
بسم الله النور

Turner syndrome

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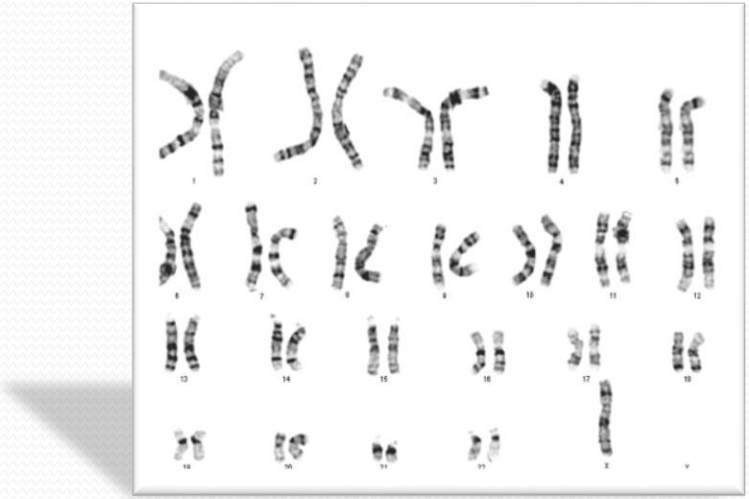
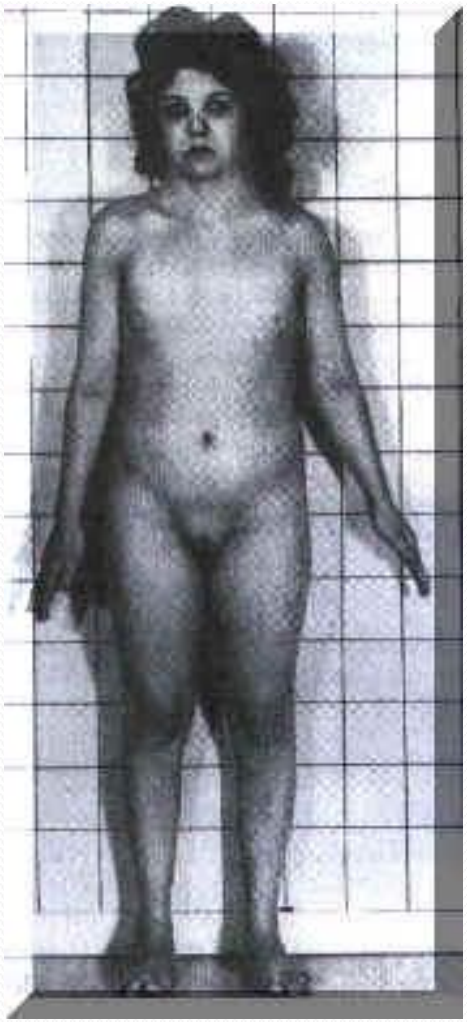
Turner syndrome

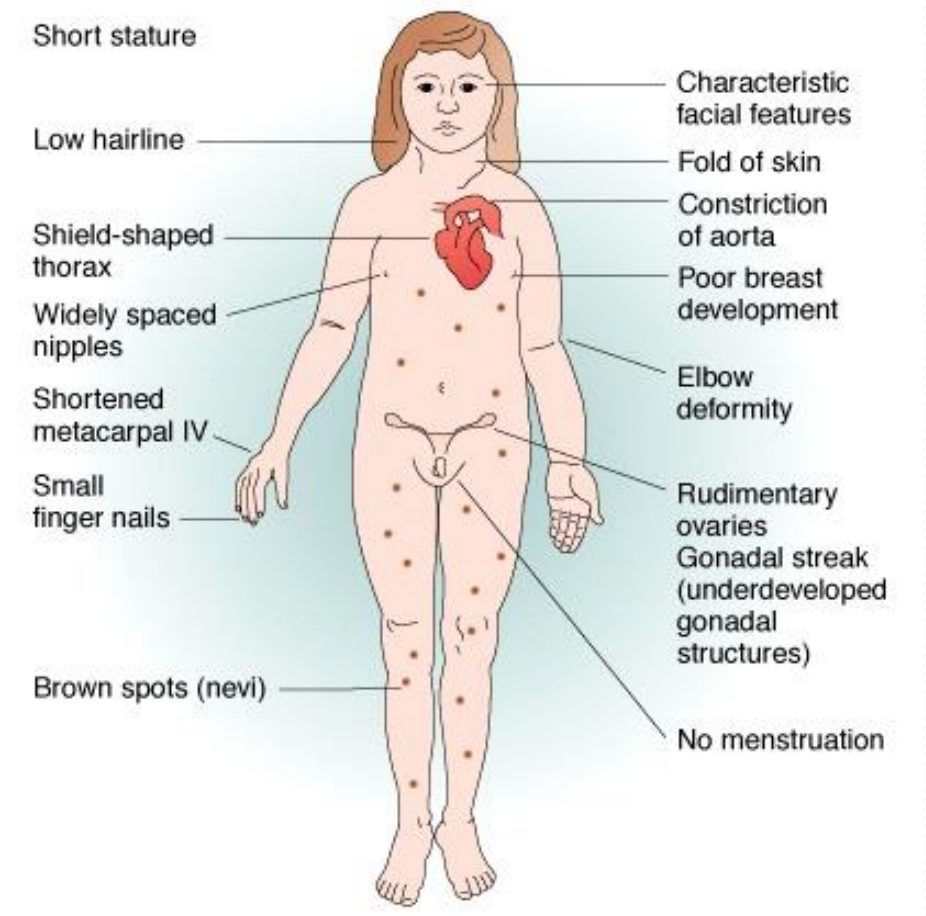
- An important cause of short stature in girls and primary amenorrhea in girls that is usually caused by loss of part or all of an X-chromosome.

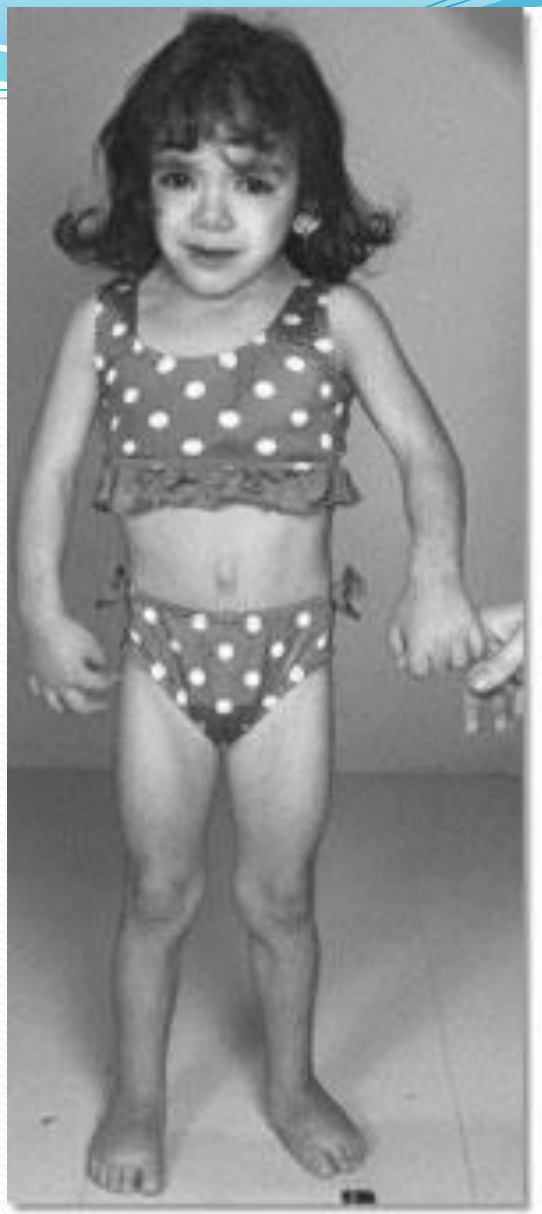


- Occurs in approximately **1 in 2000 to 1 in 2500 live** female births

Clinical phenotype







medgen.genetics.utah.edu

Lymphedema

- lymphedema usually improves over the first 1 to 2 years of postnatal life. It may even resolve, but in many patients it persists
- if the fingernails, toenails and/ or skin are compromised, professional edema therapy may need to be started early

Lymphatic obstruction

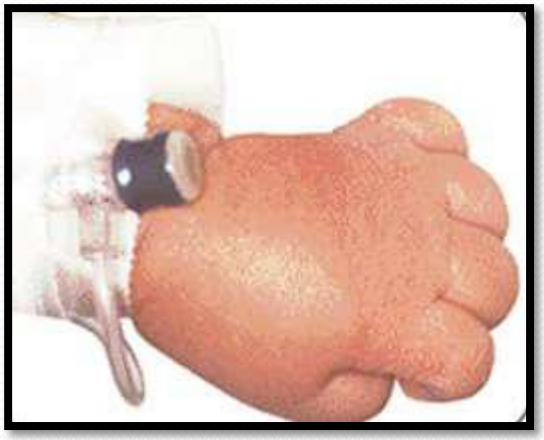
- Neck webbing
- Low posterior hairline
- Edema of hands/feet

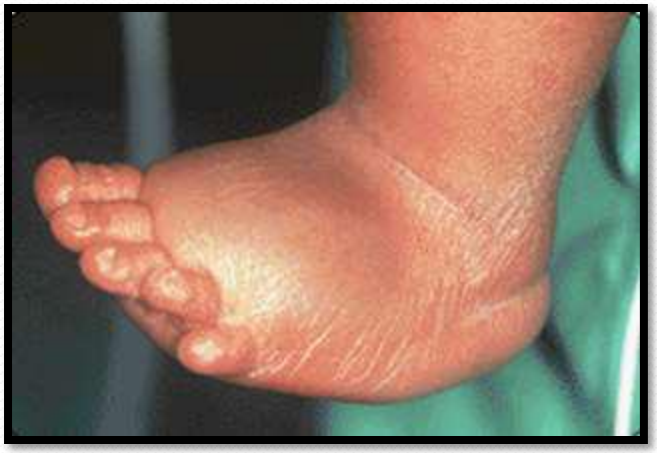
Later age Lymphedema

- Some TS individuals demonstrate intermittent worsening of their peripheral edema associated with puberty or introduction of growth hormone or sex steroid therapy
- it may occur at any later age, possibly in association with initiation of salt-/fluid-retaining therapies (estrogen).

