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Peer Review

Review of: "Hydrochloric Acid Hypersecretion as the Cause of Pathology in the Upper Digestive Tract: Literature Analysis"

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The author states that current literature often treats upper gastrointestinal diseases as separate conditions, with little exploration of shared causes and mechanisms. Besides organic diseases, there are functional disorders linked to gut-brain interaction. This study highlights the body's natural defense against hydrochloric acid and enzymes, involving myenteric reflexes, nerve plexuses, Cajal cells, enzymes, and hormones, with no central nervous system involvement. Genetic traits like lactose intolerance, food allergies, and obesity weaken this defense, leading to mucosal damage, inflammation, and intestinal dysfunction. Hypersecretion of acid harms multiple digestive organs, causing varied symptoms, including constipation due to increased digestive tract tone. The study suggests that all functional gastrointestinal disorders involve mucosal inflammation from acid, pepsin, or bile damage, proposing a new perspective on their etiology and pathogenesis.

Some considerations are needed.

As a general statement on the subject of gastric hypersecretion, to avoid confusion among readers, it is good to define what is meant by gastric hypersecretion. Likewise, it is advisable to define the criteria for diagnosis. Especially in the field of gastroenterological pathology, and in the specific case of reflux esophagitis and functional dyspepsia, there is a large literature on the use of some serum markers such as Pepsinogens I and II and their ratio, the anti-helicobacter antibody, and Gastrin 17.

I also find that some statements require substantiation by incontrovertible evidence on the histological level. Precise and accurate definition is critical in forming a basis for scientific study. Chandrasoma P, DeMeester T. A New Pathologic Assessment of Gastroesophageal Reflux Disease: The

 doi.org/10.32388/GL3JVX

Squamo-Oxyntic Gap. Adv Exp Med Biol. 2016;908:41-78. doi: 10.1007/978-3-319-41388-4_4. PMID: 27573767.

Here are some statements (in brackets) that present some critical issues:

“There is reason to believe that all so-called functional gastrointestinal disorders are accompanied by an inflammatory process in the intestinal mucosa because of damage to the wall by hydrochloric acid, pepsin, or bile.”

I find that some statements require substantiation by incontrovertible evidence also on the histological level.

“There is no detailed description of the anatomy and physiology of the upper gastrointestinal tract in modern literature.”

Below, some extrapolations from PubMed: (Soybel DI. Anatomy and physiology of the stomach. Surg Clin North Am. 2005 Oct;85(5):875-94, v. doi: 10.1016/j.suc.2005.05.009. PMID: 16139026.

Sasegbon A, Hamdy S. The anatomy and physiology of normal and abnormal swallowing in oropharyngeal dysphagia. Neurogastroenterol Motil. 2017 Nov;29(11). doi: 10.1111/nmo.13100. Epub 2017 May 25. PMID: 28547793.

Matsuo K, Palmer JB. Anatomy and physiology of feeding and swallowing: normal and abnormal. Phys Med Rehabil Clin N Am. 2008 Nov;19(4):691-707, vii. doi: 10.1016/j.pmr.2008.06.001. PMID: 18940636; PMCID: PMC2597750.)

“This is probably due to the interstitial cells of Cajal of the deep myenteric plexus (ICC-DMP), which are found exclusively in the small intestine.”

As reported in the literature, it has long been known that: "The presence of the ICC in the human gastrointestinal tract has been demonstrated over the years from the esophagus to the anal canal; however, these cells present different morphological features and different tissue distribution

(Radu P, Zurzu M, Paic V, Bratucu M, Garofil D, Tigora A, Georgescu V, Prunoiu V, Popa F, Surlin V, Strambu V. Interstitial Cells of Cajal-Origin, Distribution and Relationship with Gastrointestinal Tumors. Medicina (Kaunas). 2022 Dec 28;59(1):63. doi: 10.3390/medicina59010063. PMID: 36676686; PMCID: PMC9865743.)

Moreover: (Foong D, Zhou J, Zarrouk A, Ho V, O'Connor MD. Understanding the Biology of Human Interstitial Cells of Cajal in Gastrointestinal Motility. Int J Mol Sci. 2020 Jun 25;21(12):4540. doi:

10.3390/ijms21124540. PMID: 32630607; PMCID: PMC7352366.)

(Kaji N, Hori M. Interstitial cells of Cajal in gastrointestinal inflammatory diseases. J Smooth Muscle Res. 2023;59:1-13. doi: 10.1540/jsmr.59.1. PMID: 36792171; PMCID: PMC9926098.)

