

CLINICAL FEATURES KNOWN TO BE ASSOCIATED WITH VELO-CARDIO-FACIAL SYNDROME

The list below has been compiled based on a review of thousands of cases of VCFS plus a review of the medical literature reporting findings in the syndrome. Each finding is followed by a letter that indicates how common each finding is in the syndrome: **VH** represents "Very High Frequency" meaning that the finding occurs in at least 60% of cases; **H** represents "High Frequency" meaning that the finding is a feature in 30% to 60% of cases; **M** represents "Moderate Frequency" meaning the finding occurs in approximately 10% to 30% of cases; **L** represents "Low Frequency" meaning it is a feature of the syndrome, but occurs in less than 10% of cases; and **R** represents "Rare" in which case the finding has been reported in a very small number of cases and this may mean that the finding is not specifically caused by the 22q11.2 microdeletion that causes VCFS. These findings have been reported in the book *Velo-Cardio-Facial Syndrome, Volume I* (Plural Publishing), Robert J. Shprintzen and Karen Golding-Kushner authors, with only minor variations in the listing. The book provides an in depth explanation of each of the findings, including illustrations and videos illustrating them. Copies of this list are available on the web site of the Virtual Center for Velo-Cardio-Facial Syndrome at www.vcfscenter.com.

Craniofacial anomalies

1. Palate anomalies, including overt cleft palate, submucous cleft palate, occult submucous cleft palate, deficient muscle, and asymmetric palate **VH**
2. Asymmetric pharynx **VH**
3. Platybasia (flat skull base) **H**
4. Retrognathia (retruded lower jaw) **M**
5. Asymmetric crying facies (in infancy) **H**
6. Functional facial asymmetry (throughout life) **H**
7. Structural facial asymmetry **M**
8. Straight facial profile **H**
9. Hypotonic face **VH**
10. Vertical maxillary excess **H**
11. Small primary teeth **H**
12. Enamel hypoplasia **H**
13. Downturn oral commissures **H**
14. Microstomia **M**
15. Microcephaly **M**
16. Small posterior cranial fossa **M**
17. Cleft lip **L**

Ears and hearing

18. Over folded helices **VH**
19. Attached lobules **H**
20. Protuberant cup shaped ears **H**
21. Small ears **VH**
22. Mildly asymmetric ears **M**
23. Frequent otitis media **VH**
24. Mild conductive hearing loss (often transient) **H**
25. Sensorineural hearing loss **M**
26. Ear tags or pits **L**
27. Narrow external ear canals **H**

Eye findings

28. Tortuous retinal vessels **VH**
29. Suborbital congestion (“allergic shiners”) **VH**
30. Strabismus **M**
31. Narrow palpebral fissures **H**
32. Hooded or puffy upper eyelids **VH**
33. Posterior embryotoxon **M**
34. Small optic disk **M**
35. Prominent corneal nerves **M**
36. Cataracts **L**
37. Iris nodules **M**
38. Iris coloboma (uncommon) **M**
39. Retinal coloboma **M**
40. Small eyes **M**
41. Mild orbital hypertelorism **M**
42. Mild vertical dystopia **M**

Cardiovascular findings*

43. Ventricular septal defect (VSD) **H**
44. Atrial septal defect (ASD) **H**
45. Pulmonic atresia or stenosis **H**
46. Tetralogy of Fallot (TOF) **H**
47. Right-sided aortic arch **H**
48. Vascular ring **M**
49. Patent ductus arteriosus (PDA) **H**
50. Interrupted aortic arch type B **M**
51. Coarctation of the aorta **M**
52. Double aortic arch **M**
53. Aortic valve anomalies **M**
54. Aberrant subclavian arteries **H**
55. Truncus arteriosus **M**
56. Anomalous origin of the carotid artery **M**
57. Transposition of the great vessels **L**
58. Tricuspid atresia **L**

* Although none of the cardiac anomalies are shown to be **VH**, congenital heart anomalies in general should be listed as **VH** because nearly 70% of infants with VCFS have some type of structural heart or major outflow blood vessel abnormality.

Vascular anomalies

59. Medially displaced and ectopic internal carotid arteries **H**
60. Tortuous or kinked internal carotid arteries **H**
61. Jugular vein anomalies **M**
62. Absence of the internal carotid artery and unilaterally **M**
63. Tortuous or kinked vertebral arteries **VH**
64. Low bifurcation of the common carotid **H**
65. Raynaud's phenomenon **H**
66. Small veins **VH**
67. Circle of Willis anomalies **H**

Brain and central nervous system anomalies

68. Reduced total brain volume **VH**
69. Variations in size of various brain segments, small cerebellar vermis, and cerebellar hypoplasia **VH**
70. Periventricular cysts **H**
71. White matter hyperintensities **H**
72. Generalized hypotonia **VH**
73. Cerebellar ataxia **L**
74. Seizures **H**
75. Strokes **L**
76. Meningomyelocele **L**
77. Developmental delay **VH**
78. Enlarged Sylvian fissure **L**
79. Cavum septum pellucidum **H**
80. Pachygyria **M**
81. Polymicrogyria **M**
82. Cortical dysgenesis or dysplasia **L**
83. Arnold-Chiari anomaly **L**

