

Caring for Persons with Noonan Syndrome

Noonan syndrome is characterized by mildly distinct facial features, short stature, heart defects, bleeding problems, and skeletal malformations. Occurs in ~1 in 1,000 to 2,500 as most common RAS-opathy of cell signaling pathway which controls crucial cell functions like growth, development, and death. Cases distributed 50% males, 50% females with autosomal dominant inheritance. Diagnoses may be missed until adulthood.

System	Information	Follow-up
Genetics	▪ Mutations can be multi genes, significant proportion de novo ▪ 70% mutation identified, variants in RAS-MAPK pathway genes – PTPN 11 50%, SOS1 10%, KRAS <5%, NRAS, SHOC2, RAF1, BRAF, others	▪ Genetic referral ▪ Gene variant may stratify risk of co-morbidities
Cognition	▪ Wide range, intellectual disability 15-35%, usually mild, mean full scale IQ 85, higher in SOS1 ▪ Articulation, attention, visual-spatial, social issues	▪ Developmental screening ▪ Neuropsych. testing & supports as indicated ▪ Speech therapy common
Cardiovascular	▪ Abn. pulmonic valve 20-50%, Ao coarct 9%, ASD, VSD ▪ EKG atypical 50% ▪ Hypertrophic cardiomyopathy 20-30%, esp RAF1, RIT1, LZTR1 ▪ Lymphedema 20%, lymphangiectasia, chylothorax	▪ Cardiac echo/EKG at dx, annual until 3 yo, age 5-10 and periodically ▪ Specialized lymphedema care
Dental	▪ Dental malocclusion 50%, high palate 50-100%, small lower jaw 40%	▪ Routine dental care, referral as needed
Endocrine	▪ Short stature 70-80%, ht. & wt. nl at birth, slowed growth, pubertal delay ~ 2 yrs ▪ Low growth hormone (esp. SHOC2) ▪ Hypothyroid 5% ▪ Male lower fertility, females fertile, 3:1 transmit	▪ Monitor growth curves on Noonan graphs ▪ Evaluate GH by variant, other risks ▪ Screen thyroid q3-5yr in older child, adult ▪ Genetic counseling prior to childbearing.
ENT	▪ Hearing loss 15-40%	▪ Hearing screen annual
Face	▪ Deep philtrum groove, hypertelorism, pale blue or blue-green eyes, low-set backward-rotated ears, short neck, low hairline	▪ Features vary with age
GI	▪ Poor feeding as infants 75%, GE reflux, rarer malrotation ▪ Hepato- and/or splenomegaly 26-50%, younger age	▪ Feeding therapy as needed
GU	▪ Cryptorchidism 80% ▪ Urinary abn. 10%, solitary, pyelo-ureteral stenosis, hydronephrosis, duplicating system	▪ Orchiopexy as indicated ▪ Renal U/S at dx
Hematology	▪ Coagulation defects 30%, severe 3% ▪ Varied - factors VII, XI (25%), XII, platelet – low/ abn fnc, abn bleeding time	▪ Baseline coagulation tests aged 5+, or for earlier major surgery
MSK	▪ Pectus carinatum superiorly, pectus excavatum inferiorly 90%, cubitus valgum >50%, clubfoot 5% ▪ Hyperextensible 50%, scoliosis 15%	▪ Monitor scoliosis, can accelerate with GH Rx
Neurology	▪ Early motor delay, hypotonia ▪ Seizures 13%, craniosynostosis, hydrocephalus, Chiari malformation	▪ Lower threshold for imaging for sx, eg. headache, etc.
Oncology	▪ Higher oncogenic risk - PTPN11 – 3.5x, KRAS ▪ Increase childhood leukemia 8x, neuroblastoma, glioma, rhabdomyosarcoma	▪ No routine screening ▪ Screen for sx. or gene variant
Skin	▪ Nevi, cafe au lait, lentigines ▪ Keratosis pilaris, ulerythema, loss of eyebrows	▪ Moisturize, keratolytics
Vision	▪ Strabismus 50-60%, refractive error 60-70%	▪ Ophthal at dx, follow up at least q 2 yr

References: Stagi S, et al. Multidisciplinary Treatment of Patients with Noonan Syndrome: Consensus. *JAMA Network Open*. 2025.
 DYSCERNE Noonan Syn Guideline Dev Grp. Management of Noonan Syndrome: A Clinical Guideline, 2010.

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