Lymphatic System

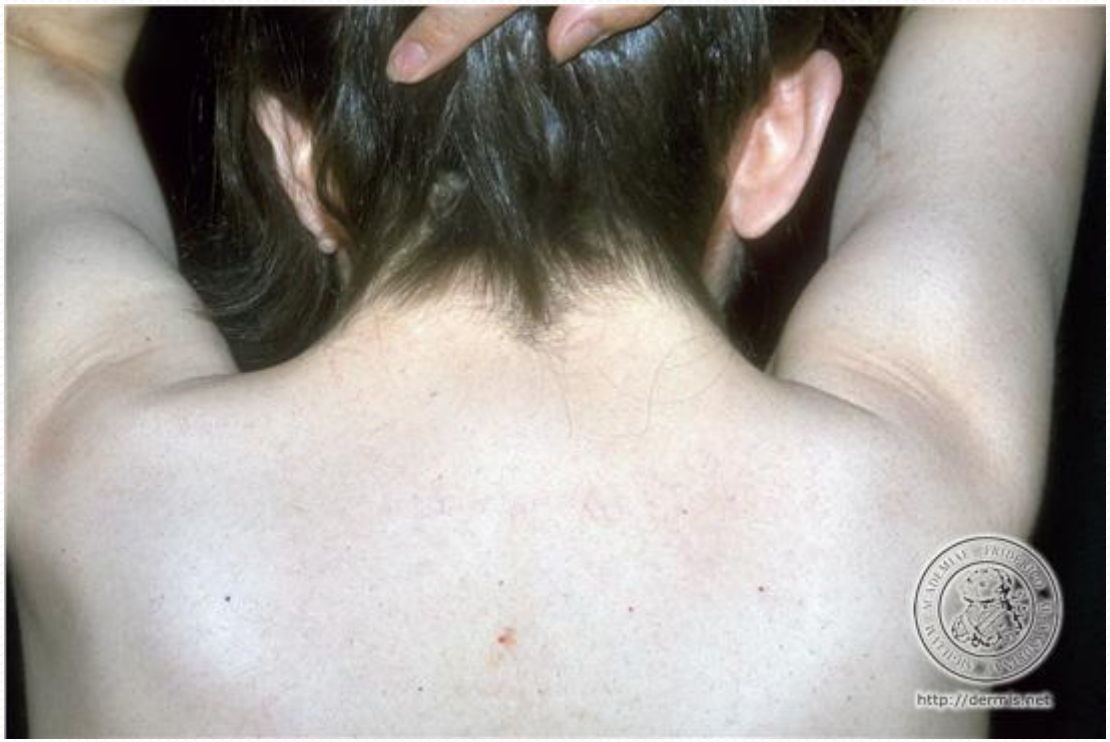
Peripheral lymphedema



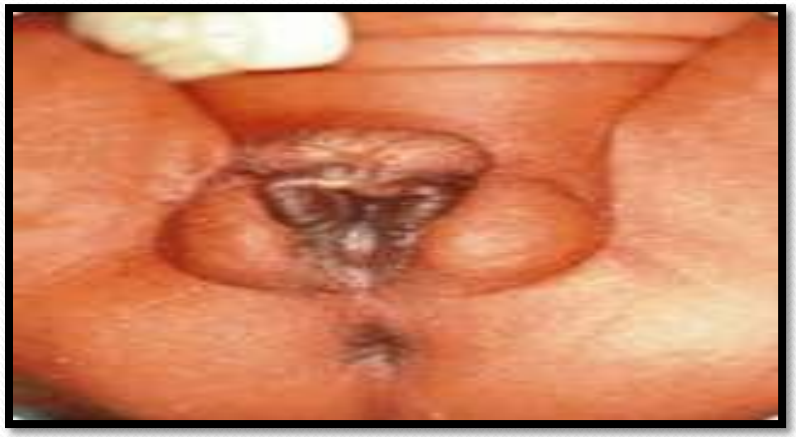


Nail hypoplasia

Low hair line



- Lymphedema of genitalia



Growth failure, Short Stature

Short Stature

- Their growth failure is disproportionate
- large trunk with broad shoulders and pelvis
- Reduced height, this renders them with a "stocky" appearance
- increased **upper-to-lower segment** ratio
- TS women ending up **about 20 cm shorter than** their non-Turner female peers.

Growth failure

- A mild degree of growth restriction During infancy and up to 3 years of age, a further mild growth deceleration can be seen.
- Continued subnormal growth is observed throughout childhood
- Between ages **3 and 13 years**, TS girls develop more deflection from both **their target percentile and the normal height curves.**

Growth hormone treatment

- We recommend initiating growth hormone (GH) treatment early **around 4–6 years of age**

SHOX deficiency

- SHOX is located at Xp22 on the pseudoautosomal region of the X chromosome.
- SHOX, **a transcription factor**, has been implicated in short stature and the skeletal anomalies associated with TS

SHOX deficiency

SHOX heterozygous variants, may cause

- Madelung wrist deformity observed in Leri-Weill dyschondrosteosis
- up to 15 % of idiopathic short stature
- Mesomelia
- Cubitus valgus
- Short metacarpals
- Short stature in TS
- Neurocognitive deficits

Gonadotropin measurement

- Between **0.5-3 year**
- Screening of FSH and AMH At 10 or 11 years of age

- it is important to note that **a normal FSH does not exclude** the possibility of Turner syndrome

Pubertal development variation

- 15 to 30 % of girls with Turner syndrome have initial breast development followed by pubertal arrest
- Complete puberty but then develop secondary amenorrhea.
- Milder phenotypes of ovarian failure are common in girls with mosaicism compared with those with 45,X
- if menarche occurs, oligomenorrhea and anovulation

are common

Spontaneous puberty

- Spontaneous puberty was observed in approximately

15% of girls with 45,X monosomy and in 30% of girls with a second cell line with more than one X chromosome

45,X/46,XX; 45,X/47,XXX

- Spontaneous pregnancy may occur in 2% to 3% of women with TS.

Adrenarche & pubarche

- Onset of adrenarche is normal but followed by delayed pubarche

Orthopedic manifestation

Orthodontic evaluation

- Begins at age 7 years
- increased risk for **root absorption**
- Small mandible
- Distal molar occlusion
- Smaller primary and permanent teeth

Orthodontic evaluation

- High arched palate in 60% of patients
- **Thinner enamel** and abnormal dentin
- Abnormal **gingival**
- Cleft palate
- paradoxically advanced dental age

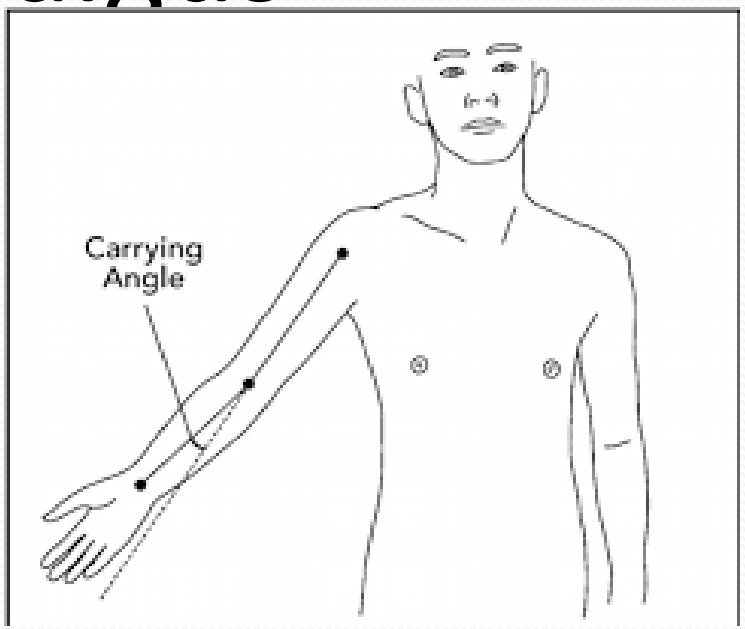
Facial bones

- Abnormalities of the development of facial bones and skull base result in a **micrognathic and retrognathic**

Cubitus valgus

Carrying Angle/Cubitus Valgus

- Formed by long axis of humerus and midline of forearm
- Male norms – 11-14 degrees
- Female norms – 13-16 degrees
- Larger angles are considered abnormal

