HIGH FAT DIET ALTERS GASTRIC HOMEOSTASIS LEADING TO METAPLASIA

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Background & Aims: High-fat diets (HFDs) are increasingly prevalent worldwide. The consumption of HFDs are known to disrupt gastrointestinal function, leading to metabolic imbalances and contributing to digestive diseases. While much research has focused on the intestinal alterations that result from HFD, the impact of HFD on the stomach remains underexplored. Given the stomach's key role in nutrient sensing and hormone secretion, cellular changes in response to HFDs may contribute to gastric disorders, including inflammation and cancer. This study investigates the effects of HFD on gastric cell composition and the resulting cellular changes. **Methods:** Male C57BL/6 mice were fed either a standard chow diet (control) or an HFD for 25 weeks. Gastric tissue was collected from mice following euthanasia and was fixed in 10% normal buffered formalin overnight. Gastric tissue was then analyzed by histology and immunostaining for markers that identify individual cell types within the gastric mucosa: tuft cells (DCLK1), enteroendocrine cells (ChgA), goblet cells (MUC2), and proliferative cells (Ki67). Quantification of cell types was performed using Image J software. **Results:** HFD led to notable changes in stomach cell composition. Analysis of H&E-stained tissue showed thickening of the gastric mucosa, loss of parietal cells and an infiltration of immune cells in mice fed a HFD compared to chow fed mice. Tuft cells, which are involved in immune responses and nutrient sensing, significantly increased in HFD fed mice. Enteroendocrine cells, crucial for hormone regulation, were significantly decreased in mice fed a HFD compared to control chow fed mice. Additionally, proliferating cells showed an upward trend, indicating increased turnover which could lead to an increased risk of cancer development. MUC2+ goblet cells were detected in 60% of the HFD mice and were absent in control mice, indicating that intestinal metaplasia was present in some of the HFD mice. **Conclusion:** Prolonged consumption of a HFD induces significant cellular changes in the stomach, including increased tuft cells, reduced hormone-secreting cells, and heightened cell proliferation, potentially contributing to inflammation and cancer risk. These data highlight the importance of understanding HFD's role in gastric disease progression.