Refractory celiac disease (RCD) is a complex autoimmune disorder much like the more common celiac disease but, unlike celiac disease, it is resistant or unresponsive to at least 12 months of treatment with a strict gluten-free diet. Gliadin, a component of the wheat storage protein gluten, together with similar proteins in barley and rye, are the villains that trigger the immune reaction in celiac disease. The diagnosis of RCD is made by exclusion, especially of any other disorder that can affect the huge number of thread-like projections that line the interior of the intestine (intestinal villi), such as intestinal lymphoma, Crohn's disease, small intestinal bacterial overgrowth or hypogammaglobulinemia. Refractory celiac disease is rare among adults and is almost never seen in children. Data regarding the true incidence and prevalence of RCD are unreliable, but some have estimated that there might be 20,000 patients in the USA. However, those estimations are based on incomplete data. In one recent study, 1.5% of patients diagnosed with celiac disease at a single US center developed RCD. Of those with RCD 85% had the less severe Type I RCD. Virtually all clinicians studying refractory celiac disease emphasize that the diagnosis is based on eliminating all other possible sources of the symptoms and intestinal injury. One article lists more than 10 conditions that must be considered and eliminated before a convincing diagnosis of refractory celiac disease may be made. As noted above, examination of the interior wall of the intestine (upper and lower) by means of an enteroscope or colonoscope as well as obtaining intestinal biopsies to be examined under a microscope is useful, especially to determine if the symptoms are the result of intestinal disorders other than RCD. Capsule endoscopy, which examines the small intestinal lining using a camera mounted on a swallowed pill, may also be useful in evaluating the degree of small intestinal inflammation and injury. Some specialized centers are able to offer sophisticated examinations of the biopsy materials that in many cases will assist in the diagnosis. These studies emphasize the presence of abnormal populations of T lymphocytes in the tissue indicating a diagnosis of the more aggressive Type II RCD. Other imaging studies (barium X-ray, CT scan, capsule enteroscopy and MRE) may be undertaken, especially if there is concern for the presence of a lymphoma. Several therapies for RCD have been tried in uncontrolled tests with inconclusive results. Among the therapies tested in this way are: elemental diet (an elemental diet is a liquid diet consisting of nutrients that require no digestion, including amino acids, carbohydrates, vitamins, minerals, and triglycerides); and total parental nutrition (TPN) that is defined as nutrition maintained entirely by intravenous injection or by some other nongastrointestinal route. Steroid therapy is a mainstay of treatment but its beneficial effect is short-lived in patients of lymphoma. Treatment involving other immunosuppressive drugs such as azathioprine, cyclosporine, enteric-coated budesonide, 5-aminosalicylic acid (5-ASA), or inflixamab has been used with a limited number of patients. More recently chemotherapy with cladribine with or without autologous stem cell transplantation has also been reported to be useful.