"Biliary system pathology, including SOD, is an acid-dependent disease and therefore is always associated with other acid-dependent diseases."

This is a very broad statement that cannot be shared in the literature because it is not true that biliary system pathology is only an acid-dependent disease. Just as an example, it is enough to mention autoimmune disease.

"It is currently believed that "functional dyspepsia (FD) is a disorder of gut-brain interaction (GBI) with an estimated prevalence of 10-40% in Western countries and 5-30% in Asia" [22]. This hypothesis has no evidence."

Normally, in cases of strong assertions, it is good to cite the bibliographical entries that support this point of view. Even better would be to also cite the opposing opinions.

“For this reason alone, the Rome IV criteria do not have scientific status and should not be considered in scientific papers. “

Rome IV and subsequent editions not only have scientific status because they were drawn up by a select board of experts in the field, but are also taken into consideration in all scientific works where they represent reference statements. Each statement obviously presents levels of evidence that vary from strong to weak, but at the time of publication, it still represents the state of the art.

As mentioned, when contradicting a piece of literature, rightly or wrongly, references must be cited to support one's assertions. Otherwise, one risks self-referentialism at the expense of logical rigor.

“The effectiveness of PPI in FD is less than in GERD, but this is not a reason to consider these diseases to be of different origin, since the symptoms of GERD are not always controlled by PPI. “

Citations are needed.

“During ontogenesis, the symptoms of GERD change. “

And

“During ontogenesis, when atrophic gastritis develops, the secretion of hydrochloric acid decreases sharply, but against the background of already existing sphincter dysfunction (lower esophageal, antral, pyloric, and all duodenal sphincters), bile is thrown into the stomach and esophagus,

evacuation from the stomach is impaired (gastroparesis), evacuation from the duodenum is impaired (SMAS, duodenitis). “

Ontogenesis: in embryology, the series of successive stages and progressive changes that the egg (or the germ), and therefore the embryo, go through to give rise to the individual of a given species.

Furthermore, neither symptoms of GERD nor chronic atrophic gastritis develop during ontogenesis, but for the latter, with the intervention of some factors such as helicobacter pylori, autoimmune processes, etc. So, this statement is difficult to prove and certainly deserves to be stated differently.

“The inflammatory process in the esophagus in the so-called non-erosive reflux disease is determined based on a histological examination of the mucosa, by the presence of eosinophils[30], by the width of the intercellular space[31], by the presence of cardiac epithelium[32].”

Biopsy of the normal squamous epithelium may show histologic changes such as intraepithelial eosinophils and basal cell hyperplasia, but these are not sufficiently sensitive or specific to have practical value. Chandrasoma P, DeMeester T. A New Pathologic Assessment of Gastroesophageal Reflux Disease: The Squamo-Oxyntic Gap. Adv Exp Med Biol. 2016;908:41-78. doi: 10.1007/978-3-319-41388-4_4. PMID: 27573767.

Reflux disease is certainly a pathology that, from a histological point of view, requires a series of parameters to be modified in a more or less marked manner. (Tripathi M, Streutker CJ, Marginean EC. Relevance of histology in the diagnosis of reflux esophagitis. Ann N Y Acad Sci. 2018 Dec;1434(1):94-101. doi: 10.1111/nyas.13742. Epub 2018 May 16. PMID: 29766511.)

“Walker et al. reanalyzed duodenal biopsy by eosinophil counts in five high power fields that had previously been assessed as normal. “

Also in this case, it would be desirable to cite the bibliographic sources along with the explanation of the number of eosinophils above which the finding is certainly pathological.

“There is reason to believe that all so-called functional gastrointestinal disorders (functional constipation without megacolon, irritable bowel syndrome, functional dyspepsia, postprandial distress syndrome, functional chest pain, functional heartburn, functional bloating[46]) are accompanied by an inflammatory process in the intestinal mucosa because of damage to the wall by hydrochloric acid, pepsin, or bile.”

This hypothesis needs to be proved, and important to test too are the amount of acid or bile reflux, reflux time, number of episodes, values in the different locations mentioned, and so on, as well.

Finally,

English flaw:

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“Peristalsis is observed only in the body and anal part of the stomach.” I believe this is a trivial error, and the correct phrase would be “Peristalsis is observed only in the body and antral part of the stomach.”

In conclusion, this work presents as a strong point an innovative approach to a part of gastrointestinal pathology but requires a complete restyling in the presentation of the evidence in favor of the working hypotheses.

Declarations

Potential competing interests: No potential competing interests to declare.