common issues present in persons diagnosed with 22q Deletion Syndrome
- To explore what may lead to suspicion of and testing for 22q Deletion Syndrome
- To review treatment of Endocrine disorders present in 22q Deletion Syndrome

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Introduction

- 22q Deletion Syndrome
  - a chromosomal disorder that results in poor development of several body systems
  - features vary widely, even among members of the same family.
  - original classifications included DiGeorge sequence/syndrome, velocardiofacial syndrome, Shprintzen syndrome, Sedlackova syndrome, and conotruncal anomaly face syndrome.
- This syndrome is caused by the deletion of a small piece of chromosome 22; the International 22q11.2 Foundation, through its "Same Name Campaign", advocates for the name 22q11.2 deletion syndrome.

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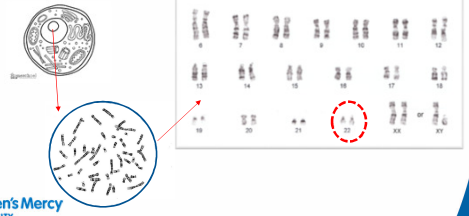
The genetic information is found in the center of the cell



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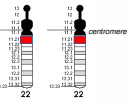
p = *short arm*

q = long *arm*



Typical Pair of Chromosomes 22

22q11.21 deletion syndrome

Pair of Chromosomes 22 with a deletion

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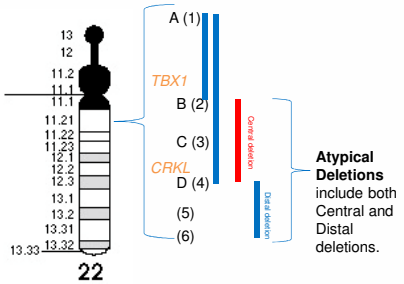

Atypical Deletions include both Central and Distal deletions.

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Case Study

- RW was born on 8/30/12.
- She was the 4th child together for her 24 y.o. mother and 23 y.o. father.
- Mother was on Zofran for morning sickness.
- Pre-term labor at 29 weeks led to bedrest.
- Ultrasound showed fetus was smaller than expected, as well as had a prenatal arrhythmia.
- She arrived at 37 weeks by spontaneous vaginal delivery, weighing 5 pounds, 4 ounces. Length unknown.

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Presentation to Genetics Clinic

RW was referred for a genetics consult at 3½ months of age due to:

- slow growth
- developmental delay
- nasal regurgitation
- dysmorphic features
- history of tracheomalacia with a possible laryngeal cleft
- failed hearing tests since birth

At the Genetics appointment, her length, weight, and HC were at the 50th percentile for a 1 month old.

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Genetics findings

- Wide spaced eyes
- Small, unusually shaped ears
- Prominent parietal bones
- Thin ala nasi (the cartilaginous flap on either side of the nostrils)
- Long slender fingers
- Decreased tone

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RW

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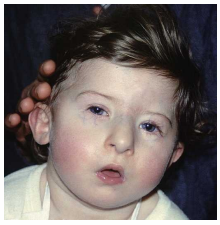

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- Diagnosed with 22q Deletion Syndrome on 12/12/12.

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22q Deletion Syndrome

- Present in 1 out of every 1,000 live pregnancies, in 1 in 68 children with congenital heart disease, and in 5 to 8 percent of children born with cleft palate
- 22q11.2 Deletion Syndrome is almost as common as Down syndrome.
- Potential to affect almost every system
  - can cause a wide range of health problems
  - no two people are ever exactly alike

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22q Deletion Syndrome

- Though not always present, the key characteristics of this syndrome include combinations and varying degrees of:

  - heart defects
  - palate differences
  - feeding and gastrointestinal difficulties
  - immune system deficiencies
  - kidney problems
  - growth delay
  - hearing loss
  - low calcium and other endocrine issues
  - cognitive, developmental and speech delays
  - behavioral, emotional and psychiatric differences (ADHD, autism, anxiety, etc.)

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Cardiac

- A congenital heart defect is present in 75-80% of patients with 22q Deletion Syndrome
- The most frequently seen cardiac malformations are "conotruncal" defects, including tetralogy of Fallot, pulmonary atresia with ventricular septal defect, truncus arteriosus, interrupted aortic arch, and ventricular septal defect.

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Immunology

- 22q11.2 Deletion syndrome is the most common congenital chromosome deletion syndrome
  - associated with developmental defects including hypoplasia or abnormal migration of the thymus
  - patients have variable defects in T-cell immunity with an increased incidence of infection and autoimmune disease.
- The thymus gland is located behind the sternum and is responsible for the maturation of T-cells to fight infections.

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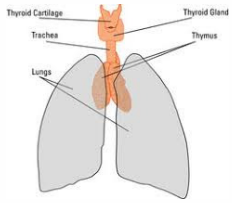
Thymus Gland



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Immunology

Three major immunological concerns can complicate 22q11 deletion syndrome.

1. The most severe clinical scenario: complete absence of the thymus, alymphocytosis and SCID-like phenotype. This is rare and affects fewer than 1% of patients with 22q11 deletion.

2. The most common clinical scenario: patients have small, often atopic, thymus development and present with T lymphocytopenia and recurrent sinopulmonary infection in early childhood, which usually resolves by adolescence.

