USE OF A NOVEL MARKER FOR DIFFERENTIATING GASTRIC INTESTINAL METASTASIS: LI-p Gastric Intestinal Metaplasia (GIM) is a condition of uncertain pathogenesis, with some increased risk of carcinoma over the general population, but much less so than for intestinal metaplasia of the esophagus or Barrett’s epithelium (BE). This may be due to the heterogeneity of IM in the stomach. While gastric IM can be easily diagnosed by routine H&E staining, there is no clear marker for predicting which cases may have an increased risk for the development of dysplasia/cancer. Special mucin stains including alcian blue/high iron diamine have been utilized to differentiate various forms of gastric IM. We developed a monoclonal antibody (moAb) 7E1H2 (IgM isotype) that reacts specifically with specialized columnar epithelium of the cardia (BE) and colon epithelium, but not with normal epithelium from caecum, stomach and small intestine (Ann Int Med 120:753, 1994). OBJECTIVE: In this study we have attempted to ascertain the reactivity rate of 7E1H2 moAb with gastric IM and compare the results with standard alcian blue staining. METHODS: 53 cases of gastric IM diagnosed by routine H&E staining from WRJU and MRMC were obtained. All were tested by a sensitive immunoperoxidase method using 7E1H2 moAb. 39 of these were also tested by alcian blue/high iron diamine staining. RESULTS: 30 samples tested by 7E1H2 and only 13 (24.5%) were reactive to metaplastic cells. CONCLUSION: Although alcian blue stained all IM in the stomach, the moAb reacted more selectively. Further studies are needed to correlate the 7E1H2 reactivity with the type of metaplasia. 7E1H2 may detect cases of colorectal type, or “incomplete gastric IM” which are thought to be prone to the development of dysplasia/carcinoma.

RECTAL GLUTATHIONE CONTENT AND GLUTATHIONE-S-TRANSFERASE ACTIVITY IN X-LINKED AGAMMAGLOBULINEMIA (XLA) PATIENTS. A COMPARISON WITH HEALTHY VOLUNTEERS AND PATIENTS WITH ADENOMYOSIS. MAJL. GLOBULINEMIA (XLA). CMM vd Braak1, WHM Peters2, JWM vd Meer2, FM Negen1ast. Deps. of Gastroenterology1 and Internal Medicine2, Universty Hospital Nijmegen, The Netherlands.

XLA is a primary immunodeficiency disorder. An increased risk for developing cancer was well established in late-onset agammaglobulinemia and less well in XLA. We noticed a 30-fold greater incidence of rectosigmoid malign tumors in patients with XLA than in age-matched controls (Lancet 1993;341:1438-40). GST activity may be involved in the metabolism and detoxification of cytotoxic and carcinogenic compounds. Tissues with low or reduced levels of GST and glutathione-S-transferases (GST) may have a reduced capacity to detoxify carcinogens, resulting in more cytotoxic damage, which could lead to a higher tumor risk. A significant negative correlation exists between GST-activity in the mucosa along the gastrointestinal tract and tumour incidence in humans (lb J Cancer 1993;67: 1413-17).

Aim and methods. We investigated GST content and GST-activity in normal rectal mucos of XLA-patients (n=8), healthy volunteers (n=10) and patients with recently removed colonic adenomas (n=10). Differences between groups were assessed by the Mann-Whitney U test.

Results. Values are given as means ± SEM.

<table>
<thead>
<tr>
<th>Age (yrs)</th>
<th>GSH (nmol/mg protein)</th>
<th>GST-activity (nmol/min/mg protein)</th>
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</thead>
<tbody>
<tr>
<td>XLA</td>
<td>34 ± 2</td>
<td>50 ± 2</td>
</tr>
<tr>
<td>Adenoma</td>
<td>49 ± 3</td>
<td>41 ± 2</td>
</tr>
<tr>
<td>Normal</td>
<td>24 ± 1</td>
<td>44 ± 1</td>
</tr>
</tbody>
</table>

XLA: p<0.02 compared to XLA, p<0.01 compared to adenoma and normal, p<0.05 compared to normal.

Conclusion. The rectal GST activity in XLA-patients and patients with adenomas is not statistically different from healthy controls. Patients with adenomas have a significantly lower rectal GST-activity compared to healthy volunteers. Further study of the reactivity of XLA patients to mutagens is needed. These findings indicate that in XLA patients the risk of colorectal cancer might be partly explained by a lower detoxification capacity in the mucosa.

THE EFFECT OF RESISTANT STARCH ON COLONIC PROLIFERATION (POLYN, FAECAL BILE ACIDS AND SHORT CHAIN FATTY ACIDS IN PATIENTS WITH COLONIC ADENOMAS: A CONTROLLED TRIAL. MAJL. GLOBULINEMIA, M. Eilenberg, M. Dithoff, CMM vd Braak, A. Tangermann, A. Schäkel, AF2 de Haani, MB Farman, FM Negenast. Agriculturally University Wageningen, Dept. of Medical Statistics and Dept. of Gastroenterology, University Hospital Nijmegen, The Netherlands.

