

Abstract

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Th1/Th2 balance: the hypothesis, its limitations, and implications for health and disease.

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BACKGROUND: One theory of immune regulation involves homeostasis between T-helper 1 (Th1) and T-helper 2 (Th2) activity. The Th1/Th2 hypothesis arose from 1986 research suggesting mouse T-helper cells expressed differing cytokine patterns. This hypothesis was adapted to human immunity, with Th1- and Th2-helper cells directing different immune response pathways. Th1 cells drive the type-1 pathway ("cellular immunity") to fight viruses and other intracellular pathogens, eliminate cancerous cells, and stimulate delayed-type hypersensitivity (DTH) skin reactions. Th2 cells drive the type-2 pathway ("humoral immunity") and up-regulate antibody production to fight extracellular organisms; type 2 dominance is credited with tolerance of xenografts and of the fetus during pregnancy.

DISCUSSION: Overactivation of either pattern can cause disease, and either pathway can down-regulate the other. But the hypothesis has major inconsistencies; human cytokine activities rarely fall into exclusive pro-Th1 or -Th2 patterns. The non-helper regulatory T cells, or the antigen-presenting cells (APC), likely influence immunity in a manner comparable to Th1 and Th2 cells. Many diseases previously classified as Th1 or Th2 dominant fail to meet the set criteria. Experimentally, Th1 polarization is readily transformed to Th2 dominance through depletion of intracellular glutathione, and vice versa. Mercury depletes glutathione and polarizes toward Th2 dominance. Several nutrients and hormones measurably influence Th1/Th2 balance, including plant sterols/sterolins, melatonin, probiotics, progesterone, and the minerals selenium and zinc. The long-chain omega-3 fatty acids EPA (eicosapentaenoic acid) and DHA (docosahexaenoic acid) significantly benefit diverse inflammatory and autoimmune conditions without any specific Th1/Th2 effect.

CONCLUSION: Th1/Th2-based immunotherapies, e.g., T-cell receptor (TCR) peptides and interleukin-4 (IL-4) injections, have produced mixed results to date.

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