VIII  Hygiene Hypothesis
A.  Review of human immune system
   1.  CD8\(^+\) cells
      a.  Develop into cytotoxic T lymphocytes (= CTLs)
      b.  Part of cell-mediated response
   2.  CD4\(^+\) cells differentiate into 2 types of helper T-cells
      a.  Th1 cells
         (1)  Part of cell-mediated response
         (2)  Bind to macrophages
            (a)  Phagocytose invaders
            (b)  Antigens of invaders on surface of macrophages
         (3)  Enhance phagocytic activity of macrophages
         (4)  Secret cytokines
            (a)  Attract more macrophages
            (b)  Kill bacteria and viruses
            (c)  Increase inflammation response
      b.  Th2 cells
         (1)  Part of the humoral response
         (2)  Bind to B-cells
         (3)  B-cells become plasma cells and produce antibodies
      c.  IgE
         (1)  Activates mast cells
         (2)  Associated with allergic response
      d.  Mast cells secrete chemicals
         (1)  Blood vessels near wound or mast cell
            (a)  Constrict
            (b)  Blood flow near a wound would decrease
         (2)  Blood vessels slightly further away from wound
            (a)  Dilate
            (b)  Increase blood, plasma, & white blood cells to
                 injured area
   B.  Biological Features of IgE
      1.  Associated with nematode infections
      2.  >99% pumped into the lumen of gut
   C.  Allergies
      1.  Rare in undeveloped countries
      2.  IgE & mast cells closely linked and play major role in producing
          immediate hypersensitivities known clinically as allergies
   D.  Helminth parasites and IgE responses
      1.  Helminths are parasitic worms
          a.  Nematodes
          b.  Trematodes
      2.  High Th2 response
3. Rapid Expulsion (=RE):
   a. Immune animals reject challenge nematodes within minutes of exposure
   b. Challenge nematodes: Pathogen given to experimental group
   c. Similar to hypersensitivity reaction

E. Mast cells and parasite rejection
   1. Evidence for . . .
      a. Mucosal mast cells degranulate following challenge infection
      b. Some inhibitors of hypersensitivity reaction reduce effectiveness of RE
   2. Conflicting evidence may be due to existence of more than one mechanism of involving mast cells

F. Parasites and allergy in human populations in undeveloped countries
   1. Nematode infections can approach 100%
      a. High levels of IgE
      b. Low levels of allergies
   2. Comparison of helminths & allergies with socio-economic status
      a. Direct relationship between IgE and helminth infections
      b. Inverse relationship between helminths and allergies
   3. Allergies & helminths in experimental systems
      a. No reports of allergies associated with helminth infections,
      b. Yet chronic helminth infections lead to elevation of components of immune system involved in allergies in developed countries

G. Modulation of allergic activity
   1. Multiple mechanisms may exist to block capacity of mast cells to react in manner associated with allergies
   2. Mechanisms activated in nematode-infected humans

H. Hypothesis
   1. Helminthic parasites have shaped the evolution, ontogeny and function of the mammalian immune system
      a. Scientists in West have considered microbes (viruses and bacteria) to have been most influential
      b. Helminths ignored in West
   2. Allergic reactions are not the mechanisms by which helminths are controlled
   3. RESTATEMENT: Th2 activity during ontogeny (= childhood) and adulthood is required for proper homeostasis of the developing (juvenile) and adult immune system