GM3 SYNTHASE DEFICIENCY

Marc E. Tischler, PhD:
University of Arizona

• glycosphingolipids, to which carbohydrates are attached, reside in cell membranes of nerve tissue

• three types of glycosphingolipids are:
  ✓ cerebroside – contain a single galactose or glucose sugar
  ✓ globoside – contain multiple sugars
  ✓ ganglioside –
    o contain multiple sugars and sialic acid
    o high concentration in ganglions of central nervous system especially nerve endings
    o letter code in name refers to number of sialic acids (e.g. M = mono [1]; D = di [2], etc)
    o number code in name refers to the specific sugar structure
    o GM3 = simplest with one sialic acid and two sugars attached
Figure 1. Gangliosides are glycosphingolipids produced mostly in ganglions especially at nerve endings and are involved in cell-signaling function. They are produced from ceramide, the simplest sphingolipid, to which are added in succession hexose sugars and sialic acid. GM3 is the simplest ganglioside with the inclusion of two sugars (i.e., glucose, galactose) and a single sialic acid. In this disease GM3 synthase is defective (X). The lack of synthesis of GM3, rather than the accumulation of lactosylceramide, may have the more significant role in terms of symptoms. This conclusion is based on GM3 being required for construction of the more complex gangliosides that have a major role in membrane and cell function.