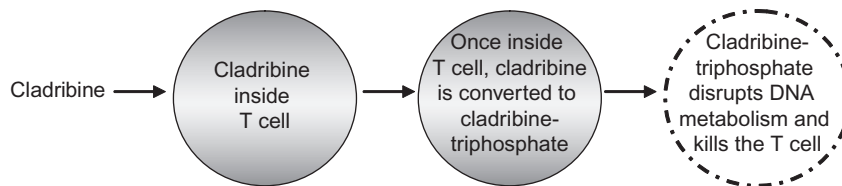


- Reduces activities of neutrophils. Interferon- β blocks production of toxic oxygen by neutrophils (30). Neutrophils are cells of the immune system that produce toxic oxygen, and have been found to contribute to the pathology of multiple sclerosis (31).
- Maintenance of the integrity of the blood–brain barrier (32). “Integrity of the blood–brain barrier” refers, in part, to the ability of the blood–brain barrier to serve as a wall against migrating immune cells.

d. Cladribine

Cladribine (2-chlorodeoxyadenosine) is a small molecule that is an analogue of deoxyadenosine. Clinical trials have demonstrated that cladribine is effective in treating multiple sclerosis (33,34). When administered, cladribine is taken up by cells, including lymphocytes, and is phosphorylated to produce cladribine-triphosphate. Cladribine-triphosphate is then incorporated into the chromosome of lymphocytes during the normal activities of cell division and DNA repair. But when cladribine is incorporated into the cell’s DNA, the result is DNA strand breaks, and cell death by apoptosis (35,36) as indicated in the following diagram.



³⁰ Huseby ES, Liggitt D, Brabb T, Schnabel B, Ohlén C, Goverman J. A pathogenic role for myelin-specific CD8(+) T cells in a model for multiple sclerosis. *J Exp Med.* 2001;194:669–676.

³¹ Sayed BA, Christy AL, Walker ME, Brown MA. Meningeal mast cells affect early T cell central nervous system infiltration and blood–brain barrier integrity through TNF: a role for neutrophil recruitment? *J Immunol.* 2010;184:6891–6900.

³² Sheremata WA, Jy W, Delgado S, Minagar A, McLarty J, Ahn Y. Interferon- β 1a reduces plasma CD31+ endothelial microparticles (CD31+ EMP) in multiple sclerosis. *J Neuroinflammation.* 2006;3:23–27.

³³ Giovannoni G, Comi G, Cook S, et al. A placebo-controlled trial of oral cladribine for relapsing multiple sclerosis. *New Engl J Med.* 2010;362:416–426.

³⁴ Barten LJ, Allington DR, Procacci KA, Rivey MP. New approaches in the management of multiple sclerosis. *Drug Des Devel Ther.* 2010;4:343–366.

³⁵ Szondy Z. The 2-chlorodeoxyadenosine-induced cell death signalling pathway in human thymocytes is different from that induced by 2-chloroadenosine. *Biochem J.* 1995;311:585–588.

³⁶ Van Den Neste E, Cardoen S, Husson B, et al. 2-Chloro-2'-deoxyadenosine inhibits DNA repair synthesis and potentiates UVC cytotoxicity in chronic lymphocytic leukemia B lymphocytes. *Leukemia.* 2002;16:36–43.