Resistant starch (RS) is fermented in the large bowel, resulting in the production of short chain fatty acids (SCFA), CH3CO, and H2. Possibly through acidification of colonic contents the lowering of the concentration of the secondary bile acids and colonic mucosal proliferation has been shown to decrease subsequently in healthy volunteers (Dig Dis Sci 1994;39:834-842). These intermediate biomarkers may play a role in colonic carcinogenesis. RS seems to influence these biomarkers in a favourable way.

We therefore studied the effect of supplementation of Hydron VII (45 g/day) to a normal Dutch diet on patients (pts) with recently removed adenomas in a controlled trial. After this period pts were randomly assigned to either Hydron VII (67, 69, mean age 67.8, BMI 26.7 ± 1.3 kg/m²) or H2O (69, mean age 58.8, BMI 24.8 ± 0.8 kg/m²) for another four weeks. At 4 and 8 weeks rectal biopsies and 48 hours faeces were collected. Differences in data's (M±SD) between 4 and 8 weeks of both groups were assessed by Mann-Whitney U test. Results. The PNA (Proliferating Cell Nuclear Antigen) labeling index in rectal biopsies was not influenced by RS intake (df: M ± SD). The faecal and dry weight as well as the pH, the total SCFA concentration and excretion did not change significantly in the RS group. The total faecal soluble bile acid concentration decreased in the RS group (df: M ± SD: 2.6 ± 2.6; RS: 27.8 mmmol, p=0.05). The concentration and percentage primary bile acid increased (esp. df: M ± SD: 14:2 ± 2; RS: 11.6 mmmol, p=0.05 and df: M ± SD: 14:2 ± 2; RS: 16%, p=0.01). The percentage secondary and dihydroxy bile acids decreased (esp. df: M ± SD: 14:2 ± 2; RS: -12%, p=0.01) in the RS group. No changes in dietary composition were observed during the study period. Conclusion. These results partially confirm our previous observations in healthy subjects (bile acids), but are at odds with respect to the SCFA excretion and colonic cell proliferation. An alternative explanation can be found in a relatively higher basal fibre and lower fat intake in these patients, compared to the previously studied healthy subjects.

GENETIC INSTABILITY AND CLINICOPATHOLOGICAL FEATURES OF COLORECTAL CANCER IN YOUNG PATIENTS. B. Squib, S. Gallinger, B. Bapat, E. Holody, R. McLaughlin, M. Redston. Samuel Lunenfeld Research Institute, Mount Sinai Hospital, University of Toronto, Canada.

Background. A significant proportion of colorectal cancers (CRC) in young patients may be due germline mutations in mismatch repair genes as demonstrated by microsatellite instability (MIN). Recent studies suggest that sporadic CRC with MIN exhibits a number of distinct clinical and pathologic features. Purpose: To determine the frequency and clinicopathological relevance of MIN in CRC from young patients. Methods: Twenty-five patients ≤15 years old (average age=30.7 years) with CRC in whom Familial Adenomatous Polyposis was excluded, were identified from the population-based Ontario Cancer Registry. Paraffin-embedded specimens were histologically reviewed, CRC of >70% cellularity and normal mucosa were microdissected and digested, DNA amplified by PTC with β2M and microsatellites (DSS123, DSS346, DST519, D1S1044 & D17S871), separated by denaturing gel electrophoresis and exposed to film. Results: MIN was seen in 12 of 25 CRC patients, 7 of which displayed MIN at 32 loci. Loss of heterozygosity of the chromosome 5 or 17 microsatellite occurred in 6 of the tumors. Six of 12 CRC with MIN and 6 of 13 CRC without MIN occurred proximal to the splenic flexure. Synchronous adenomas or hyperplastic polyps were noted in 6 patients without MIN, while only 1 patient with MIN had a synchronous polyp. Patients with CRC exhibiting MIN and those without were similar for Duke's staging and survival at a average follow up of 2.0 years. CRC with MIN was more likely to be poorly differentiated (MIN+ 58% vs. MIN- 15%), and exhibit peritumoral (MIN+ 12% vs. MIN- 5%) or intratumoral (MIN+ 83% vs. MIN- 58%) lymphocytic infiltration. The occurrence of MIN in CRC was unrelated to other pathological features previously described in hereditary nonpolyposis CRC (HNPPC) such as extracellular mucinosis. Creola's lymphoid reaction or expansive tumor margins. Conclusions: MIN is very common in CRC in young patients, suggesting that defects in mismatch repair are important in the pathogenesis of these tumors. The presence of MIN in this young age group correlates strongly with some pathologic features of XLA patients of HNPPC. However, the relationship of the molecular phenotype of MIN to other features of HNPPC remains unclear.