Turner Syndrome: Merging Clinical Care and Practice Guidelines

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Conflict of Interest Disclosure

Conflicts of Interest: none

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It is a journey

Journey varies depending on age at diagnosis
- Each age group has unique set of issues
  - Prenatal
  - Newborn
  - School age
  - Adolescence
  - Late adolescence

Variables that shape the journey
- Age at diagnosis
- Complexity of medical issues
- Psychological and emotional aspects
- Severity of short stature
- Growth hormone therapy or not
Working with families throughout the journey

Providing direction

Multidisciplinary approach

- Genetics
- Endocrinology
- Cardiology
- Nephrology
- Audiology
- ENT
- Ophthalmology
- Dental
- Speech

- Developmental Pediatrics
- Dermatology
- Orthopedics
- Nutrition
- Social Work
- Psychology
Overview of Turner syndrome

Diagnosis requires characteristic features coupled with complete or partial absence of the second sex chromosome.

Phenotype of TS is very broad.

No predictable phenotype-genotype correlation.

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Classic features

*Any of the features can be seen with any of the chromosome results

- Short stature (98-99%)
- Lack of ovarian function
- Lack of pubertal onset or stunted puberty
- High arched palate
- Low set ears
- Ptosis
- Small mandible
- Webbed neck
- Low hairline
- Broad (shield) chest

Cardiac anomalies
- Hypoplastic nipples
- Wide carrying angle
- Shortened 4th metacarpals and tarsals
- Spoon shaped (convex) nails
- Pigmented nevi

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How presents?

Prenatal:
- CVS, amniocentesis, ultrasound findings
- Genetic counseling

Postnatal:
- Karyotype (peripheral blood) should be done postnatally in all cases!
- FISH test for Y material
- Toddlerhood and school age: short stature
- Adolescence: lack of pubertal onset
Prenatal counseling

- Accuracy!
- Providers involved in counseling families must be accurately informed about the diagnosis, outcome, treatment options and overall quality of life.
- Important to discuss the variability of presentation
- Individuals with TS have normal intelligence
- Short stature, ovarian failure, infertility are the most common challenges

Delayed diagnosis

Late diagnosis is an ongoing challenge!

If not identified in newborn period, diagnosis is often delayed until short stature in school age years or lack of pubertal onset during adolescence lead to diagnosis

Psychosocial aspects

<table>
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<tr>
<th>Bullying</th>
<th>Social skills groups</th>
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<tbody>
<tr>
<td>Fitting in</td>
<td>Individual counseling</td>
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<tr>
<td>Being social</td>
<td>Child Study Team: NVLD; IEP</td>
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<tr>
<td>Treated younger than age</td>
<td>Art therapy</td>
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<tr>
<td>because of short stature</td>
<td>Camps programs: specifically for development of social skills</td>
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</table>
**Growth**
- Average final height: 4'7"-4'8"
- Can have IUGR
- Slow growth rate in infancy
- Slow growth rate in childhood
- Lack of the typical growth spurt of puberty

**Etiology of short stature**
- Haploinsufficiency of the SHOX gene
- Also responsible for other skeletal anomalies

**Growth Hormone Therapy**
- Increases rate of growth
- Increases final height outcome
- Best outcome if started at young age
- When to start? No specific age has been identified but recommended as soon as growth failure is demonstrated
- Growth hormone dose: 0.375 mg/kg/week as daily injections
Gonadal Failure

- Along with short stature, one of the most common features of TS
- Results in lack of spontaneous pubertal development in majority
- However, approximately 30% will show some spontaneous pubertal development
- Estrogen therapy used to initiate pubertal changes
- Estrogen patch therapy is most common
- Add progesterone once breakthrough bleeding occurs
- Feminization process: 2-4 years

Cardiac Defects

- Bicuspid aortic valve (BAV): prevalence is about 16%
- Aortic coarctation: prevalence is about 11%
- BAV and aortic coarctation occur at a 4 fold increase in patients with webbed neck
- Hypertension: 25% of girls
- Risk for aortic dilation, dissection or rupture