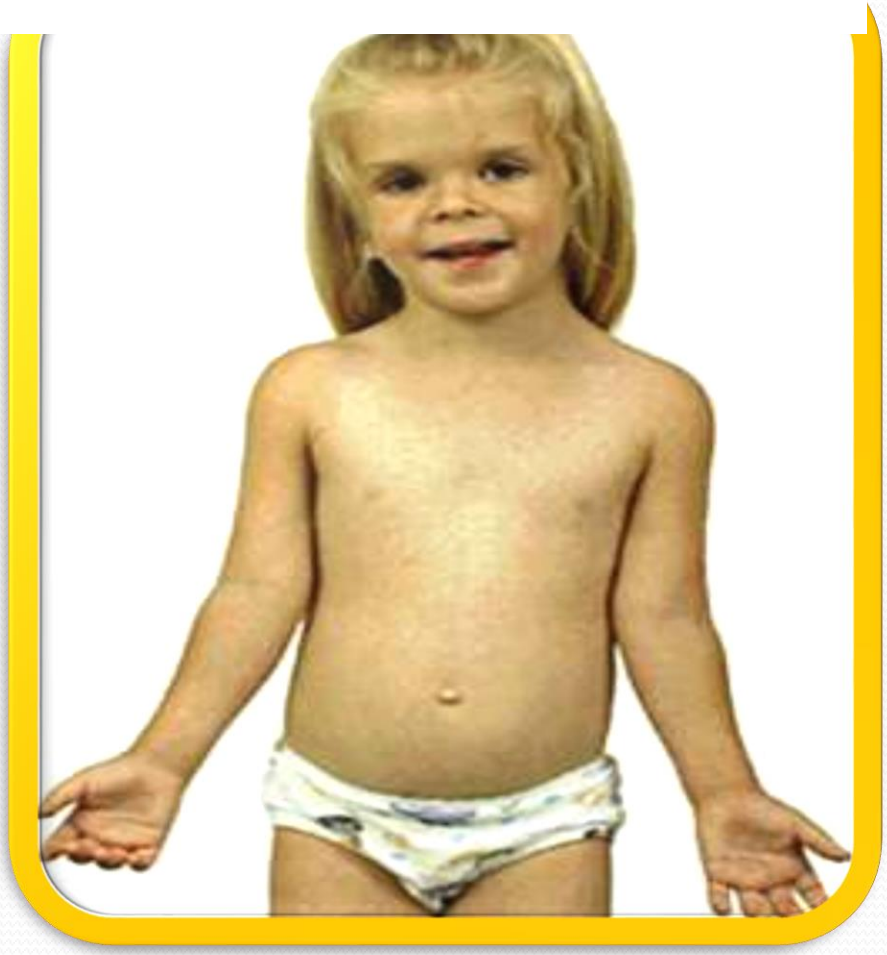


This carrying angle is the angle of intersection of the long axis of the upper arm with the long axis of the fully extended and supinated forearm.

Skeletal Anomalies

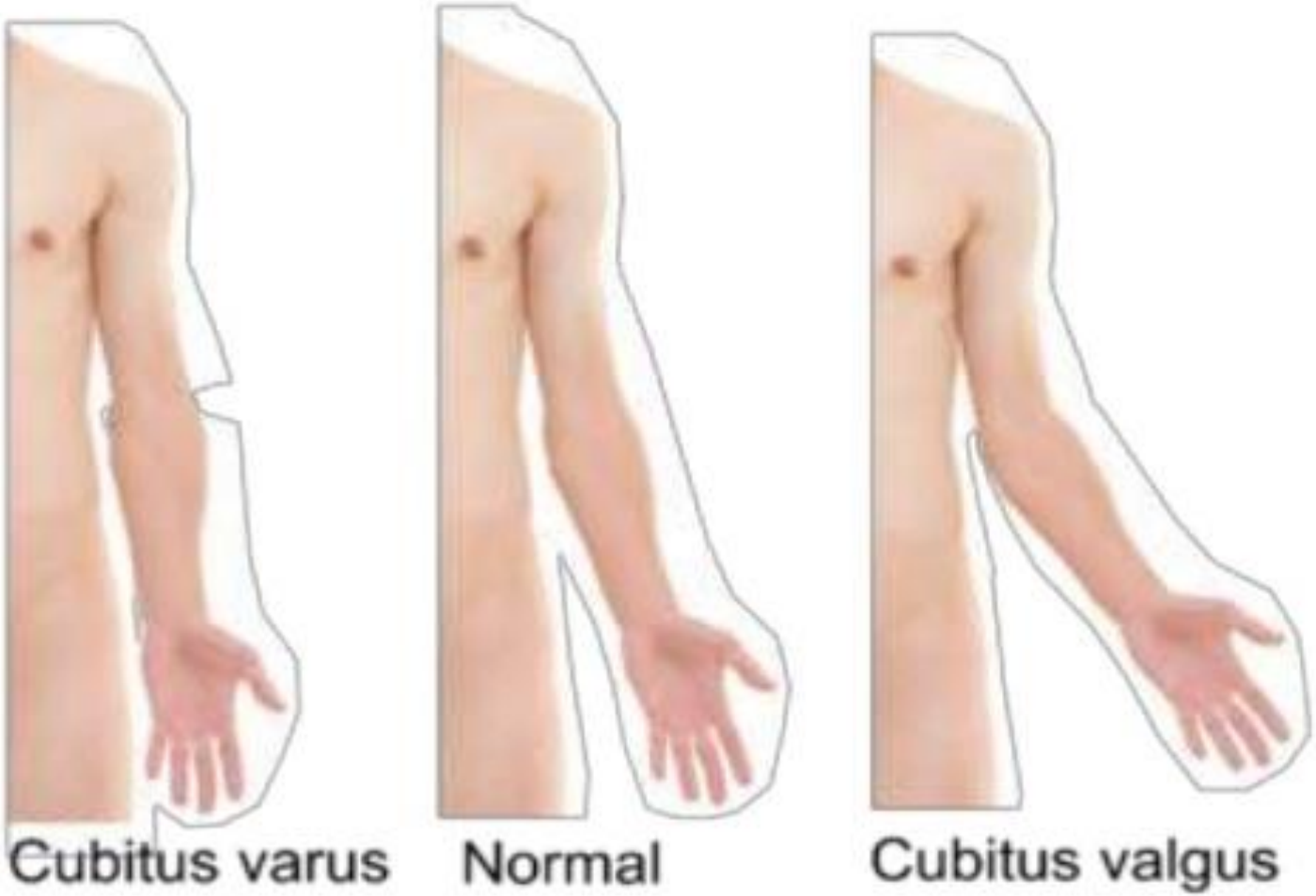
Cubitus valgus

present in approximately 50 percent of individuals with Turner syndrome



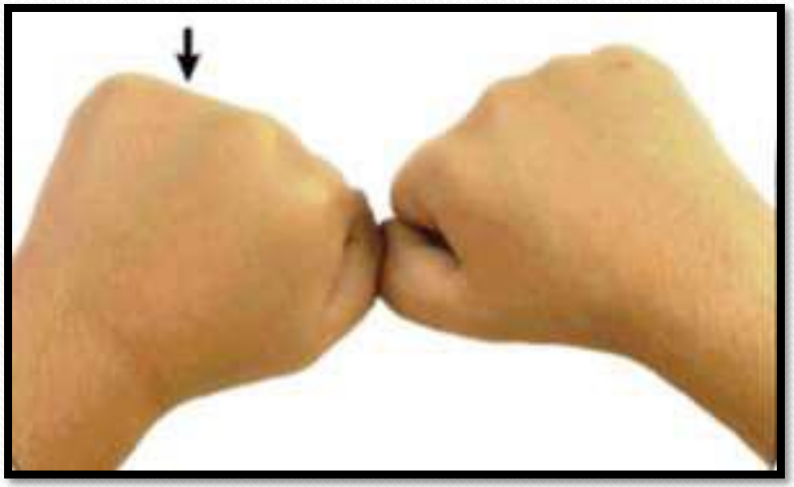
2-arms out straight

To detect cubitus valgus of Turner and Noonan.



