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# Histamine intolerance and microbiota changes in patients with Painful Bladder Syndrome / Interstitial Cystitis

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## Hypothesis / aims of study

The cause of Painful Bladder Syndrome / Interstitial Cystitis is currently unknown.Histamine seems to play a major role in IC as neurogenic inflammation is one of the hypothesis of IC.Antihistamines are part of the guideline recommendations, foods high in histamine (e.g. Shorter-Moldwin Food Sensitivity Questionnaire) aggravate IC symptoms.
Objective: Within this retrospective case collection the role of histamine overload in the gut and vagina is highlighted.

## Study design, materials and methods

Between September 2012 and March 2016 a total of 71 women (range 19 to 75 years, mean age 48) were surveyed.Histamine in fecal samples was measured with a commercially available ELISA kit (LDN Labor Diagnostika Nord GmbH &Co. KG, Nordhorn, Germany).The results were compared to an age-matched cohort of 57 healthy women.Additionally, vaginal swabs were analysed for histamine producing bacteria of the Enterococcus and Enterobacteriaceae family. Furthermore a complete gut microbiota analysis was done in all women.

## Results

**Stool results**
In 50 of the 71 analysed women elevated histamine levels were found in fecal samples (Figure 1) compared to a control-group of 57 healthy women (Figure 2).

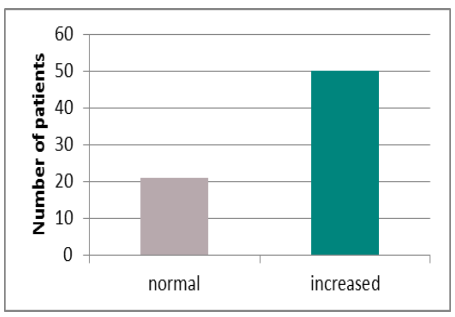


Figure 1: Histamine in stool

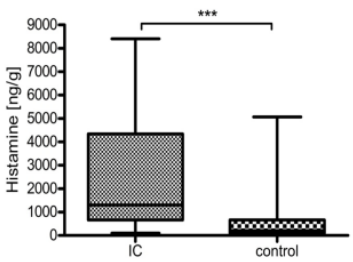


Figure 2: Histamine in ng/g stool in IC-group (n=57; Median=1299ng/g) and control-group (n=57; Median=205ng/g)
***p>0,0001 (Mann-Whitney)

Moreover in most of the patients the protective anaerobic indicator microbiota (mainly lactobacilli and bifidobacteria) was also diminished (Figure 3).

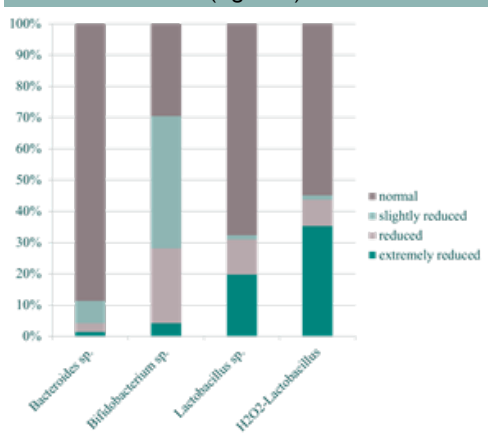


Figure 3: Protective gut microbiota

**Vaginal swab results**
In 37 out of the 50 women with the elevated histamine level the presence of Enterococcus ssp. and / or Enterobacteriaceae in vaginal swabs was also detected. In 8 women only the presence of Enterococcus ssp. and / or Enterobacteriaceae was found. Only 4 women did neither show elevated histamine levels nor the presence of histamine producing bacteria in vaginal swabs (Figure 4).

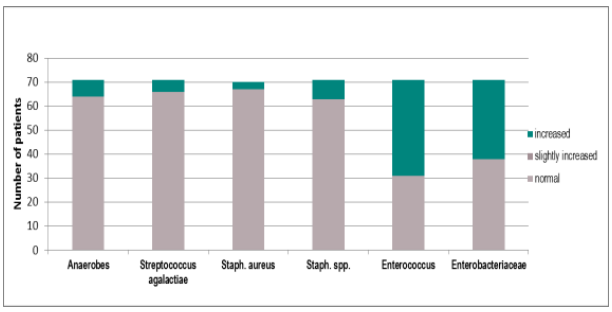


Figure 4: Vaginal microbiota

## Interpretation of results

There are paralleles between IC and histamine intolerance: prevalence of 1%, 80% female and middle aged, symptom improvement in pregnancy because of a 500 fold higher level of the diamine oxidase (histamine eliminating enzyme). Histamine intolerance is a poorly described disease which can present with a variety of symptoms like e.g. migraine, irritable bowel syndrome, urticaria, tachykardia, nasal congestion and perhaps also IC? Histamine can increase intestinal permeability causing a leaky gut which prompts the body to initiate immune reactions causing autoimmune diseases. Irritable bowel syndrome and autoimmune diseases are both comorbidities of IC.

## Concluding message

In irritable bowel syndrome it has been demonstrated that abdominal pain correlates with activated mast cells in proximity to colonic nerves which leads to the hypothesis of a neural-mediated crosstalk between colon and bladder afferents. Moreover histamine alone as shown in mice can also cause pelvic pain. Another consequence of the leaky gut is a toll-like receptor (TLR)-4 inflammatory response leading per se to pain.
That TLR-4 plays a role in pain has been recently demonstrated in IC patients by the MAPP research group.
Pre- and probiotics could be a new therapeutic approach for IC as they can repair the gut layer and can influence TLRs.

## References

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## Disclosures

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