

#### 4. Crohn's disease and ulcerative colitis

Crohn's disease and ulcerative colitis constitute inflammatory bowel disease (IBD) (11,12). Crohn's disease involves gut bacteria, the gut mucosa, macrophages, and T cells. In this disease, defects in the ability of macrophages to respond to bacteria allow the bacteria to breach the gut mucosa, and enter interstitial spaces. The result is the formation, in the gut wall, of granulomas – pathological structures containing T cells. In lesions of Crohn's disease, CD4<sup>+</sup> T cells express large amounts of the Th1-type cytokine, interferon-gamma. In contrast, in ulcerative colitis, the lesion results from the Th2-type cytokines, IL-4 and IL-13. Both diseases involve IL-17 producing T cells. These diseases result in gastrointestinal pain, and require diet therapy and the services of a dietician.

#### 5. Asthma

Asthma is initiated by inhaled allergens. The disease is mediated by Th2-type cytokines, IL-4, IL-5, IL-9, and IL-13. The immune cell most responsible for the pathology of asthma is eosinophils. The consequence is constriction of the airways and difficulty in breathing.

#### 6. Chronic obstructive pulmonary disease (COPD)

COPD is mainly caused by long-term cigarette smoking (13,14). The disease involves a decreased ability to breathe, as measured by forced expiratory volume per second, with consequent disability and death. Cytokines that mediate COPD include IL-6, TNF-alpha, and IL-1beta, while the immune cells most responsible for this disease are macrophages, neutrophils, and T cells. While COPD and asthma both involve the airways (bronchial tree) and alveoli, COPD is distinguished in that its pathology is mostly caused by *neutrophils*, while that of asthma is caused mostly by *eosinophils*.

## II. DETAILED EXAMPLE OF MULTIPLE SCLEROSIS MECHANISM OF ACTION

Multiple sclerosis is a severe disorder of the central nervous system (CNS) characterized by chronic inflammation, myelin loss, and progressive neurological dysfunction (15). Symptoms that occur most commonly in multiple sclerosis include tremor, optic

<sup>11</sup> Casanova JL, Abel L. Revisiting Crohn's disease as a primary immunodeficiency of macrophages. *J Exp Med.* 2009;206:1839–1843.

<sup>12</sup> Shih DQ, Targan SR. Insights into IBD pathogenesis. *Curr Gastroenterol Rep.* 2009;11:473–480.

<sup>13</sup> Halpin DM, Tashkin DP. Defining disease modification in chronic obstructive pulmonary disease. *COPD.* 2009;6:211–225.

<sup>14</sup> van der Molen T. Co-morbidities of COPD in primary care: frequency, relation to COPD, and treatment consequences. *Prim Care Respir J.* 2010, September 2009.

<sup>15</sup> Nicot AB. Gender and sex hormones in multiple sclerosis pathology and therapy. *Front Biosci.* 2009;14:4477–4515.