Skeletal Anomalies

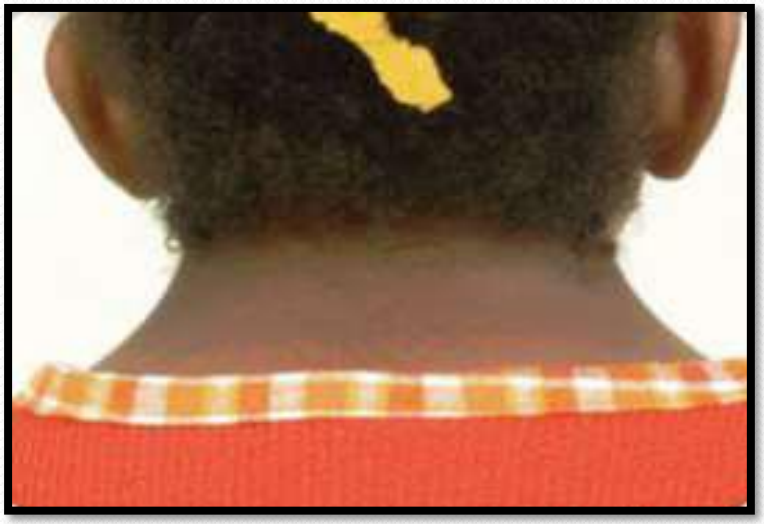
Short 4th (5th) metacarpals



Genu valgum

Skeletal Anomalies

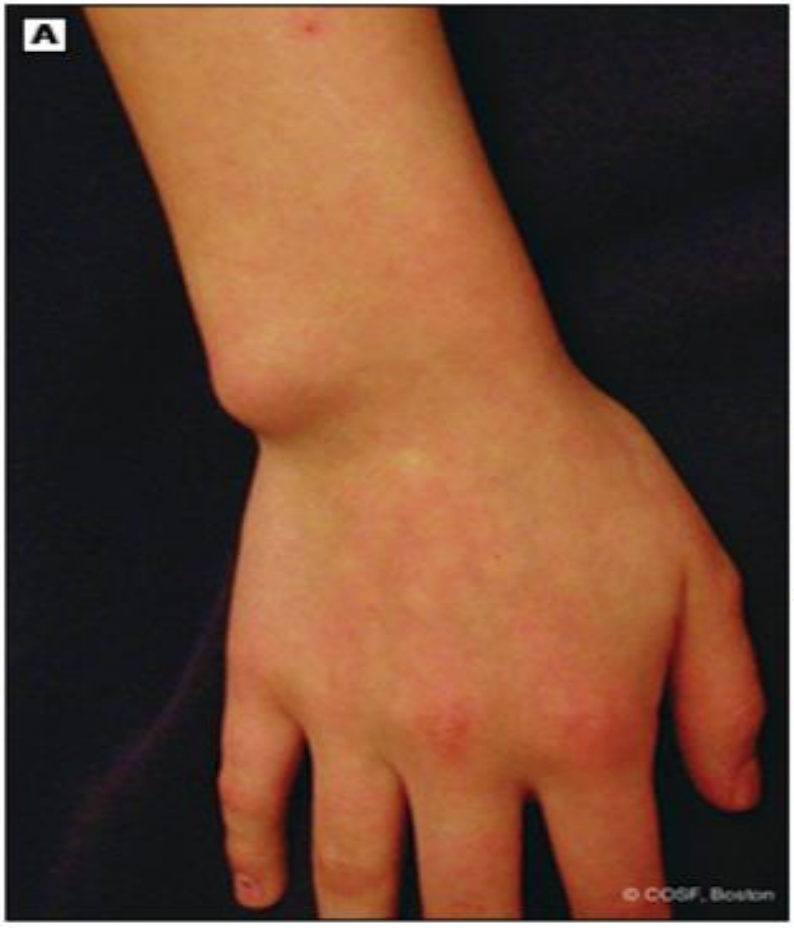
Short neck

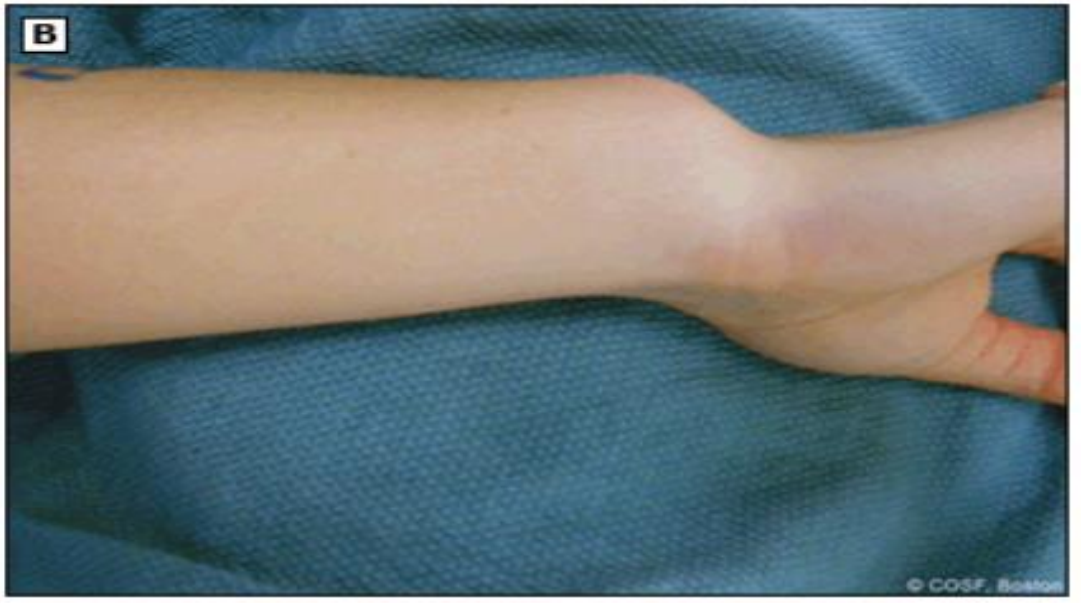


Scoliosis

Madelung deformity of the forearm and wrist

Madelung deformity of the forearm





caused by a curvature of the distal radius in addition to a dorsal subluxation of the distal ulna

Scoliosis &kyphosis

- Scoliosis develops in **20 %**
- kyphosis in nearly **50%**
- vertebral wedging

- Between 5 and 20 years of age develop scoliosis

- The presence of scoliosis or kyphosis does not preclude growth hormone therapy **but warrants close monitoring during therapy**

Scoliosis &kyphosis

Visual inspection of the spine

- Annually
- **Every six months** during GH therapy
- or annually until growth is completed

Additional radiographic assessment around

- School entry **five to six years of age**
- During mid-puberty **12 to 14 years of age**
- when **concerns arise.**

- Slipped capital femoral epiphysis has been reported with and without GH therapy
- Hip dislocation

Vitamin D deficiency

- Screen begins between 9 and 11 years of age and every **two to three years thereafter**
- lower 25-OH D
- Maintaining 25-OHD is important because girls and women with Turner syndrome have an increased risk of fracture even if they have normal BMD
- Increased PTH and bone resorption markers
- impaired renal vitamin D metabolism

Bone mineral density

- Screening of BMD should begin when patients reach adult estrogen replacement doses **late adolescence or early adulthood** , **18 yr**
- Repeated BMD **every 3-5 years**
- Additional follow-up is done when the patient stops estradiol replacement (around 50 years of age).

Osteoporosis

Osteoporosis and fractures have been reported to be common in women with Turner syndrome
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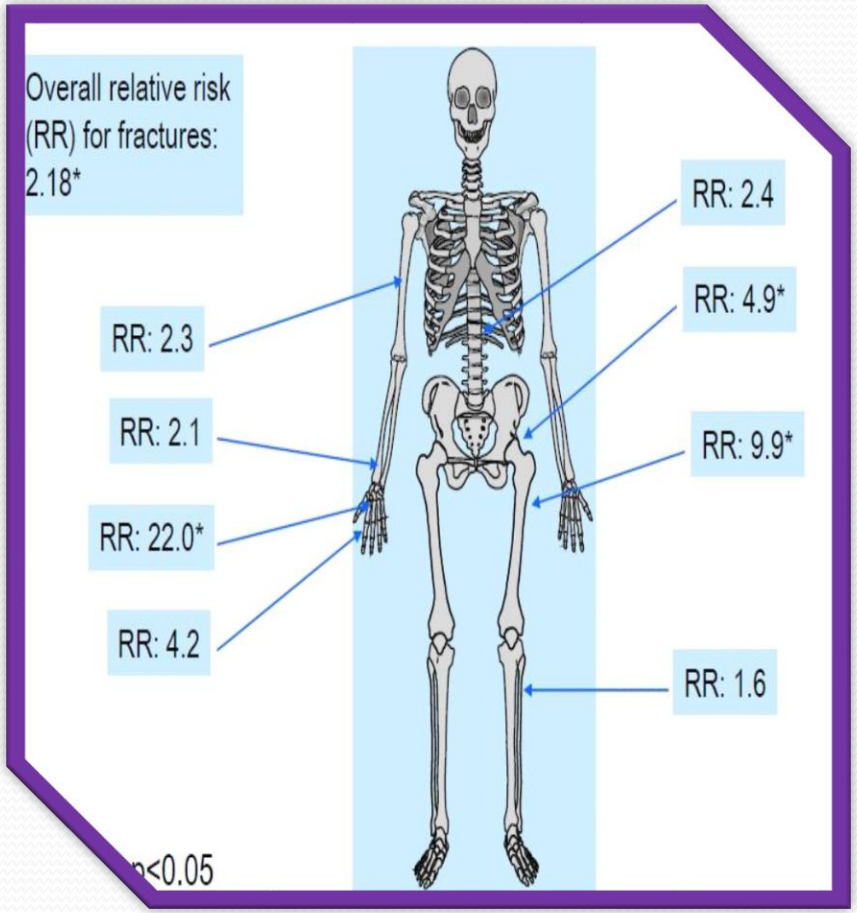


Diagnostic methods

- DXA is not good ,can be affected by bone size. Consequently, subjects with short stature could be over-diagnosed with osteoporosis
- **phalangeal quantitative ultrasound**

Bone mineral density

Women with Turner syndrome have an increased risk for osteoporosis and fractures even with normal BMD **because of**

- **Suboptimal estrogen replacement**
- **Intrinsic bony abnormalities**
- A selective reduction in cortical forearm BMD
- History of parental fracture
- Enhanced osteoclastogenesis
- Calcium and vitamin D deficiency
- Coeliac disease
- Diabetes

