Fecal alpha-1-antitrypsin is recommended as a marker of enteric protein loss and in patients with Crohn's disease as an index of intestinal inflammatory activity. We describe our experience in 88 patients with chronic diarrhea or suspicion of protein-losing enteropathy. We measured alpha-1-antitrypsin concentration in random stool samples \((n = 7)\), quantitative alpha-1-antitrypsin excretion in a 24 h feces collection \((n = 59)\) and fecal alpha-1-antitrypsin clearance \((n = 22)\). 13 of 88 patients with the following diagnoses had increased values: Crohn's disease \((3/9)\), other inflammatory diseases of the small intestine \((3/3)\), Whipple's disease, eosinophilic gastroenteritis, celiac disease), hypertrophic gastropathy \((1/4)\), infectious diarrhea \((2/6)\), irritable bowel syndrome \((2/29)\), chronic pancreatitis \((2/32)\) and diarrhea of other reasons \((0/5)\). In patients with Crohn's disease, alpha-1-antitrypsin excretion correlated with the clinical disease activity. All 3 patients with other inflammatory diseases of the small intestine showed increased fecal alpha-1-antitrypsin. All but 2 of the 32 patients with diarrhea due to chronic pancreatitis had normal values. Of 29 patients with idiopathic diarrhea, only 2 showed slightly increased fecal alpha-1-antitrypsin. 10 of the 11 patients with increased alpha-1-antitrypsin excretion in 24 h stool collection had normal alpha-1-antitrypsin concentration in random stool samples. Of the 5 patients with increased alpha-1-antitrypsin clearance, 4 also had increased alpha-1-antitrypsin in 24 h stool collection, but only one had increased alpha-1-antitrypsin concentration in random stool sample. Fecal alpha-1-antitrypsin measurement proved helpful in differing between inflammatory and non-inflammatory diarrhea.