Wolf-Hirschhorn syndrome (WHS) is an extremely rare chromosomal disorder caused by a missing piece (partial deletion or monosomy) of the short arm of chromosome 4. Major symptoms may include extremely wide-set eyes (ocular hypertelorism) with a broad or beaked nose, a small head (microcephaly), low-set malformed ears, growth deficiency, heart (cardiac) defects, intellectual disability, and seizures. The symptoms of this syndrome vary from person to person based the size and location of the missing piece of chromosome 4. WHS is an extremely rare disorder. Studies undertaken about 25 years ago suggested that the disorder occurred in approximately 1 in about 50,000 live births with a female to male ratio of 2:1. More recent studies suggest that the frequency of the disorder is underestimated because of misdiagnosis. A diagnosis of WHS may be suggested by the characteristic facial appearance, growth failure, developmental delays, and seizures. The diagnosis is confirmed by detection of a deletion of the Wolf-Hirschhorn syndrome critical region (WHSCR) by cytogenetic (chromosome) analysis. Conventional cytogenetic analysis detects less than half of the deletions that cause WHS. Fluorescence in situ hybridization (FISH) using a WHSCR probe has much better detection rate than standard karyotype and will detect most patients. However, the diagnostic test of choice is chromosomal microarray, which detects essentially all deletions of the WHSCR and defines the size of the deletion. Chromosomal microarray can also find other chromosome rearrangements, such as extra pieces of other chromosomes that are seen in many patients with WHS.