Intrinsic bony abnormalities

- These intrinsic abnormalities of bone may be due to haploinsufficiency for **bone-related X chromosome genes**
- *SHOX gene*
- Bone morphogenetic protein 2
- insulin-like growth factor
- placental growth factor
- prostaglandin endoperoxide synthase 1
- Secreted frizzled-related protein 1

Increased FSH secretion

- **FSH** can affect the formation and activity of Ocs
- There are **two main windows for prevention**
- Early childhood 6-7 years of age
- prepubertal age.
- These two periods are characterized by high FSH levels which activate the osteoclast function
- An enhanced spontaneous osteoclastogenesis appears to be more active in girls before the induction of puberty, possibly supported by the high FSH

Increased FSH secretion

- A neutralizing FSH antibody could be useful to modulate the high FSH levels observed during the prepubertal age.
-

Bone fracture

increased risk of bone fractures are typically localized 25%

- Metacarpal bones
- Femoral neck
- lower spine
- Forearm

Treatment of osteoporosis

Important preventive measures include

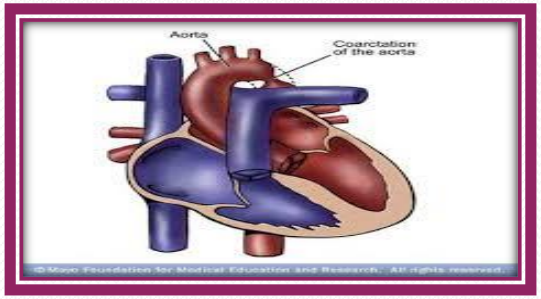
- Optimal estrogen replacement
- To ensure intake of calcium and vitamin D
- Weight bearing exercise.
- perhaps growth hormone therapy
- Denosumab and Romosozumab further studies are required to determine the safety of their potential use on children

Treatment of osteoporosis

- After adjustment for body size, the prevalence of osteoporosis and fractures in the Turner syndrome patients who had been treated with estrogen was the same as age-matched controls without Turner syndrome

Cardiovascular anomalies

- **Prevalence is 23 to 50%**
- All patients should be studied by echocardiography or MRI to detect cardiovascular anomalies
- Defects is higher in patients harboring a 45,X compared to X chromosome mosaicism
- Repeat echo or MRI for asymptomatic patients every 5 years
- yearly if aortic root >3 cm
- MRI for older girls and adults



Blood pressure

- Blood pressure in all extremities should be monitored annually or every visit
- A prevalence as high as 30 % in children and 60% in adults
- Hypertension is defined
- As **>130/80 mmHg** for adults and children >13 years
- or **>95th percentile** for younger children

Pathogenesis of Hypertension

- Neither the presence of renal or cardiac abnormalities, nor treatment with growth hormone or estrogen therapy, had an effect on blood pressure.
- **Sympathetic hyperactivity, increased activity of the renin-angiotensin-aldosterone system, and estrogen deficiency** may all be contributory.

Risk for Premature Atherosclerotic Disease

- 3-fold increased risk of coronary and cerebrovascular disease among women with TS.
- Atherogenic risk factors, including abdominal adiposity and lipid profile, are higher in women with turner

Vasculopathy

- increased **vascular resistance and stiffness** in patients as young **as 9 or 10 years of age**
- Cardiovascular risk factors of hypertension, dyslipidemia, and dysglycemia
- Estrogen deficiency is a contributor to this risk
- Mean carotid intima-media thickness was increased
- Enlarged diameter of the carotid and brachial arteries
- Aneurysms of other arteries

The coagulation system

- **CVA occur in excess** of the general population
- Whether related to systemic hypertension or other TS-specific causes **is unknown**
- Normal clotting factors and clotting times
- Normal or increase procoagulant values of clotting and fibrinolytic factors
- Normal or increase Fibrinogen
- **Reduce proteins C and S**
- factor V Leiden is more prevalent
- Even clotting system is activated outcome data are lacking

Renal screening

- We recommend a renal ultrasound at the time of diagnosis
- Screen for creatinine, and urinalysis begins **around ten years of age**
- **Repeat kidney sono every 5 years**

Mortality related to renal disease **is sevenfold higher than** that in the general population

Renal anomalies

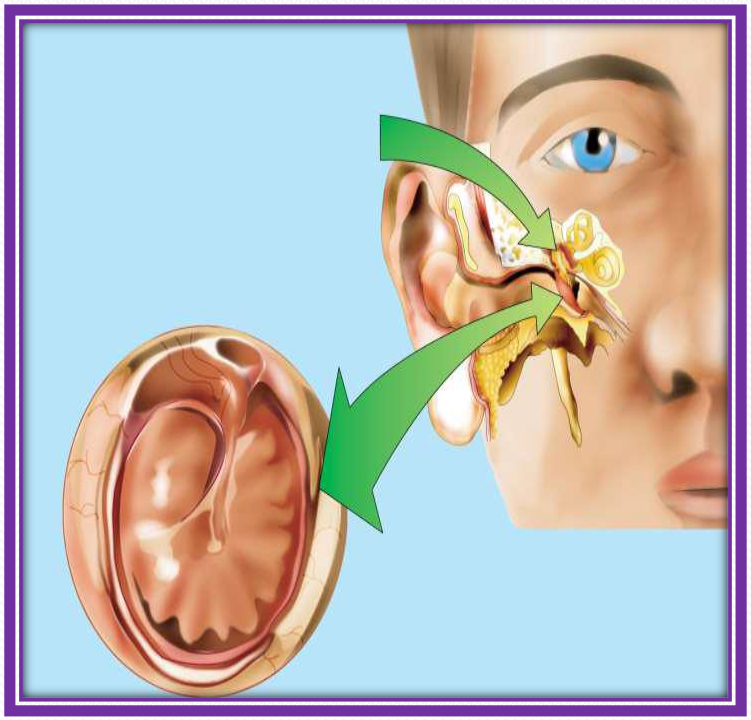
Congenital renal abnormalities present in 30 to 40 percent of patients.

- Collecting system malformations
- positional abnormalities (Malrotated kidneys)
- Horseshoe kidneys
- Obstruction of the ureteropelvic junction
- Hydronephrosis
- Pyelonephritis.
- Renovascular abnormality
- Renal aplasia
- multicystic

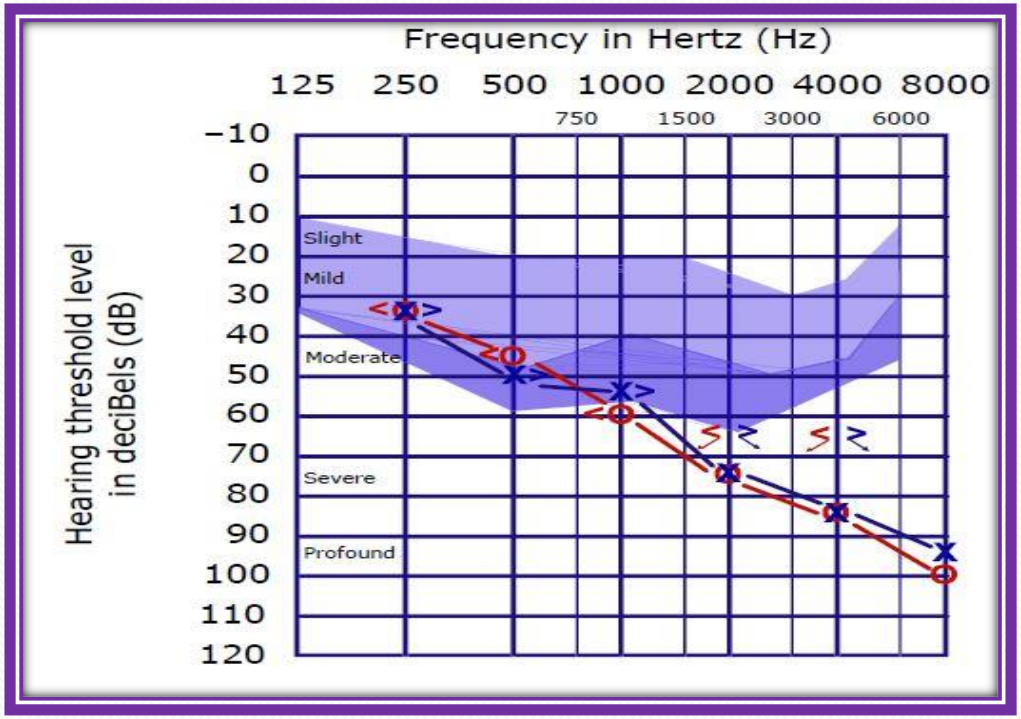
Tympanometry and audiology

- Mild malformation of the outer ear and low set ears occur in 30–50% of individuals with TS
- **TS with Conductive hearing loss** have a karyotype with deletion short arm of the X chromosome (Xp) seems to predispose to this

Tympanometry and audiology



- SNHL More than 50 % adult
- . Recurrent Serous otitis media



Inner ear

- Sensorineural dip can occur as early **as 6 years**
- **Estrogens deficiency** might be a contributory factor particularly in SNHL
- Periodic examinations throughout the lifespan are mandatory even after the resolution of the middle-ear disease to detect SNHL
- SNHL predominantly at a frequency of 1000 to 2000 Hz has been noted in more than **50 percent of adult Turner syndrom**
- SNHL occure in 45,X or 45,X/46,i(Xq) karyotype

