Tay–Sachs disease (also known as GM2 gangliosidosis or hexosaminidase A deficiency) is a rare autosomal recessive genetic disorder. In its most common variant (known as infantile Tay–Sachs disease), it causes a progressive deterioration of nerve cells and of mental and physical abilities that begins around 7 months of age and usually results in death by the age of four. The disease occurs when harmful quantities of cell membrane components known as gangliosides accumulate in the brain's nerve cells, eventually leading to the premature death of the cells. A ganglioside is a form of sphingolipid, which makes Tay–Sachs disease a member of the sphingolipidoses. There is no known cure or treatment.

The disease is named after the British ophthalmologist Waren Tay, who in 1881 first described a symptomatic red spot on the retina of the eye; and after the American neurologist Bernard Sachs of Mount Sinai Hospital, New York, who described in 1887 the cellular changes of Tay–Sachs disease and noted an increased disease prevalence in Ashkenazi Jewish people.

Research in the late 20th century demonstrated that Tay–Sachs disease is caused by a genetic mutation in the HEXA gene on (human) chromosome 15. A large number of HEXA mutations have been discovered, and new ones are still being reported. These mutations reach significant frequencies in specific populations. French Canadians of southeastern Quebec have a carrier frequency similar to that seen in Ashkenazi Jews, but carry a different mutation. Cajuns of southern Louisiana carry the same mutation that is seen most commonly in Ashkenazi Jews. HEXA mutations are rare and are most seen in genetically isolated populations. Tay–Sachs can occur from the inheritance of either two similar, or two unrelated, causative mutations in the HEXA gene.

As an autosomal recessive disorder, two Tay–Sachs alleles are required for an individual to exhibit symptoms of the disease. Carriers of a single Tay–Sachs allele do not exhibit symptoms of the disease but appear to be protected to some extent against tuberculosis. This accounts for the persistence of the allele in certain populations in that it confers a selective advantage—in other words, being a heterozygote is advantageous.[1]

- **Infantile Tay–Sachs disease.** Infants with Tay–Sachs disease appear to develop normally for the first six months after birth. Then, as neurons become distended with gangliosides, a relentless deterioration of mental and physical abilities begins. The child may become blind, deaf, unable to swallow, atrophied, and paralytic. Death usually occurs before the age of four.[2]

- **Adult/Late-Onset Tay–Sachs disease.** A rare form of this disease, known as Adult-Onset or Late-Onset Tay–Sachs disease, usually has its first symptoms during the 30s or 40s. In contrast to the other forms, late-onset Tay–Sachs disease is usually not fatal as the effects can stop progressing. It is frequently misdiagnosed. It is characterized by unsteadiness of gait and progressive neurological deterioration. Symptoms of late-onset Tay–Sachs –
which typically begin to be seen in adolescence or early adulthood — include speech and swallowing difficulties, unsteadiness of gait, spasticity, cognitive decline, and psychiatric illness, particularly a schizophrenia-like psychosis. People with late-onset Tay–Sachs may become full-time wheelchair users in adulthood.