

# Increased neutrophil apoptosis in chronic fatigue syndrome

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**Introduction:** Many patients with chronic fatigue syndrome (CFS) have symptoms that are consistent with an underlying viral or toxic illness. Considering that increased neutrophil apoptosis occurs in patients with infection, we examined whether patients with CFS also demonstrate increased numbers of neutrophils undergoing apoptosis.

**Methods:** Forty-seven patients (18 M & 29F, mean age 47.5 years [19-63 years]) who fulfilled the Centers for Disease Control classification for CFS were enrolled into the study. Thirty-four sex- and aged-matched healthy volunteers (13 M & 21F, 45.9 years [19-63 years]) were also recruited. The apoptotic process was measured isolating the neutrophils and incubating them with annexin V and or propidium iodide (PI) and by measuring leukocyte TNF-RI surface expression levels using a fluorescent-labeled antibody. An ELISA was used to measure platelet poor plasma levels of TGF-b1.

**Results:** Patients with CFS had significantly higher levels of neutrophil annexin V and TNFR-1 expression (37.4 vs. 22.8%;  $P = 0.001$  [Mann-Whitney U-test] and 12.5 vs. 3.9%;  $P = 0.004$ , respectively) and increased plasma levels of TGF-b1 (2.24 vs. 1.89 pg mL<sup>-1</sup>;  $P = 0.005$ ) when compared with controls. The patient group had significantly lower number of viable neutrophils (63.0 vs. 77.0%;  $P = 0.002$ ) and an increased number of early apoptotic neutrophils (32.0 vs. 19.6%;  $P = 0.002$ ).

**Conclusion:** We have shown that patients with CFS also have increased neutrophil apoptosis and higher levels of TGF-b1. We suggest that increased neutrophil apoptosis and inhibition of transmigration of neutrophils by higher TGF-b1 levels may be indicative of a persistent viral infection or a toxic state giving rise to many of the symptoms which characterize CFS. It might also be that increased apoptosis merely reflects a quicker turnover of neutrophils in this condition, but either way the data presented here provides convincing evidence that many patients with CFS have an underlying detectable abnormality.

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