# ABSTRACT

## The Mechanism of Secretory Diarrhoea in Trichuris Dysentery Syndrome

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The mechanism of the diarrhoea occurring in Trichuris Dysentery Syndrome was investigated by voltage clamping, in Ussing chambers, rectal biopsies taken from previously infected patients. Twelve patients (2 years and 4 months - 9 years and 8 months) who had previously been infected with *Trichuris trichiura* and 16 controls (1 week - 11 years) that had never been infected with *Trichuris trichiura* or any other helminths were studied. Prior to the voltage clamping experiments, preliminary studies examining the chloride ion concentration in stools collected from ten infected patients before and after treatment showed a statistically significant fall in the chloride ion concentration following worm expulsion by chemotherapy. Mean chloride ion concentration was 64.29 ± 39.30 (SD) mM before treatment and 46.86 ± 37.70 (SD) mM after treatment (2 tailed Wilcoxon $p < 0.05$).

In the voltage clamping studies the rectal biopsies were challenged on the mucosal surface with excretory-secretory *T.trichiura* antigen. An increase in the short-circuit current (ΔIsc) was observed in the previously infected group while in the control

group, no response was obtained. The mean peak ΔIsc upon mucosal antigenic challenge was 3.63 ± 1.16 $\mu A/cm^2$. A serosal antigenic challenge in one infected patient resulted in a ΔIsc of 11.99 $\mu A/cm^2$.

Selective blockers such as the specific chloride channel blocker, anthracene-9-carboxylic acid, and the $Na^+$-$K^+$-$2Cl^-$ cotransporter inhibitor, furosemide, were used to show that the change in the short-circuit current was due to the movement of chloride ions across the rectal mucosa from the serosal to the luminal surface. The histaminergic blocker diphenhydramine, and indomethacin, an inhibitor of prostaglandin $E_2$, were used to demonstrate that histamine was the inflammatory mediator of prime importance in the pathway.

Electron microscopic studies of the rectal biopsies taken from two infected patients and two uninfected controls, after antigenic challenge, revealed the presence of degranulated mast cells in patients and undegranulated mast cells in the controls. These findings indicate that in Trichuris Dysentery Syndrome: (1) the observed diarrhoea is secretory in nature and is due to chloride ions moving across the rectal mucosa from the serosal to luminal surface; (2) the response is mediated by histamine released by degranulation of mast cells upon exposure to excretory-secretory *Trichuris* antigen, in previously sensitized individuals.