PDE is considered to be a rare disease, and only a few epidemiologic studies have been published. For example, a study from the United Kingdom and the Republic of Ireland reported a point prevalence of 1:687,000 for definite and probable cases of PDE, while a survey conducted in the Netherlands reported an estimated birth incidence of 1:396,000. PDE is quite likely under-diagnosed and a higher birth incidence is suspected. This notion is supported by a study from a German center where pyridoxine administration is part of a standard treatment protocol for neonatal seizures and a birth incidence of probable cases of 1:20,000 was reported. While pyridoxine-dependency should be considered when evaluating possible causes of intractable seizures in young patients, other more common causes must be ruled out, including a variety of brain malformation syndromes, serious acquired disorders of the central nevous system (such as hemorrhagic conditions and infections), and other inborn errors of metabolism. A closely related neonatal metabolic epilepsy is PNPO deficiency. Babies with this genetic disorder also have intractable seizures, but the seizures in these patients respond to pyridoxal-5'-phosphate (P5P, the biologically active form of pyridoxine) but in most instances do not respond to pyridoxine. Other genetic pyridoxine-dependency states have been described (e.g. pyridoxine-dependent anemia and pyridoxine-dependent forms of homocystinuria, xanthurenic aciduria and cystathioninuria), but these conditions are not genetically related to PDE, and intractable seizures are not a feature of these other disorders.