Cancer Association of South Africa (CANSA)

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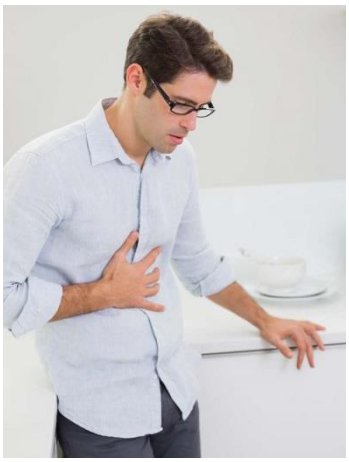
Fact Sheet
on
Atrophic Gastritis

Introduction

Atrophic gastritis (also known as Type A or Type B Gastritis) is a process of chronic inflammation of the stomach mucosa, leading to changes in stomach juice excretion.



[Picture Credit: Atrophic Gastritis]

Those with the autoimmune version of atrophic gastritis are statistically more likely to develop gastric carcinoma (stomach cancer).

Atrophic Gastritis (AG)

Atrophic gastritis (AG) is a type of chronic inflammation of the gastric mucosa with loss of gastric glandular. The two main causes of atrophic gastritis result in distinct types of gastritis (inflammation of the stomach). *H pylori*-associated atrophic gastritis is usually a multifocal process that involves the mucosa of the stomach. Individuals with autoimmune gastritis may develop pernicious anaemia because of extensive loss of parietal cell mass and anti-intrinsic factor antibodies.

H pylori- associated atrophic gastritis is frequently asymptomatic (without symptoms), but individuals with this disease are at increased risk of developing gastric carcinoma (stomach cancer). Patients with chronic atrophic gastritis develop low gastric acid which may lead to carcinoid tumours.

Raza, M. & Bhatt, H. 2020.

"Gastric atrophy (GA) and intestinal metaplasia of the gastric mucosa (GIM) are collectively known as chronic atrophic gastritis (CAG). These early conditions can lead to the development of gastric adenocarcinoma (GC). This review focuses on the current evidence and guidelines in diagnosis, management, and surveillance of chronic atrophic gastritis to identify those at risk of progression to gastric adenocarcinoma. Chronic atrophic gastritis is considered a precursor lesion for gastric cancer, which is the fifth most common cancer globally and carries third-highest cancer-related mortality in the world. This aggressive cancer presents late in most countries with no screening program and leads to numerous deaths due to late diagnosis. The common etiologies of this premalignant lesion

are *Helicobacter pylori (H. pylori)* and autoimmune gastritis. Chronic inflammation leads to the loss of gastric mucosa leading to an acid depleted environment hypothesized as an early precursor to distal gastric cancer. *H. pylori* is a microaerophilic gram-negative bacterial pathogen. Its role has been implicated in not only atrophic gastritis but also peptic ulcers, gastric adenocarcinoma, and mucosa-associated lymphoid tissue lymphoma (MALT). Identification and eradication of the pathogen have a significant role in reducing the risk of CAG. It is of utmost importance to identify the precancerous lesions by identifying those at risk. It is also crucial to follow-up with surveillance endoscopy and, if needed, endoscopically intervening to avoid major resection surgery in advanced stage gastric cancer. The popular Correa Cascade suggested the linear progression from chronic atrophic gastritis (CAG) with metaplastic intestinal epithelium to low-grade dysplasia (LGD), high-grade dysplasia (HGD), and eventually gastric adenocarcinoma."

Kim, Y.J., Lee, S-Y., Yang, H., Kim, J.H. Sung, I-K. & Park, H.S. 2019.
Background/aims: Chronic atrophic gastritis (CAG) and metaplastic gastritis (MG) are precancerous conditions of *Helicobacter pylori* (*H. pylori*)-related gastric cancer. This study aimed to identify the characteristics of nodular gastritis (NG) showing CAG or MG after nodule regression.
Methods: *H. pylori*-infected patients with NG were included after upper gastrointestinal endoscopy. Patients were excluded if their latest endoscopy had been performed ≤36 months after the initial diagnosis of NG. Small-granular-type NG was defined as the condition with 1-2 mm regular subepithelial nodules. Large-nodular-type NG was defined as those with 3-4 mm, irregular subepithelial nodules. The endoscopic findings after nodule regression were recorded.
Results: Among the 97 *H. pylori*-infected patients with NG, 61 showed nodule regression after a mean follow-up of 73.0±22.0 months. After nodule regression, 16 patients showed a salt-and-pepper appearance and/or transparent submucosal vessels, indicating CAG. Twenty-nine patients showed diffuse irregular elevations and/or whitish plaques, indicating MG. Sixteen patients with other endoscopic findings (14 normal, one erosive gastritis, and one chronic superficial gastritis) showed a higher proportion of *H. pylori* eradication (12/16, 75.0%) than those in the CAG group (5/16, 31.3%) and MG group (6/29, 20.7%; p=0.001). Patients with small-granular-type NG tended to progress toward CAG (14/27, 51.9%), whereas those with large-nodular-type NG tended to progress toward MG (25/34, 73.5%; p<0.001).
Conclusions: In patients with a persistent *H. pylori* infection, NG tended to progress to CAG or MG when the nodules regressed. Small-granular-type NG tended to progress to CAG, whereas large-nodular-type NG tended to progress to MG.

