

Alpha1-antitrypsin deficiency: A position statement of the Canadian Thoracic Society

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OBJECTIVE: To prepare new guidelines for the Canadian Thoracic Society (CTS) regarding severe alpha1-antitrypsin (AAT) deficiency and AAT replacement therapy.

MATERIALS AND METHODS: Previously published guidelines and the medical literature about AAT deficiency and AAT replacement were reviewed. The prepared statement was reviewed and approved by the CTS Standards and Executive Committees.

RESULTS: Three studies evaluated AAT replacement. The National Heart, Lung and Blood Institute's AAT Registry was a nonrandomized comparison of patients receiving and not receiving AAT replacement, and evaluated the decline in forced expiratory volume in 1 s (FEV1) in 927 subjects. The rate of FEV1 decline was significantly less in those receiving AAT treatment ($66 \pm SE 5$ mL/year versus $93 \pm SE 11$ mL/year; $P=0.03$) only in the subgroup with FEV1 35% to 49% predicted. In another study comparing 198 German patients receiving weekly AAT infusions and 97 untreated Danish patients, the mean annual decline in FEV1 was significantly less in treated patients only in the subgroup with FEV1 31% to 65% predicted (62 mL versus 83 mL, $P=0.04$). Neither of these studies was a randomized, controlled study and, thus, cannot be taken as proof of efficacy. A randomized, double-blind, placebo controlled trial of monthly replacement therapy over three years in 56 exsmokers with severe AAT deficiency and moderate emphysema showed a trend ($P=0.07$) favouring slower progression of emphysema by computed tomography scan in the group receiving AAT replacement.

CONCLUSIONS: AAT replacement therapy has not been proven definitively to be clinically effective in reducing the progression of disease in AAT-deficient patients, but there is a possible benefit to selected patients. A placebo controlled, randomized clinical trial of AAT replacement therapy is required. The authors recommend reserving AAT replacement therapy for AAT-deficient patients with impaired FEV1 of 35% to 50% predicted who have quit smoking and are on optimal medical therapy but continue to show a rapid decline in FEV1, and participation of all AAT-deficient subjects in the Canadian AAT Registry.