## History of Turner and Noonan Syndromes

<table>
<thead>
<tr>
<th>Noonan Syndrome</th>
<th>Turner Syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Web neck</td>
<td>Web neck</td>
</tr>
<tr>
<td>Low-set ears</td>
<td>Low-set ears</td>
</tr>
<tr>
<td>Pedal edema +</td>
<td>Pedal edema ++</td>
</tr>
<tr>
<td>Wide-spaced nipples</td>
<td>Wide-spaced nipples</td>
</tr>
<tr>
<td>Short stature +</td>
<td>Short stature ++</td>
</tr>
<tr>
<td>CHD (right sided)</td>
<td>CHD (left sided)</td>
</tr>
<tr>
<td>Both sexes, nl chromosomes</td>
<td>Females only: 45,X</td>
</tr>
<tr>
<td>15% familial (dominant)</td>
<td>Not inherited</td>
</tr>
<tr>
<td>Subnormal intelligence</td>
<td>Normal intelligence</td>
</tr>
<tr>
<td>Normal fertility</td>
<td>1° amenorrhea</td>
</tr>
</tbody>
</table>
Noonan Syndrome

- Webbed neck, neonatal lymphedema
- Pulmonary valve stenosis
- Wide spaced nipples, pectus
- Low set ears, downslanted eyelids with ptosis
- Learning delay
- Etiology: RAS-MAPK signal transduction path
  - PTPN11 (50% have mutations). Other genes include: KRAS, SOS1, RAF1, SHOC2, NRAS and others
Individuals with the Noonan syndrome
Noonan Syndrome and Related Conditions

- Related genes with proteins involved in common signaling pathway
- May be grouped as the “Noonan-phenotype” conditions
- Syndromes:
  - Noonan
  - Cutaneous-Cardio-Facial (CFC)
  - Costello
  - LEOPARD
Example of some of the genes that can cause the Noonan phenotype
- **Noonan Phenotype**
  - Craniofacial
  - Cardiovascular
  - Developmental

- **Costello**
  - Coarse face
  - relative/absolute macrocephaly
  - Tumor predisposition

- **LEOPARD**
  - Lentigenes, nevi
  - Hearing loss
  - Leftward QRS axis

- **Cardio-Facial-Cutaneous (CFC)**
  - Sparse, wooly hair
  - Hyperkeratotic, scaly skin

- **Costello**
  - Coarse face
  - relative/absolute macrocephaly
  - Tumor predisposition

- **LEOPARD**
  - Lentigenes, nevi
  - Hearing loss
  - Leftward QRS axis

- **CFCsyndrome.org**

- **Noonan Phenotype Core Features**
  - Craniofacial
  - Cardiovascular
  - Developmental
LEOPARD Syndrome

Lentigines
EKG abnormalities
Ocular hypertelorism
Pulmonic stenosis
Abnormalities of genitalia
Retardation of growth
Deafness

Left axis deviation