Epidermal nevus syndromes (ENSs) are a group of rare complex disorders characterized by the presence of skin lesions known as epidermal nevi associated with additional extra-cutaneous abnormalities, most often affecting the brain, eye and skeletal systems. Epidermal nevi are overgrowths of structures and tissue of the epidermis, the outermost layer of the skin. The different types of epidermal nevi can vary in size, number, location, distribution and appearance. Neurological abnormalities that can be associated with ENSs can include seizures, cognitive impairment, developmental delays and paralysis of one side of the body (hemiparesis). Skeletal abnormalities can include abnormal curvature of the spine, malformation of the hip and abnormalities of the arms and legs (e.g., underdevelopment or absence or overgrowth of limbs). Ocular abnormalities may include cataracts, clouding (opacity) of the cornea or partial absence of tissue of the iris or retina (colobomas). Endocrine abnormalities such as vitamin D-resistant rickets have been associated with Schimmelpenning syndrome. The specific symptoms and severity of ENSs can vary greatly from one person to another. Most ENSs occur randomly for no apparent reason (sporadically), most likely due to a gene mutation that occurs after fertilization (postzygotic mutation) and is present in only some of the cells of the body (mosaic pattern). Epidermal nevi (including as an isolated finding) have been reported to occur in approximately 1 to 3 per 1,000 live births. The percentage of individuals with epidermal nevi who also have extra-cutaneous malformations is much lower but likewise unknown. The prevalence and incidence of individual ENSs is unknown. A diagnosis of an epidermal nevus syndrome is made based upon identification of characteristic symptoms, a detailed patient history and a thorough clinical evaluation. In some cases, a small sample of affected skin may be taken for microscopic study (biopsy). Additional tests may be required to detect the presence and extent of associated symptoms. Such tests include a skeletal survey, chest x-rays and specialized imaging techniques to evaluate the brain. Such imaging techniques may include computerized tomography (CT) scanning and magnetic resonance imaging (MRI). Whether a child with an epidermal nevus should undergo such imaging techniques is controversial. Some researchers believe that these tests should be avoided unless there are clinical signs of central nervous involvement. In three of the well-defined ENSs (type 2 segmental Cowden disease, García-Hafner-Happle syndrome, CHILD syndrome), molecular testing is now possible.