Cardiac Recommendations

- Cardiology evaluation
- ECHO (if fetal ECHO done, repeat it)
- ECG
- Cardiac MRI: is recommended once can be done without sedation
- Screening is essential; an abnormal aortic valve can be silent
- Blood pressure screening annually
- Ongoing: even if no cardiac defect, return for MRI in late adolescence
- Education on risk for aortic dissection
**Lymphedema**

- Results from abnormalities in lymphatic system
- Usually resolves in first 2 years
- Therapeutic options if does not resolve:
  - Compression stockings
  - Referral to Orthopedics if needed

**Renal Defects**

- Renal issues in 30-40%
  - Collecting system: 20%
  - Horseshoe kidney: about 10%
- Renal ultrasound required at diagnosis

**Dermatology**

- Pigmented nevi
- Keloid formation: anticipatory guidance
- No increased risk for melanoma
Orthopedic Issues

- Scoliosis 10-20%
- Kyphosis
- Nail beds
- Hips: increased risk for dislocation (infants)

Autoimmune

- Thyroiditis: about 25%
  - Annual thyroid function tests starting at age 4 years
- Celiac disease: 4-6%
  - Begin screening at age 4 years
  - Repeat every 3-5 years

Dental/Orthodontic Issues

- Small mandible
- Dental crowding issues
- Abnormalities in tooth development can occur
- Can have early eruption of secondary teeth
- Recommendation: see pediatric dentist by age 2 years and orthodontist by age 7 years
### Ophthalmologic Concerns

- Ptosis
- Strabismus: 25-35%
- Hyperopia: 25-35%
- Ophthalmology evaluation by age 12-18 months

### ENT and Audiology

- Otitis Media
- Hearing loss
  - Conductive related to OM
    - Middle ear effusions
    - May require myringotomy tube placement, adenoidectomy, tonsillectomy
    - May cause speech issues
  - Sensorineural hearing loss
  - Recommendations: audiology every 2-3 years

### Merging Practice Guidelines and EMR

- Diagnosis specific **progress notes**
- Diagnosis specific **smart phrases**
- Data retrieval through **flow sheets**
- **Consult** feature of EMR if an option
Practice Guidelines

Newly diagnosed versus established diagnosis

Age groups:
- Prenatal/newborn
- Birth-4 years
- School age (4-10 years)
- Adolescence

Practice Guidelines Newly Diagnosed: NEWBORN

Genetics: if diagnosed prenatally, confirm dx with karyotype

Endocrine

Birth hx: BW, BL

ROS: cardiac issues, nutrition, growth assessment

PE: height, weight, BP, phenotypic features of TS

Education: GH option/future planning

Cardiology

Nutrition

Social Work

Screening tests:
- Renal Ultrasound
- Audiology
- Cardiac ECHO

Education

Anticipatory guidance

Resources

Practice Guidelines Newly Diagnosed: birth-4 years

Genetics evaluation: if dx prenatally, do karyotype

Endocrine

Birth hx: BW, BL

ROS: otitis media, vision, hearing, cardiac issues, nutrition, growth assessment, development

PE: height, weight, BP, BMI, phenotypic features, growth

Education: GH option

Cardiology

ENT: if otitis media

Ophthalmology: eye exam by age 12-18 months

Dental: start age 2 yrs

Nutrition: as indicated

Social Work

Screening tests:
- Renal ultrasound
- Audiology
- Cardiac ECHO
- Bone age as indicated

Resources
**Practice Guidelines Newly Diagnosed: School Age 4-10 yrs**

**Genetics**

**Endocrine**

**Birth hx:** BW, BL

**ROS:** otitis media, vision issues, hearing deficits, cardiac, UTIs, nutrition, growth, social interactions/social skills, learning

**PE:** H, W, BP, BMI, growth, otoscopic exam, phenotype features, scoliosis exam

**Education:** discuss GH, resources

**Cardiology**

**ENT:** if otitis media

**Ophthalmology:** annual eye exam

**Dental/Orthodontia:** starting age 7 yrs

**Orthopedics:** if scoliosis

**Nutrition**

**Social Work**

**Educational evaluation**

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**Practice Guidelines Newly Diagnosed: Adolescent**