Cholesteatoma

Risk factors included

- 45,X and 46,XisoXq karyotypes
- A history of chronic OM
- Retraction of the tympanic membrane
- persistent otorrhea and older age

Chronic otitis media

- Otitis media occurs particularly between 1 and 6 yr of age
- With a maximum incidence 60% at 3 yr of age because of
- A subnormal immune response
- The effects of X chromosome-related factors (estrogen deficiency
- Decreased T helper-cell

Tympanometry and audiology

- Audiomeric evaluation Begins 9-12 month
- Audiology evaluation every three years in children and **every five years in adults**

Ophtalmologic Evaluation

- starting in the second year of life and repeated **every three years thereafter**

Eye Anomalies

Strabismus 15%

Petosis 10%

Eye Anomalies

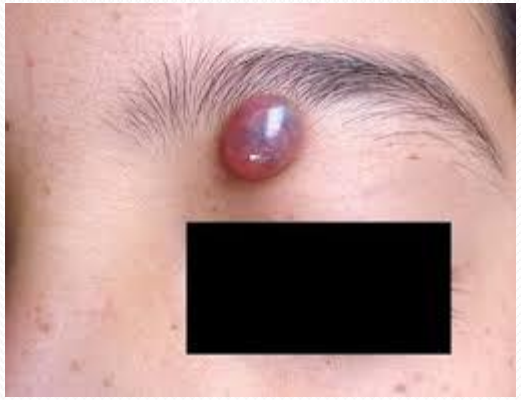
Prominent epicanthal folds with telecanthus %20

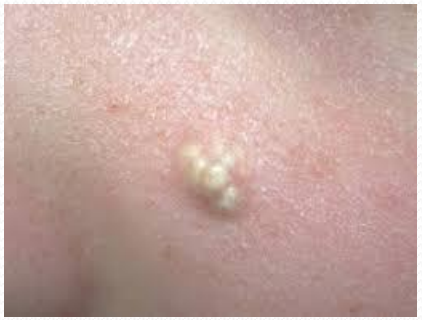
Prominent epicanthal folds with down-slanting palpebral fissures

Ophtalmologic Evaluation

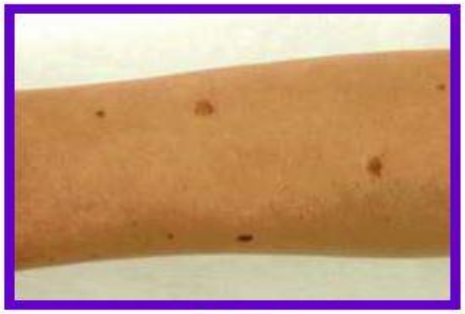
- Amblyopia
- Strabismus
- Ptosis
- Red-green color blindness 8 to 10%
- Keratoconus
- Glaucoma
- Anterior lenticonus
- Cataracts
- Retinal vascular changes
- Retinal detachment
- Refractive errors

pilomatricoma

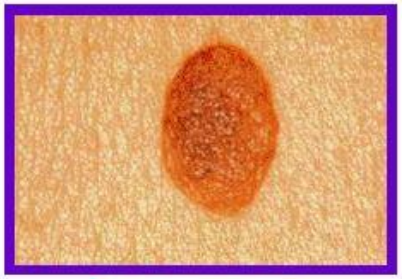




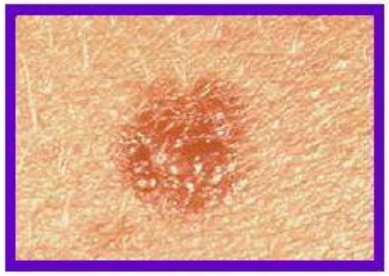
Dermatologic finding



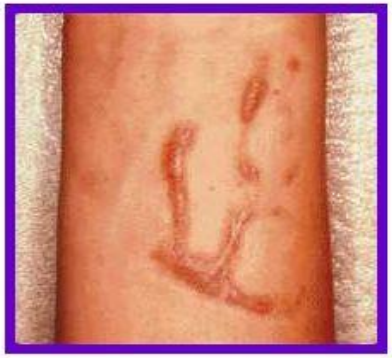
Nevi



Compound nevus



Dysplastic nevus



Keloid scars

Single transverse palmar crease

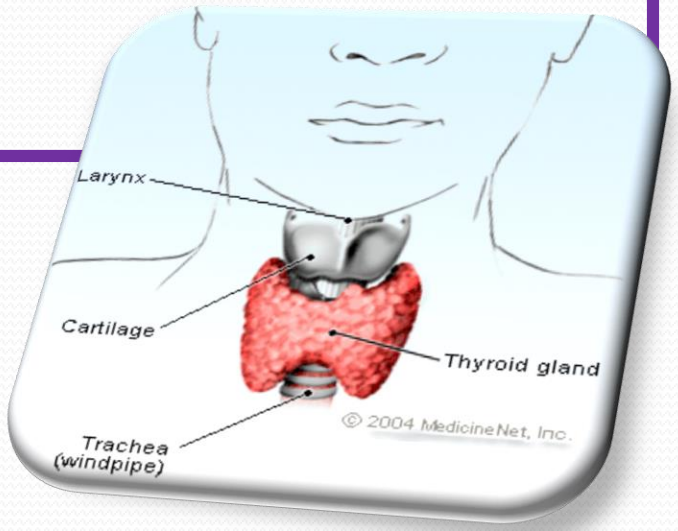
Autoimmunity

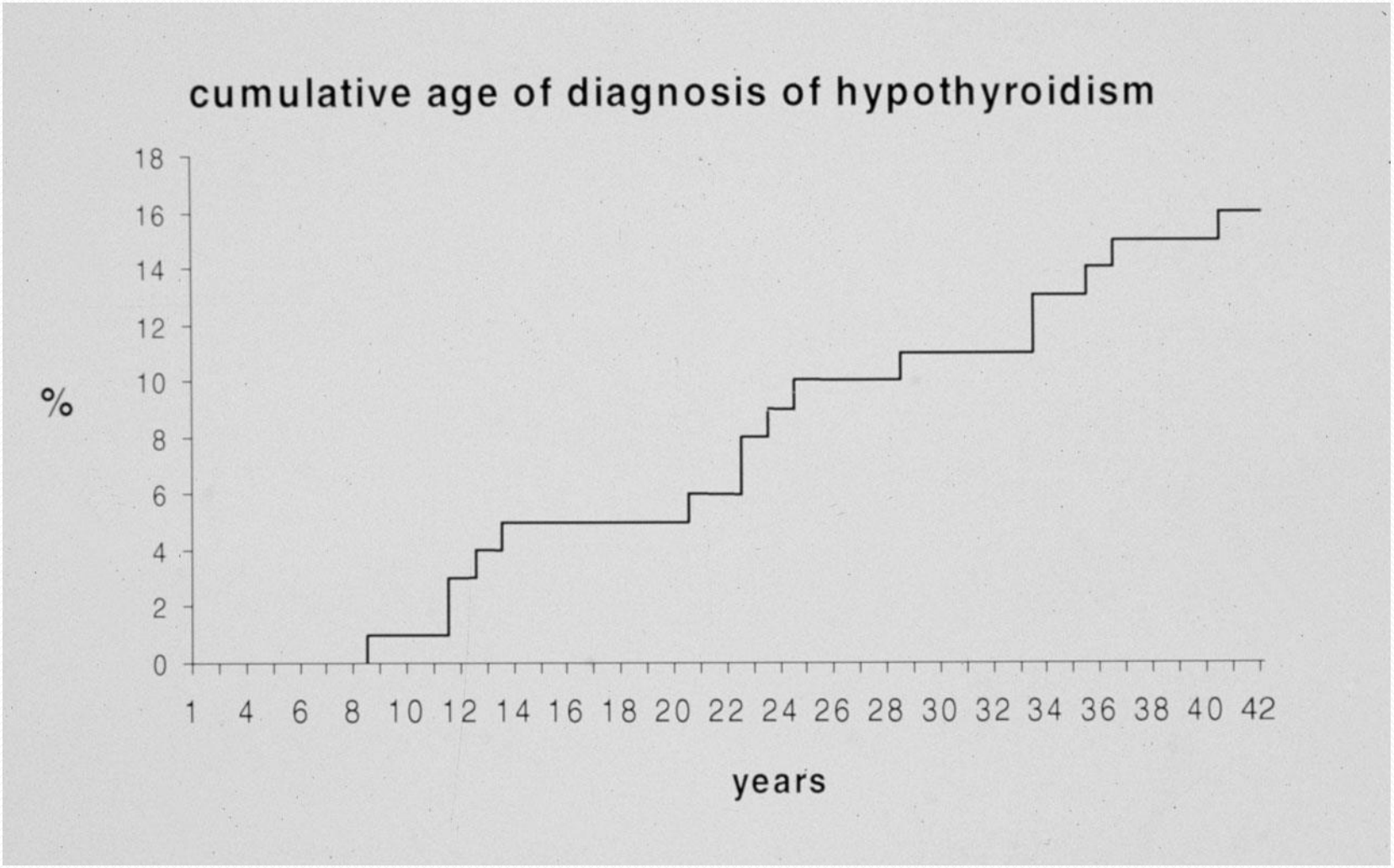
- **Decrease in the CD4–CD8 suggesting an immune alteration that may predispose to autoimmunity**
- **Absence of a second X chromosome**
- Thyroiditis, hyperthyroidism and hypothyroidism
- Celiac disease
- Type 1 diabetes mellitus
- Alopecia areata
- Juvenile rheumatoid arthritis
- Uveitis
- Inflammatory bowel disease

