

amniotic fluid, usually at 16 weeks of gestation. Cells can be collected and submitted for karyotype analyses, FISH, and mutational analysis of selected genes ([Table 466-4](#)). The main indications for amniocentesis include advanced maternal age (>35 years), presence of an abnormality of the fetus on ultrasound examination, an abnormal serum “quad” test (α fetoprotein, β human chorionic gonadotropin, inhibin-A, and unconjugated estriol), a family history of chromosomal abnormalities, or a Mendelian disorder amenable to genetic testing. Prenatal diagnosis can also be performed by *chorionic villus sampling* (CVS), in which a small amount of the chorion is removed by a transcervical or transabdominal biopsy. Chromosomes and DNA obtained from these cells can be submitted for cytogenetic and mutational analyses. CVS can be performed earlier in gestation (weeks 9–12) than amniocentesis, an aspect that may be of relevance when termination of pregnancy is a consideration. Later in pregnancy, beginning at ~18 weeks of gestation, percutaneous umbilical blood sampling (PUBS; cordocentesis) permits collection of fetal blood for analysis. Prenatal cfDNA allows DNA analyses from the mother and fetus from a maternal blood sample to screen for certain chromosomal abnormalities and fetal sex. These approaches enable screening for clinically relevant and deleterious alleles inherited from the parents, as well as for de novo germline mutations, and they have the potential to identify genetic disorders in the prenatal setting.

In combination with in vitro fertilization (IVF) techniques, it is possible to perform genetic diagnoses in a single cell removed from the four- to eight-cell embryo or to analyze the first polar body from an oocyte. Preconceptual diagnosis thereby avoids therapeutic abortions but is costly and labor intensive. It should be emphasized that excluding a specific disorder by any of these approaches is never equivalent to the assurance of having a normal child. Postnatal indications for cytogenetic analyses in infants or children include multiple congenital anomalies, suspicion of a known cytogenetic syndrome, developmental delay, dysmorphic features, autism, short stature, and disorders of sexual development, among others ([Table 466-4](#)).