

VACTERL [vertebral defects, anal atresia, cardiac defect, tracheoesophageal fistula, and renal and limb defects] association). When a single anomaly leads to a cascade of additional anomalies, the pattern of defects is referred to as a **sequence**. Pierre Robin sequence begins with the abnormal development of the mandible, resulting in abnormal placement of the tongue during development. The normal developmental process for the palate is prevented because the tongue obstructs the migration of the palatal shelves toward the midline, and a cleft palate remains. Consequently, infants born with Pierre Robin sequence have a recessed mandible and an abnormally placed tongue and are at risk for obstructive apnea. NTDs, cleft lip and palate, deafness, congenital heart defects, and cognitive impairment are examples of congenital malformations that can occur in isolation or as part of a syndrome, association, or sequence and can have different causes, such as single-gene or chromosome abnormalities, prenatal exposures, or multifactorial causes.

Disorders of the Intrauterine Environment

The intrauterine environment can have a profound and permanent effect on developing fetuses with or without chromosome or single-gene abnormalities. Intrauterine growth restriction, for example, can occur with many genetic syndromes, such as Down, Russell-Silver, Prader-Willi, and Turner syndromes ([Rimoin, Pyeritz, and Korf, 2013](#)), or it can be caused by nongenetic factors, such as maternal alcohol ingestion. Placental abnormalities are increasingly being found to be the etiologic factor in neurodevelopmental disorders (e.g., cerebral palsy and cognitive impairment) that were previously attributed to asphyxia during delivery ([McIntyre, Taitz, Keogh, et al, 2013](#)).

Teratogens, agents that cause birth defects when present in the prenatal environment, account for the majority of adverse intrauterine effects not attributable to genetic factors. Types of teratogens include drugs (phenytoin [Dilantin], warfarin [Coumadin], isotretinoin [Accutane]), chemicals (ethyl alcohol, cocaine, lead), infectious agents (rubella, cytomegalovirus), physical agents (maternal ionizing radiation, hyperthermia), and metabolic agents (maternal PKU). Many of these teratogenic exposures and the resulting effects are completely preventable. For example,