Incidence of Atrophic Gastritis (AG) in South Africa
Because Atrophic Gastritis is not a cancerous condition, but rather a possible precursor to stomach cancer, the outdated National Cancer Registry (2017) does not provide any information regarding the incidence of this condition.

Causes of Atrophic Gastritis (AG)
The main causes of Atrophic Gastritis may include:

Helicobacter pylori usually infects the stomach in childhood and the infection progresses if not treated. This type of bacteria can be passed from person to person through direct contact with faeces, vomit, or saliva, and can also be spread through contact with contaminated food or water.

Autoimmune atrophic gastritis occurs when the body produces antibodies that attack the stomach cells responsible for acid production. Antibodies also attack a substance released by these cells known as intrinsic factor. Intrinsic factor helps one to absorb vitamin B_{12}. Its destruction can cause an illness known as pernicious anaemia, in which a lack of vitamin B_{12} leaves one unable to make enough red blood cells.

Chief, C., Sanderson, P.R., Willeto, A.A.A., Yazzie, A., McKinley, A., Monroy, F.P., Harris, R.B. & Oren, E. 2020.
"Stomach cancer is the third leading cause of cancer death globally. Helicobacter pylori plays a role in the healthy human gut, but is also associated with multiple chronic diseases, including stomach cancer. Though H. pylori prevalence is declining in parts of the world, it remains high among certain populations. In Arizona, stomach cancer rates are 3-4 times higher among the Navajo Nation population as compared with the non-Hispanic white population. This pilot project assessed adult Diné (Navajo) individuals' understanding and awareness regarding H. pylori infection and stomach cancer. Focus groups were held in three Diné communities. Data were analyzed thematically using a multi-investigator consensus approach. Participants had limited knowledge of H. pylori infection and stomach cancer and perceived local medical providers as also having limited knowledge on these conditions. Participants described poor health care experiences, structural inequalities, and environmental concerns and associated these with H. pylori infection and stomach cancer. This study highlights the need for additional research and education on current knowledge and perceptions of stomach cancer and H. pylori infections in Navajo Nation."

Nieminen, A.A., Kontto, J., Puolakkainen, P., Virtamo, J. & Kokkola, A. 2019.
OBJECTIVES: The aim of this study was to evaluate long-term gastric cancer risk in male smokers with and without atrophic gastritis.
MATERIALS AND METHODS: A total of 22,346 elderly male smokers participated in the Helsinki Gastritis Study between the years 1989 and 1993. Serum pepsinogen I (PGI) was measured for the men, and 2,132 men with low PGI (<25 μg/L; a marker of atrophic corpus gastritis) were invited to undergo gastroscopy because of increased gastric cancer risk. Endoscopy was performed to 1,327 men, who were followed up for a median of 13.6 years and a maximum of 25.3 years thereafter. In addition, the gastric cancer risk of men with low PGI was compared to that of the men with normal PGI and to the general Finnish male population of the same age.
RESULTS: Thirty-five cases of gastric cancer were diagnosed in men with gastroscopy during the follow-up. The incidence rate was 1.94 per 1000 patient years. The men with a history of gastric surgery (n = 180) due to a benign cause had even higher gastric cancer incidence (3.2 per 1000 patient-years). Gastric cancer risk was highest in men with marked intestinal metaplasia in primary biopsies. Compared to the general Finnish male population of the same age, the cancer risk was 1.13 times higher in male smokers with normal serum PGI, and 2.43 times higher in men with low serum PGI.
CONCLUSION: In male smokers, atrophic gastritis and intestinal metaplasia increase the risk of gastric cancer.

Signs and Symptoms of Atrophic Gastritis (AG)
Often there are no symptoms, and as a result, many cases of AG go unrecognised.