Pharyngeal, laryngeal, and airway anomalies

84. Upper airway obstruction in infancy **H**
85. Absent or small adenoids **H**
86. Large palatine tonsils **H**
87. Large pharyngeal airway **VH**
88. Laryngomalacia **H**
89. Tracheo-bronchomalacia (compression by aberrant blood vessels) **H**
90. Laryngeal web **M**
91. Arytenoid/corniculate hyperplasia **H**
92. Pharyngeal hypotonia **VH**
93. Thin pharyngeal muscle **VH**
94. Asymmetric pharyngeal movement **H**
95. Asymmetric pharyngeal structure **H**
96. Asymmetric laryngeal structure **H**
97. Unilateral vocal fold paresis **H**

- 98. Unilateral or bilateral vocal fold paralysis **L**
- 99. Reactive airway disease (asthma) **M**

Abdominal and visceral anomalies

- 100. Hypoplastic or absent kidney **M**
- 101. Cystic kidneys **L**
- 102. Inguinal hernia **M**
- 103. Umbilical hernia **H**
- 104. Diastases recti **H**
- 105. Diaphragmatic hernia **L**
- 106. Malrotation of bowel **L**
- 107. Hepatoblastoma and other tumors **R**

Limb anomalies

- 108. Small hands and feet **H**
- 109. Tapered digits **VH**
- 110. Short fingernails **VH**
- 111. Rough red scaly skin on the hands and feet **H**
- 112. Contractures **L**
- 113. Triphalangeal thumbs **L**
- 114. Polydactyly **L**
- 115. Mild soft tissue syndactyly **L**

Problems in infancy

- 116. Feeding difficulties **VH**
- 117. Failure to thrive **H**
- 118. Chronic constipation **VH**
- 119. Gastroesophageal reflux **H**
- 120. Nasal regurgitation **VH**
- 121. Irritability **H**
- 122. Poor temperature regulation **M**
- 123. Diabetes insipidus **L**
- 124. Slow gastric emptying **H**

Genitourinary and rectal anomalies

- 125. Hypospadias **M**
- 126. Cryptorchidism **M**
- 127. Vesicoureteral reflux **M**
- 128. Hydrocele **M**
- 129. Anteriorly displaced anus **M**
- 130. Imperforate anus **L**

Skeletal, muscle, spinal, an orthopedic anomalies

- 131. Scoliosis **H**
- 132. Vertebral anomalies **H**
- 133. Spina bifida occulta **M**

- 134. Syrxinx **L**
- 135. Tethered cord **L**
- 136. Osteopenia **H**
- 137. Sprengel anomaly **H**
- 138. Talipes equinovarus **M**
- 139. Valgus anomaly **M**
- 140. Hypoplastic skeletal muscles **VH**
- 141. Hyperextensible or lax joints **VH**
- 142. Joint dislocations **L**
- 143. Flat foot arches **VH**
- 144. Chronic leg pains **VH**
- 145. Extra ribs **L**
- 146. Rib fusions **L**
- 147. Cervical spine anomalies including fusions **M**

Endocrine problems

- 148. Hypocalcemia **H**
- 149. Hypoparathyroidism **M**
- 150. Hypothyroidism **M**
- 151. Autoimmune thyroiditis (Hashimoto's syndrome) **M**
- 152. Hypoglycemia **L**
- 153. Altered growth velocity (see growth charts on web site www.vcfscenter.com) **VH**
- 154. Small pituitary gland **L**

Immune disorders

- 155. Immune deficiency or immune disorder **H**
- 156. Absent or small thymus **H**
- 157. Abnormal placement of the thymus **H**
- 158. Chronic upper and/or lower respiratory illness in infancy **H**

Speech and language disorders

- 159. Velopharyngeal insufficiency **VH**
- 160. Severe hypernasality **VH**
- 161. High-pitched voice **H**
- 162. Hoarseness **H**
- 163. Language impairment **VH**
- 164. Severe articulation impairment **VH**

Cognitive, learning, and attentional disorders

- 165. Learning disabilities **VH**
- 166. Concrete thinking, difficulty with abstraction and problem-solving **VH**
- 167. Executive functioning impairment **VH**
- 168. Low IQ (below 70, cognitive impairment) **M**
- 169. Deterioration in IQ scores in adolescence **M**
- 170. Attention deficit hyperactivity disorder (ADD/ADHD) **H**

- 171. Autism spectrum disorder (ASD) **L**
- 172. Working memory disorder **H**
- 173. Auditory processing disorder **H**

Psychiatric disorders

- 174. Psychosis (all subtypes) **H**
- 175. Mood disorders **H**
- 176. Depression **H**
- 177. Impulsiveness **H**
- 178. Flat affect **H**
- 179. Social immaturity **VH**
- 180. Obsessive-compulsive disorder (OCD) **M**
- 181. Generalized anxiety disorder **VH**
- 182. Simple phobias **VH**
- 183. Severe startle response **H**
- 184. Separation anxiety **H**

Miscellaneous anomalies

- 185. Thrombocytopenia **VH**
- 186. Bernard-Soulier syndrome **L**
- 187. Juvenile rheumatoid arthritis **L**
- 188. Vasomotor instability **L**

Secondary sequences

- 189. Robin sequence **M**
- 190. DiGeorge sequence **M**
- 191. Potter sequence **Unkown, but has been reported**
- 192. Holoprosencephaly sequence **Unknown, but has been reported**