Altered gastrointestinal mucosal permeability in asthma

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Background
Abnormal gastrointestinal permeability (GIP) has been implicated in immunologic disease, including Crohn’s disease and celiac disease, but also including non-intestinal diseases such as diabetes and multiple sclerosis. Abnormal GIP may lead to entry of allergens from the gut into the systemic circulation and may prime the immune system, inciting inflammation outside the gut.

Hypothesis
Adult asthmatics demonstrate abnormal small bowel GIP.

Methods
GIP in ten patients followed in a regional referral centre in Northern Alberta was assessed. Patients were classified as allergic versus non-allergic on the basis of skin allergen testing. GIP was evaluated using an assay with established normal range values. Patients ingested a solution containing sucrose, mannitol and lactulose and urine was collected and assayed using high-performance liquid chromatography. Retrospectively, patient records were reviewed, and in addition to demographics, airway physiology, atopy, and sputum cell counts (SCCs) were captured.

Results
5 of 10 patients had increased GIP (Figure 1). Patients with abnormal GIP were not more likely to have evidence of active airway inflammation as assessed by SCC. There was no association between atopy and abnormal GIP.

Discussion
This study demonstrates an increase in GIP in the MALT-rich small intestine of asthmatic patients, illustrating an association between abnormal GIP and current asthma.

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Figure 1 GIP is increased in patients with asthma. Panel A represents the lactulose to mannitol ratio (Lac/Man) among the study cohort, measured by HPLC. Panel B represents the absorbed sucrose levels among the same patients. Each data point represents an individual patient. Circled data points indicate the patient had an abnormal sputum analysis (solid circles, eosinophilia; dashed circles, neutrophilia). In both panels, the dashed X-axis has been set at the value corresponding to the established upper limit of normal in healthy control patients.
Abnormal GIP did not correlate with concurrent airway inflammation. Abnormal GIP may be an important determinant of allergenic entry into the systemic circulation, and the absence of a correlation between active airway inflammation and increased GIP suggests a primary defect in the immunologic barrier.

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