Hypothyroidism

Adolescents 15 %

- Adults 25 to 30%
- Up to 50 % have thyroid antibodies




cumulative age of diagnosis of hypothyroidism
%
0
2
4
6
8
10
12
14
16
18
1 4 6 8 10 12 14 16 18 20 22 24 26 28 30 32 34 36 38 40 42
years

Thyroid disease

Relative risk for

- Thyroiditis 16.6%
- Hypothyroidism 5.8%
- Graves disease %1.7-3

Association between ovarian failure *per se and chronic lymphocytic thyroiditis*

Autoimmune thyroiditis

- It is rare in the first four years of life
- Screen for autoimmune thyroiditis annually beginning **around four years of age**
- Patients with 46,X,i(X)q) are at a higher risk for autoimmune disorders
- Antibody measurement recommended **at first detection of thyroid dysfunction and/or with thyroid enlargement**

Gastrointestinal Bleeding

The bleeding episodes have been caused by

- intestinal telangiectasia
- Hemangiomatosis
- Angiodysplasia in the intestinal tract
- venous ectasias

Inflammatory Bowel Disease

- Crohn disease
- Ulcerative colitis

inflammatory bowel disease

- The prevalence of IBD in women with Turner syndrome is approximately **3 to 4 percent**
- Which is substantially higher than in women with POI or the general population
- Patients with an isoXq encompass more than **half of those with IBD**

Celiac disease

- The risk is increased 4 to 6%.
- RR **2 and 5 times** the general population
- *Periodic screening with Anti TTG should begin* **around 2-4 years of age**
- *Should be repeated every two*. throughout childhood
- *Every five years in adulthood*

Liver disease

- Screen for liver disease by measuring ALT, AST, GGTP and alkaline phosphatase **annually after 10 years of age**.
- Patients with persistent aminotransferase elevations >twice should be evaluated for other causes of liver disease
- Liver ultrasound required for markedly raised **liver enzymes**
- Consider special scans measuring fibrosis and steatosis, and biopsy if structural defects identified on US

Pathogenesis of liver disease

The pathogenesis for these findings is unclear

- Hepatic disorder could be caused by intrinsic vascular changes/vasculopathy affecting normal liver physiology
- The risk of cirrhosis is sixfold more than that in the general population
- Nonalcoholic fatty liver disease
- Steatosis
- Autoimmune process
- Obesity and metabolic syndrome
- primary sclerosing cholangitis

Abnormal liver enzymes

- Raised liver enzyme 35 to 45 % of adult turner patients
- ***Yearly testing of liver enzymes is recommended***

improve liver enzymes

- Although liver enzymes may remain elevated throughout childhood and in the adolescent years
- They may improve or resolve with estrogen replacement therapy

Obesity

- Higher BMI
- Higher percent body fat
- larger waist circumference
- lower percent lean body mass
- Central obesity

Abnormalities of Carbohydrate Metabolism

Glucose intolerance with unknown etiology, increased adiposity 15-50%

- insulin deficiency
- insulin resistance
- Decreased insulin sensitivity
- impaired insulin secretion
- Decreased beta-cell function
- Type 2 diabetes was more than 2-4 among women with an isochromosome Xq compared
- Type 1 diabetes 10-fold
- IGT

Treatment with GH may lead to lower adiposity and less IGT

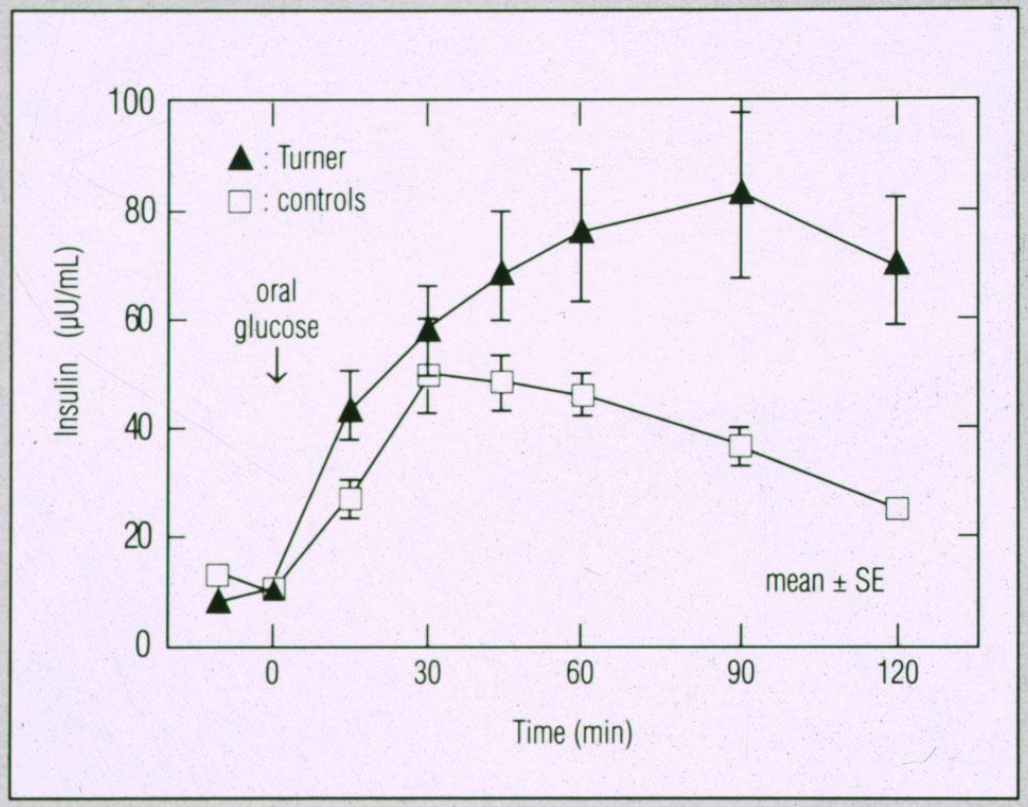
Metabolic disease

- Dyslipidemia
- Type 2 diabetes mellitus
- Obesity
- *Annual tests of fasting blood sugar and lipids are recommended.*

Metabolic disease

- Screen for hyperglycemia by measuring hemoglobin A1c, with or without fasting glucose,
- Annually beginning at 10 years of age.
- Consider OGTT if HbA1c is elevated
- Screen for dyslipidemia by measuring a lipid panel annually if at least one cardiovascular disease risk factor is present

Insulin Resistance



Insulin release following stimulation by oral glucose in24 adult TS women (filled triangles) and 10 control women (open squares). In the Turner group, insulin release is significantly elevated ($P < 0.006$) and the secretory response delayed peak concentration reached after 90 minutes versus 30 minutes in controls.

Reprinted with permission from Holl RW, et al. *Eur J Pediatr* 1994;153:11-6.

Relative risk for:

Type II diabetes:

4.4

Dyslipidemia

- lipid screening around 10 years of age
- Annually if at least cardiovascular risk factor
- Hypercholesterolemia 30%
- Hypertriglyceridemia. 32.5%
- LDL-C>95th 15%
- HDL-C <5th 7.5%

- **Treatment could follow the recommendations for the general population**.

Cognitive function and learning disabilities

Screening

- At start of primary school age 5 years
- At entry to high school or equivalent age 15 years
- Annual developmental and behavioral screenings

Neuropsychiatric disorders

- Intelligence is usually **normal**
- About 10% of girls with TS particularly those with a small ring X may present with intellectual disability

Role of Ovarian failure for neuropsychological problem

Ovarian failure contributes to the neuropsychological profile of tuner syndrom

- Major depression 5%
- Anxiety disorder 8%.
- Shyness
- Social anxiety
- Need of dependence

Neuropsychiatric disorders

- Lower self-esteem
- Social isolation
- Anxiety
- Autism spectrum disorder

Neuropsychiatric disorders

Challenges

- Task handling وظیفه شناسی
- working memory حافظه فعال
- processing speed سرعت پردازش
- visual–spatial perception (difficulty in driving)
- Mathematics
- Hyperactivity disorder

Neuropsychiatric disorders

- Reading comprehension درک مطلب
- Facial expression recognition تشخیص حالت چهره
- Motor coordination
- Motor learning یادگیری حرکتی
- Autism spectrum disorders
- Nonverbal problem-solving tasks such as mathematics
- کارهای غیرکلامی برای حل مسئله
- Attention deficit

Cognitive and academic performance

- Defects in social cognition شناخت اجتماعی
- psychomotor deficits (clumsiness)

Role of estrogen therapy on cognitive function

- Some benefits on cognitive function
- low doses of ethinyl estradiol improved verbal and nonverbal memory
- improved nonverbal processing speed and motor function
- Decrease dementia

Effect of Androgen

Androgen replacement might have an effect on

- Cognitive function
- working memory حافظه فعال
- Arithmetic learning یادگیری علم حساب

Evaluation

- **Yearly evaluation**
  - Height, weight
  - Heart exmination
  - BP
  - Creatinine, blood urea nitrogen,
  - LFT
  - TFT
  - Lipid profile
  - FBS
  - Hemoglobin A1c

Gonadoblastoma risk

Screen for Y chromosome mosaicism recommended in

- Any Turner syndrome patient
- Who develops virilization
- Streak gonads do not need to be explored or removed in patients **without Y chromosome mosaicism**
- Frequency of Turner syndrome and Y chromosome material was **7.9% by age 25 years**
- Risks for other cancers are probably similar to or minimally increased compared with the general population

Gonadoblastoma risk

- The rate of gonadoblastoma among TS patients with Y chromosome sequences that were detected by PCR or FISH varied from 4 to 60%

Cancer surveillance

- Overall risk of cancer is possibly slightly raised with standardized incidence ratios between 0.9 and 1.34
- incidence of breast cancer is reduced 30%
- Risk of melanoma increased **twofold and threefold**
- Risk of CNS malignancy increased **4.3- and 6.6-fold**
- Meningioma increased 12 -14%.

