PATHOLOGICAL CONDITIONS RELATED TO HYPO- AND ACHLORHYDRIA

INTRODUCTION

The scope of this paper is to clearly define the usefulness of determining the pH of gastric juice in patients submitted to EGD.

The following fact sheets provide a brief overview of possible correlations between gastric pH and pathological conditions. The information provided is underpinned by bibliographical references that have no claim to exhaustiveness.

Said correlations indicate the significant advantage of knowing this parameter (pH), specifically:

- to define a better biopsy taking strategy;
- to improve diagnosis;
- to inform and sensitise the pathologist;
- to contribute towards the formulation of therapeutic prescriptions.

The possibility of knowing the value of gastric pH in real time during the performance of the endoscopic investigation is essential to achieve the above-mentioned goals that enhance the potential of the endoscopic investigation by combining the visual examination with the chemical analysis that is contextually conducted.

Hypo- and achlorhydria:

- Are conditions that entail the risk of neoplasia
- Are correlated with the presence of atrophic gastritis
- Are associated with an increase in gastrinaemia
- Cause contamination of the small intestine
- Reduce vitamin B12 absorption
- Reduce iron absorption
- Significantly influence the absorption of several drugs
- Do not need treatment with antisecretory drugs

Enable to detect other autoimmune disease

Are associated with alterations in bone metabolism, predisponing the subject to pathological fractures

Indirectly enable to verify the efficacy of antisecretory treatment

Are not significantly affected by the presence of bile

Predispose the subject to intestinal infections on the part of pathogens (e.g. Yersinia enterocolitica, Salmonella, Citrobacter, Clostridium)

Are an independent risk factor for well-differentiated squamous cell carcinoma in the oesophagus

pH testing of gastric aspirate does not feel the “focal” effect of intragastric tests performed with the pH electrode

pH testing of gastric juice (static measurement) is strongly correlated with the acid secreting function of the stomach (dynamic function)

1- HYPO- AND ACHLORHYDRIA ARE CONDITIONS THAT ENTAIL THE RISK OF NEOPLASIA

Several authors claim that hypo- and achlorhydria are risk factors that are independent from atrophic gastritis for stomach cancer. Said implication arises from the carcinogenic effect produced by gastric nitrates (ingested with food) that are transformed into nitrosamines, powerful carcinogens, when acid is absent.

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2 - HYPO- AND ACHLORHYDRIA ARE CORRELATED WITH THE PRESENCE OF ATROPHIC GASTRITIS

Along with *Helicobacter pylori*, this disorder is an important risk factor for stomach neoplasms (adenocarcinoma and endocrine tumours). The oxyntic mucosa variant is often undiagnosed due to the absence, in the majority of cases, of specific endoscopic patterns and to the patchy distribution of histological lesions. Very often, even bioptic sampling does not lead to a diagnosis, if it is not adequate (numerous samples taken at the antrum, angulus, body and fundus). Moreover, alerting the pathologist is an important factor that influences the diagnosis. In routine endoscopy, atrophic gastritis involving the oxyntic mucosa records an incidence of about 1%. Percentages in the range of 5-12% have, instead, been reported by dedicated studies conducted in Italy. Even higher percentages have been reported in other countries. Determination of the pH value and of a condition of hypo- and achlorhydria enables to fill this gap by leading to the detection of almost all cases of gastritis involving the oxyntic mucosa.

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3. HYPO-AND ACHLORHYDRIA ARE ASSOCIATED WITH AN INCREASE IN GASTRINAEMIA

When hypo- and achlorhydria are underpinned by moderate to severe impairment of oxyntic gland parenchyma, they are associated with an increase in the population of gastrin-producing antral G cells and, subsequently, increase gastrin levels in blood. This hormone has a proliferation-stimulating action on ECL cells of oxyntic mucosa with the subsequent possibility of a neoplastic transformation (endocrine cell tumours).
Said population of antral G cells can undergo a neoplastic transformation (gastrinoma) when exposed to the stimulating effect of hypo- and achlorhydria.

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4. HYPO- AND ACHLORHYDRIA CAUSE CONTAMINATION OF THE SMALL INTESTINE

This is an all but rare event that is characterised by bacterial overgrowth in the small intestine, often caused by hypo- and achlorhydria (and by the subsequent reduction in antimicrobial activity of gastric juice against germs ingested with food). Clinically, the symptoms developed can be easily confused with irritable bowel syndrome (diarrhoea, tympanites, abdominal disorders and pain). The lactulose breath test is useful to detect the condition.

