**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](http://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. Syrinx \textbf{L}
135. Tethered cord \textbf{L}
136. Osteopenia \textbf{H}
137. Sprengel anomaly \textbf{H}
138. Talipes equinovarus \textbf{M}
139. Valgus anomaly \textbf{M}
140. Hypoplastic skeletal muscles \textbf{VH}
141. Hyperextensible or lax joints \textbf{VH}
142. Joint dislocations \textbf{L}
143. Flat foot arches \textbf{VH}
144. Chronic leg pains \textbf{VH}
145. Extra ribs \textbf{L}
146. Rib fusions \textbf{L}
147. Cervical spine anomalies including fusions \textbf{M}

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

\textbf{Immune disorders}
155. Immune deficiency or immune disorder \textbf{H}
156. Absent or small thymus \textbf{H}
157. Abnormal placement of the thymus \textbf{H}
158. Chronic upper and/or lower respiratory illness in infancy \textbf{H}

\textbf{Speech and language disorders}
159. Velopharyngeal insufficiency \textbf{VH}
160. Severe hypernasality \textbf{VH}
161. High-pitched voice \textbf{H}
162. Hoarseness \textbf{H}
163. Language impairment \textbf{VH}
164. Severe articulation impairment \textbf{VH}

\textbf{Cognitive, learning, and attentional disorders}
165. Learning disabilities \textbf{VH}
166. Concrete thinking, difficulty with abstraction and problem-solving \textbf{VH}
167. Executive functioning impairment \textbf{VH}
168. Low IQ (below 70, cognitive impairment) \textbf{M}
169. Deterioration in IQ scores in adolescence \textbf{M}
170. Attention deficit hyperactivity disorder (ADD/ADHD) \textbf{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 Unknown, but has been reported
192. Holoprosencephaly sequence Unknown, but has been reported