Malignancy risk

A possible increased risk for

- Meningioma or colon cancer, bladder, and uterine cancer
- long-term estrogen use in women with Turner syndrome is not associated with an increased risk of breast cancer

Survival and Death Causes in TS

- TS women have a decreased life span
- Mean survival age is 69 years
- 50% died from cardiovascular diseases
- ~20% died from malignancies
- Diabetes was observed in 25%

Gravholt CH et al J clin Epidemiol 1998; 51: 147-158

Mortality

- Overall mortality rates increased approximately threefold when compared with the general population
- Estrogen deficiency is also thought to play a role.
- Pneumonia, diabetes, epilepsy, liver disease, and kidney disease,CVD
- Which accounted for a 3- to 11-fold increase in mortality.

Evaluation

Every 3-5 years

- ✓ Celiac s disease
- ✓ Audiogram
- ✓ Cardiac evaluation
- ✓ BMD

Evaluation

Age 10 years and older

- Fasting blood glucose
- A1C
- ALT,AST
- serum creatinine
- Urinalysis
- Lipid profile

Indications for chromosome analysis to diagnose Turner syndrome

Indications for chromosome analysis to diagnose Turner syndrome

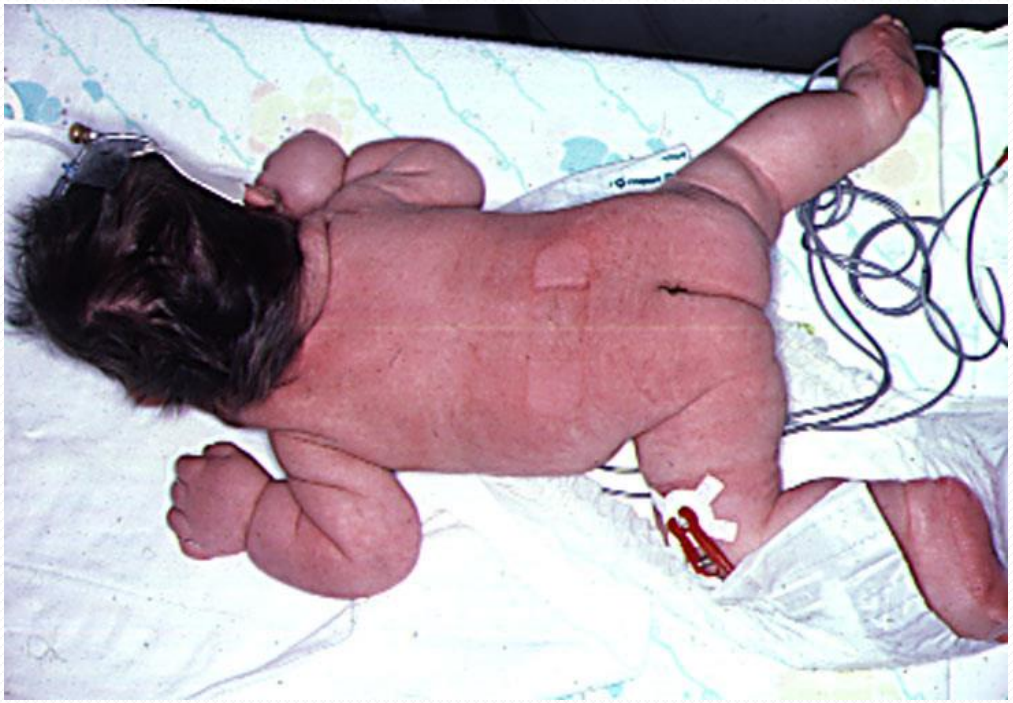
As the only clinical feature:
▪ Fetal cystic hygroma, or hydrops, especially when severe
▪ Idiopathic short stature
▪ Obstructive left-sided congenital heart defect*
▪ Unexplained delayed puberty/menarche
▪ Couple with infertility
▪ Characteristic facial features in a female ¶
At least two of the following:
▪ Renal anomaly (horseshoe, absence, or hypoplasia)
▪ Madelung deformity
▪ Neuropsychologic problems, and/or psychiatric issues
▪ Multiple typical or melanocytic nevi
▪ Dysplastic or hyperconvex nails
▪ Other congenital heart defects Δ
▪ Hearing impairment <40 years of age together with short stature

Prenatal diagnosis

- Increased nuchal translucency on ultrasound, but may be observed in several trisomic syndromes.
- presence of a cystic hygroma.
- Coarctation of the aorta
- left-sided cardiac defects
- Brachycephaly
- Renal anomalies
- polyhydramnios
- Oligohydramnios
- Growth retardation
- increased nuchal translucency

Postnatal diagnosis

- Edema of the hands or feet
- Hypoplastic left heart;
- low hairline
- low set ears
- Small mandible



Up to date 2012

Newborn period

- Congenital lymphedema of the hands and feet
- webbed neck
- Nail dysplasia
- Narrow and high-arched palate
- Short fourth metacarpal.

Infants and children

- unexplained growth failure
- Lymphedema
- webbed neck
- left-sided cardiac defects
- High-arched palate
- Short fourth metacarpal
- Strabismus
- Recurrent otitis media
- Nail dysplasia
- learning difficulties

Adolescence

- Fail to start or complete breast development
- Secondary amenorrhea, especially if short stature and/or other features suspicious of Turner syndrome are present

Recommendations for screening in Turner syndrome (excluding cardiac and neuropsychological screening recommendations)

	At diagnosis	After diagnosis (childhood)	After diagnosis (adults)
Weight/BMI	Yes	Every visit	Every visit
Blood pressure	Yes	Every visit	Every visit
Thyroid function tests (TSH and T4 or free T4)	Yes	Annually, beginning around 4 years of age	Annually
Lipids			Annually if at least 1 cardiovascular risk factor* or regional recommendation
Liver enzymes (ALT, AST, GGTP, and alkaline phosphatase)		Annually after 10 years of age	Annually
HbA1c with or without fasting plasma glucose		Annually after 10 years of age	Annually
25-hydroxyvitamin D		Every 2 to 3 years after 9 to 11 years of age	Every 3 to 5 years
Celiac screen		Starting at 2 years; thereafter, every 2 years	With suggestive symptoms
Renal ultrasound	Yes		
Audiometric evaluation	Yes ¶	Every 3 years	Every 5 years
Ophthalmologic examination	Yes Δ	Every 3 years	
Dental evaluation	Yes, if no previous care has been established		
Clinical investigation for congenital hip dysplasia	Yes, in newborns		
Skin examination	Yes	Annually	Annually
Bone mineral density			Every 5 years and when discontinuing estrogen
Skeletal assessment		Spine radiographs at 5 to 6 years and at 12 to 14 years of age	

TABLE 2. Health care checklist for individuals with TS[a]

Problems	Screening test/referral	Timing of Tests			
		At Dx	Q visit	Q year	Other
Hip dislocation	Physical examination (including height, weight, BP, and calculation of BMI)	X	In infancy		
Feeding problems		X	In Infancy		
Strabismus		X	4 months to 5 yr		
Otitis media		X	All childhood		
Growth failure		X	All childhood		
Pubertal delay		X	Adolescence		
Scoliosis/kyphosis		X	While growing		
Dysplastic nevi		X	School-age on		
Lymphedema		X	Lifelong		
Hypertension		X	Lifelong		
Needs information/support	Refer to TSS, other support groups	X			
Structural renal abnormalities	Renal ultrasound	X			
Cardiac abnormality[b]	Examination by cardiologist; EKG; MRI/echo	X			Q 5–10 yr
Conductive and SNHL	Formal audiology exam	X			Q 1–3 yr
Gonadal dysfunction	FSH, LH	X			At ages 0.5–3 and 10–12 yr
Strabismus and hyperopia	Formal eye examination	X			At 1–1.5 yr
Celiac disease	Serum IgA, TTG IgA Ab	X			Q 2–5 yr (begin about age 4 yr)
Autoimmune thyroid disease	T_4, TSH	X		Begin about age 4 yr	
Developmental, educational, social problems	Developmental, educational, and/or psychosocial examination	X			Before school entry
Palatal/occlusive abnormalities	Orthodontic evaluation				At age 7 yr
Sexuality; school and/or work plans	Counseling			Begin about age 10 yr	
Renal and liver dysfunction	Cr, BUN, LFTs, CBC	X		Begin about age 15 yr	
Metabolic dysfunction	Fasting BG and lipids			Begin about age 15 yr	
Low BMD	DEXA scan				At about age 18 yr
GH action	IGF-I/IGFBP-3			During GH tx	

Approach to the Patient with Turner Syndrome J Clin Endocrinol Metab, April 2010, 95(4):1487–1495

Thank you for your attention