An *H. pylori* infection may cause:

- nausea and vomiting
- loss of appetite
- stomach pain
- ulcers of the stomach
- cancer of the stomach
- difficult to treat iron deficiency anaemia
- loss of weight loss

Autoimmune atrophic gastritis may also lead to vitamin B_{12} deficiency, with symptoms of anaemia, including:
- feeling weak
- lightheadedness
- dizziness

Vitamin B_{12} deficiency can lead to nerve damage:
- numbness and tingling in the limbs
- unsteady walking
- mental changes

Carabotti, M., Esposito, G., Lahner, E., Pilozzi, E., Contil, L., Ranazzi, G., Severi, C., Bellini, M. & Annibaie, B. 2019.
AIM: In patients affected by atrophic body gastritis (ABG) gastro-oesophageal reflux (GER) related symptoms have been reported, despite the presence of hypochlorhydria.
OBJECTIVE: Objectives of this single-centre study was to assess in ABG the occurrence of GER-related symptoms and their relationship with histopathologic oesophageal findings.
MATERIALS AND METHODS: Fifty-four consecutive patients (20.4%male, 57.6 ± 14 years) undergoing to follow-up for ABG, underwent assessment of GER-related symptoms and gastroscopy with multiple gastric and oesophageal biopsies to investigate the presence of microscopic esophagitis (ME).
RESULTS: At least one typical GER symptoms were reported in 24.1% with 9.2% of patients complaining of heartburn and 18.5% regurgitation. One or more atypical GERD symptoms were reported in 44.4% of patients. Two symptomatic ABG patients presented oesophageal lesions at endoscopy (one with erosive esophagitis (LA-C) and one with Barrett's oesophagus (C2M2)), 49% reported a mild ME and 24.5% a severe ME. No significant differences regarding GERD prevalence were found among patients with or without ME, but cough was the only symptom significantly more frequent in patients with ME (38.95% vs. 7.7%, p = .042).
CONCLUSIONS: These data showed that GERD is present in a quarter of ABG patients, suggesting that hypochlorhydria not exclude per se arising of oesophageal symptoms. In ABG we found that ME is a frequent finding but its clinical relevance remains to be investigated with further studies.

Diagnosis of Atrophic Gastritis (AG)
The diagnosis of atrophic gastritis can only be ascertained histologically. This is usually done by endoscopy. The endoscopy does not directly contribute to making a diagnosis, however, it is necessary to perform biopsies of the stomach to make a histologically-based diagnosis.

Diagnosis of *H pylori*-associated atrophic gastritis is made following histologic examination of a gastric biopsy with *H pylori* special stains

Diagnosis of autoimmune gastritis is made by identifying the absence or lowered production of gastric acid in the stomach and anti-intrinsic factor in the serum.

Kotelevets, S.M. & Chekh, S.A. 2020.
Aim: Develop a program to identify, treat, and prevent severe atrophic gastritis to reduce gastric cancer incidence and mortality.
Materials and methods: In total, 2,847 people aged > 40 years old underwent serological noninvasive screening for atrophic gastritis by identifying postprandial gastrin-17 and pepsinogen-1 in the fasting state. Anti-H pylori IgG was found in 2,134 patients. Seven years later, 2,220 patientswho had undergone serological noninvasive screening were asked to fill out a questionnaire survey (were interviewed). We could not find any information on 627 of 2,847 patients. Next, 75 patients with multifocal atrophic gastritis who underwent gastroscopy and biopsies (the Updated Sydney System (USS)) were selected. To study gastrin-17 production, morpho-functional correlation was studies in 75 patients with multifocal atrophic gastritis.
Results: During seven years, no reported case of gastric cancer was done among 2,220 persons who underwent serological screening and treatment. In the same population, 4.3 persons who did not receive screening during the same period, developed gastric cancer and died of it. In this study, we can say that 4.3 lives were saved out of 2,220 tested persons. The cost for screening this number of people amounted to €23,750. A comparison of the prevalence rate of the four stages of multifocal atrophic gastritis based on the data of the histopathology tests and noninvasive serologic screening in accordance with OLGA classification showed a strong correlation (the correlation coefficient is 0.812). This finding suggested that using this classification not only for histopathology tests for atrophic gastritis but also for serologic markers of antral mucosa and corpus ventriculi atrophy: gastrin-17 and pepsinogen-1.
Conclusion: Complex pathogenetic treatment of atrophic gastritis significantly reduced gastric cancer risk and incidence for such patients.
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Kishikawa, H., Ojiro, K., Nakamura, K., Katayama, T., Arabata, K., Takarabe, S., Miura, S., Knai, T. & Nishida, J. 2020.
“Individuals with chronic atrophic gastritis who are negative for active H. pylori infection with no history of eradication therapy have been identified in clinical practice. By excluding false-negative and autoimmune gastritis cases, it can be surmised that most of these patients have experienced unintentional eradication of H. pylori after antibiotic treatment for other infectious disease, unreported successful eradication, or H. pylori that spontaneously disappeared. These patients are considered to have previous H. pylori infection-induced atrophic gastritis. In this work, we define these cases based on the following criteria: absence of previous H. pylori eradication; atrophic changes on endoscopy or histologic confirmation of glandular atrophy; negative for a current H. pylori infection diagnosed in the absence of proton-pump inhibitors or antibiotics; and absence of localized corpus atrophy, positivity for autoantibodies, or characteristic histologic findings suggestive of autoimmune gastritis. The risk of developing gastric cancer depends on the atrophic grade. The reported rate of developing gastric cancer is 0.31%-0.62% per year for successfully eradicated severely atrophic cases (pathophysiologically equal to unintentionally eradicated cases and unreported eradicated cases), and 0.53%-0.87% per year for spontaneously resolved cases due to severe atrophy. Therefore, for previous H. pylori infection-induced atrophic gastritis cases, we recommend endoscopic surveillance every 3 years for high-risk patients, including those with endoscopically severe atrophy or intestinal metaplasia. Because of the difficulty involved in the endoscopic diagnosis of gastric cancer in cases of previous infection, appropriate monitoring of the high-risk subgroup of this understudied population is especially important.”