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5. HYPO- AND ACHLORHYDRIA REDUCE VITAMIN B12 ABSORPTION

Hypochlorhydria and atrophy of oxyntic mucosa are often associated with a deficient production of Intrinsic Factor without which vitamin B12 taken with food cannot be absorbed, with a subsequent deficiency of this important nutrient.
The clinical picture that is correlated with vitamin B12 deficiency is pernicious anaemia (macrocytic anaemia).
But, at times, macrocytosis is not detected due to the concurrent presence of iron malabsorption and, typically, a picture of asiderotic anaemia “without microcytosis” appears (this must arouse the suspicion of a joint deficiency of both factors, namely iron and vitamin B12). Moreover, vitamin B12 deficiency can cause important and “irreversible” neurological damage in the peripheral nervous system (sensitivity disorders, pain, etc).
It is important and essential to detect conditions of hypo- and achlorhydria because they contribute to the detection of anaemia and concurrently enables to intervene therapeutically and in the most suitable manner (with parenteral administration of the vitamin because the oral route would not be effective).

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6. HYPO- AND ACHLORHYDRIA REDUCE IRON ABSORPTION

Hypochlorhydria often entails low absorption of iron taken by mouth (both as a drug and contained in food).
This produces asiderotic anaemia that is “not responsive” to iron administration by mouth.
It is important and essential to detect conditions of hypo- and achlorhydria because they contribute to the detection of anaemia and concurrently enables to intervene therapeutically and in the most suitable manner (with parenteral administration of the vitamin because the oral route would not be effective).

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7. HYPO- AND ACHLORHYDRIA SIGNIFICANTLY INFLUENCE THE ABSORPTION OF SEVERAL DRUGS

The absorption of certain drugs is affected by the presence of acid in the stomach. For example, the absorption of Thyroxin (a drug that is administered for hypothyroidism) is impaired by possible conditions of hypo- and achlorhydria. The impairment is such as to require an important increase (37%) in the therapeutic dose.
The absorption of several other drugs was significantly impaired by conditions of gastric hypoacidity (e.g. drugs for heart diseases, antibiotics, antiviral drugs, etc).

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8. HYPO- AND ACHLORHYDRIA DO NOT NEED TREATMENT WITH ANTISECRETORY DRUGS

Said treatment is contraindicated because it would aggravate a physiological function that is already impaired.
Very often patients with undiagnosed atrophic gastritis involving the oxyntic mucosa and hypo- and achlorhydria are inappropriately submitted to treatments with antisecretory drugs even for years. This might have many and serious consequences, such as:

- induced contamination of the small intestine
- aggravation of the already deficient digestive processes
- aggravation of the clinical picture.

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Scand J Gastroenterol 1990 Oct;25(10):1084-8.

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Clinical usefulness of gastric-juice analysis in 2007
Gastrointestinal Endoscopy 2007; Volume 66, No. 5 :881-890.

9. IDENTIFYING CONDITIONS OF HYPO- AND ACHLORHYDRIA ENABLES TO DETECT OTHER AUTOIMMUNE DISEASES

When hypo- and achlorhydria are produced by autoimmune atrophic gastritis, they are often associated with other immune-based diseases, such as Hashimoto's thyroiditis, primary biliary cirrhosis, vitiligo, diabetes mellitus type I, collagenopathies, etc. Detecting hypo- and achlorhydria could lead to the diagnosis of important diseases that risk remaining undiagnosed for a long time.

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10. HYPO- AND ACHLORHYDRIA ARE ASSOCIATED WITH ALTERATIONS IN BONE METABOLISM, PREDISPOSING THE SUBJECT TO PATHOLOGICAL FRACTURES

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11. IDENTIFYING A CONDITION OF HYPOCHLORHYDRIA INDIRECTLY ENABLES TO VERIFY THE EFFICACY OF ANTISECRETORY TREATMENTS

Treatment with antisecretory drugs of any type always records exceptional "non-responder" cases in which administration of the drug does not reduce gastric acid secretion.
Instead, at times the reduction occurs but is scarcely important for clinical purposes.
Both these conditions can be detected by testing gastric pH. Very acidic pH values strongly indicate one of the above-mentioned two conditions, and are hardly correlated with an effective therapeutic response.
Therefore, failure to detect a condition of hypochlorhydria in patients under treatment with antisecretory agents leads to an ineffective therapeutic response.

12. HYPO- AND ACHLORHYDRIA ARE NOT SIGNIFICANTLY AFFECTED BY THE PRESENCE OF BILE

The presence of bile in gastric juice does not significantly influence pH values. Despite contributing hydroxide ions (OH^-), bile cannot (except in very rare cases) increase pH above 4, determining a condition of hypochlorhydria.

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15. PH TESTING OF GASTRIC ASPIRATE DOES NOT FEEL THE "FOCAL" EFFECT OF INTRAGASTRIC TESTS PERFORMED WITH THE PH ELECTRODE.

16. PH TESTING OF GASTRIC JUICE (STATIC MEASUREMENT) IS STRONGLY CORRELATED WITH THE ACID SECRETING FUNCTION OF THE STOMACH (DYNAMIC FUNCTION).