**Genetics**

**Endocrine**

**Birth hx:** BW, BL

**ROS:** otitis media, cardiac issues, UTI, vision, hearing, nutrition, growth, social interactions/social skills, learning, puberty

**PE:** H, W, BP, BMI, otoscopic exam, nevi, scoliosis, Tanner staging

**Education:** discuss GH, puberty,

**Cardiology**

**ENT:** if otitis media

**Ophthalmology:** annual eye exam

**Dental/Orthodontia:** as indicated

**Orthopedics:** if scoliosis

**Nutrition**

**Social Work**

**Educational evaluation**

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**Practice Guidelines: BIRTH-4 years Ongoing Assessments**

*patients with no renal/cardiac anomalies noted at diagnosis*

**Review of Systems**

Growth, nutrition, otitis media, vision, hearing, nutrition, cardiac status, learning, social interactions/social skills

**Physical Examination**

H, W, BP annual; BMI, otoscopic exam, assess for nevi

**Screening Tests**

Renal ultrasound

Audiology

Cardiac ECHO/MRI

**Labs**

TFT: begin age 4 yrs

Celiac screen: begin at 4 yrs

Bone age

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**Practice Guidelines: BIRTH-4 years Ongoing Assessments**

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**Review of Systems**

Growth, nutrition, otitis media, vision, hearing, nutrition, cardiac status, learning, social interactions/social skills

**Physical Examination**

H, W, BP annual; BMI, otoscopic exam, assess for nevi

**Screening Tests**

Renal ultrasound

Audiology

Cardiac ECHO

**Bone age:** if indicated

**DXA:** > 18 yrs

**Labs**

Thyroid studies: annual; start at 4 yrs

Celiac screen: start at 4 yrs; q 2-3 yrs

Growth factors if on GH

**Evaluation**

**ENT:** if recurrent OM

Ophthalmology: first assessment by 12-18 months

Dental: yearly

**Audiology:** if normal at dx, repeat every 2-3 yrs

Nutrition: based on weight/BMI

**Educational evaluation**

**Social work**
Practice Guidelines: School Age (4-10 yrs) Ongoing Assessments*

*patients with no renal/cardiac anomalies noted at diagnosis

**Review of Systems**
- otitis media, vision, hearing, cardiac status, nutrition, growth, learning, social interactions/social skills

**Physical Examination**
- Height, Weight, Annual BP, BMI
- Otoscopic exam until age 7-8 years or ongoing if recurrent otitis, nevi, scoliosis, Tanner staging

**Labs**
- TFT, LFT: annual
- Celiac screen: every 2-3 yrs
- Growth factors: if on GH

**Evaluations**
- Ophthalmology: annually
- Audiology: if normal at dx do every 2-3 years
- ENT: if recurrent otitis media
- Dental/Orthodontia
- Orthopedics: if scoliosis
- Nutrition: based on BMI
- Educational evaluation
- Counseling

Practice Guidelines: Teen-young adult ongoing assessment*

*patients with no renal/cardiac anomalies noted at diagnosis

**Review of Systems**
- growth, pubertal changes, vision, hearing, nutrition, cardiac status, dental/orthodontic issues, education/learning needs, social skills, peer relationships, teen issues

**Physical Examination**
- Height
- Weight
- Blood pressure yearly
- Tanner staging
- Otoscopic exams: if otitis media
- Scoliosis

**Labs**
- TFT, starting age 15 yrs: fasting lipids, HgbA1c, LFT, CBC, Cr, BUN
- Growth factors if on GH
- LH/FSH
- Celiac panel: every 2-3 years
- DXA: >18 years

**Evaluations**
- Cardiology: return visit in early teens; ECHO +/- MRI q 5-10 years
- Audiometry: q 2-3 years
- Ophthalmology: yearly
- Orthopedics: if indicated
- Nutrition: if indicated per weight or BMI
- Transition: ongoing discussion
- Counseling

Transition

Start early
Identify providers
Discuss options
Education and Support Opportunities

- Learn and Connect Sessions
- Shared Medical Appointments with social worker
- Networking and Education Day
- Parent organized toddler play group
- Parent to parent connections
- Patient to patient connections

References


Thank you!