3. An increasingly recognized scenario: autoimmunity, a common feature of many immunodeficiencies.

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GI

Feeding difficulties
- Nasal regurgitation, which may happen because of a cleft palate
- Spitting up or vomiting due to esophageal dysmotility
- Gastroesophageal reflux disease (GERD)
- Tracheoesophageal fistula

Gastrointestinal problems
- Mild to severe constipation
- Intestinal malrotation
- Hirschsprung's disease
- Diaphragmatic hernia
- Inguinal and umbilical hernia

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Development and Behavioral

- **Delayed development**
  - Mild speech delays
  - Delay in emergence of language
  - Delayed motor skills development

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Endocrine

- Midline defects are common
- 3 major Endocrine concerns:
  - Calcium
  - Thyroid
  - Growth

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Thyroid

- The thyroid gland is in front of the neck and is shaped like a butterfly or bowtie. The main job of the thyroid is to make thyroid hormones (T4 and T3). Thyroid hormones help maintain normal metabolism, growth, and development.
- A thyroid disorder may be present at birth (congenital) or might develop later in life. The thyroid may make too little hormone (hypothyroidism) or too much (hyperthyroidism).

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Thyroid Concerns

- Congenital hypothyroidism
  - May be transient
  - Higher etiology of being autoimmune
  - May be less likely to come off treatment

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Thyroid treatment

- Monitor with TSH and Free T4 in order to not miss a central hypothyroidism
- Standard treatment for hypothyroidism or hyperthyroidism

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RW was found to have central hypothyroidism on 8/5/13. First Endocrine evaluation on 8/7/13.

TSH 0.4 mcIU/ml (0.35-7.6)

Free T4 0.6 ng/dL (0.8-1.9)

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Hypocalcium

- Hypocalcemia is almost always related to hypoparathyroidism

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Calcium - Hypoparathyroidism

- The four parathyroid glands are located adjacent to the thyroid gland in the neck and regulate calcium in the blood through the production of parathyroid hormone.

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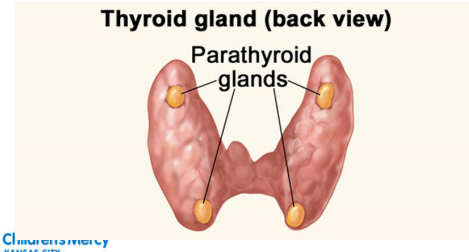
Parathyroid Glands



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Hypoparathyroidism

- Hypoparathyroidism is the presence of a low calcium level in the presence of an inappropriately normal or low PTH
- Congenital hypoparathyroidism tends to be transient

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Treatment of Hypoparathyroidism

- Treatment is 2-fold:
  - Calcium
  - Calcitriol

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Calcium

- Obtain a baseline renal ultrasound

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Calcium

- 50-100 mg elemental calcium/kg/day divided into 3-4 doses
  - Use gut when possible
  - The intestine can only absorb so much.
- Titrate to target a slightly low to normal calcium level.

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Calcitriol

- Calcitriol is the active form of Vitamin D.
  - PTH converts the inactive to the active form of Vitamin D. With a low PTH level, this conversion is unable to take place.
- Calcitriol helps retain calcium in the body.

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Growth

- Concerns with growth hormone needs
- Celiac disease

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Growth

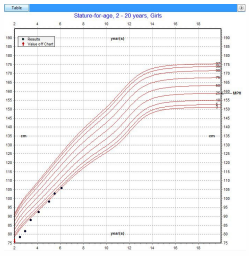

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Table II. Recommended assessments for 22q11.2 deletion syndrome*

Assessment	At diagnosis	Infancy (0-12 months)	Preschool age (1-5 years)	School age (6-11 years)	Adolescence (12-18 years)	Adulthood (>18 years)
Ionized calcium, parathyroid hormone†	✓	✓	✓	✓	✓	✓
Thyrotropin (thyroid-stimulating hormone)†	✓		✓	✓	✓	✓
Complete blood cell count and differential (annual)	✓	✓	✓	✓	✓	✓
Immunologic evaluation‡	✓	✓	✓			
Ophthalmology	✓		✓			
Evaluate palate§	✓	✓	✓			
Audiology	✓	✓	✓			✓
Cervical spine (>age 4 years)			✓			
Scoliosis examination	✓		✓		✓	
Dental evaluation			✓	✓	✓	✓
Renal ultrasound	✓					
Electrocardiogram	✓					✓
Echocardiogram	✓					
Development**	✓	✓	✓			
School performance				✓	✓	
Socialization/functioning	✓	✓	✓	✓	✓	✓
Psychiatric/emotional/behavioral††	✓		✓	✓	✓	✓
Systems review	✓	✓	✓	✓	✓	✓
Deletion studies of parents	✓					
Genetic counseling‡‡	✓				✓	✓
Gynecologic and contraceptive services					✓	✓

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Conclusion

- This disorder is autosomal dominant - A person with 22q Deletion Syndrome has a 50% chance of passing the syndrome on to any offspring.

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Conclusion

- 22q Deletion Syndrome can affect many different bodily systems.
- Endocrine Concerns
  - Calcium
  - Thyroid
  - Growth

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