Zhang, Y., Li, F., Yuan, F., Zhang, K., Huo, L., Dong, Z., Lang, Y., Zhang, Y., Wang, M., Gao, ., Qin, Z. & Shen, L. 2020.

Background: The sensitivity of endoscopy in diagnosing chronic atrophic gastritis is only 42%, and multipoint biopsy, despite being more accurate, is not always available.

Aims: This study aimed to construct a convolutional neural network to improve the diagnostic rate of chronic atrophic gastritis.

Methods: We collected 5470 images of the gastric antrums of 1699 patients and labeled them with their pathological findings. Of these, 3042 images depicted atrophic gastritis and 2428 did not. We designed and trained a convolutional neural network-chronic atrophic gastritis model to diagnose atrophic gastritis accurately, verified by five-fold cross-validation. Moreover, the diagnoses of the deep learning model were compared with those of three experts.

Results: The diagnostic accuracy, sensitivity, and specificity of the convolutional neural network-chronic atrophic gastritis model in diagnosing atrophic gastritis were 0.942, 0.945, and 0.940, respectively, which were higher than those of the experts. The detection rates of mild, moderate, and severe atrophic gastritis were 93%, 95%, and 99%, respectively.

Conclusion: Chronic atrophic gastritis could be diagnosed by gastroscopic images using the convolutional neural network-chronic atrophic gastritis model. This may greatly reduce the burden on endoscopy physicians, simplify diagnostic routines, and reduce costs for doctors and patients.

Treatment of Atrophic Gastritis (AG)

Once atrophic gastritis is diagnosed, treatment is usually directed:

(1) to eliminate the cause
(2) to correct complications of the disease
(3) to attempt to revert the atrophic process.

Pimentel-Nunes, P., Libânio, D., Marcos-Pinto, R., Areia, M., Leia, M., Esposisto, G., Garrido, M., Kikuste, I., Megraud, F., Matysiak-Budnik, T., Annibale, B., Dumonceau, J-M., Barros, R., Fléjou, J-F., Carneiro, F., van Hooft, J.E., Kuipers, E.J. & Dinis-Ribeiro, M. 2019.

"Patients with chronic atrophic gastritis or intestinal metaplasia (IM) are at risk for gastric adenocarcinoma. This underscores the importance of diagnosis and risk stratification for these patients. High definition endoscopy with chromoendoscopy (CE) is better than high definition white-light endoscopy alone for this purpose. Virtual CE can guide biopsies for staging atrophic and metaplastic changes and can target neoplastic lesions. Biopsies should be taken from at least two topographic sites (antrum and corpus) and labelled in two separate vials. For patients with mild to moderate atrophy restricted to the antrum there is no evidence to recommend surveillance. In patients with IM at a single location but with a family history of gastric cancer, incomplete IM, or persistent *Helicobacter pylori* gastritis, endoscopic surveillance with CE and guided biopsies may be considered in 3 years. Patients with advanced stages of atrophic gastritis should be followed up with a high quality endoscopy every 3 years. In patients with dysplasia, in the absence of an endoscopically defined lesion, immediate high quality endoscopic reassessment with CE is recommended. Patients with an endoscopically visible lesion harboring low or high grade dysplasia or carcinoma should undergo staging and treatment. *H. pylori* eradication heals nonatrophic chronic gastritis, may lead to regression of atrophic gastritis, and reduces the risk of gastric cancer in patients with these conditions, and it is recommended. *H. pylori* eradication is also recommended

for patients with neoplasia after endoscopic therapy. In intermediate to high risk regions, identification and surveillance of patients with precancerous gastric conditions is cost-effective."

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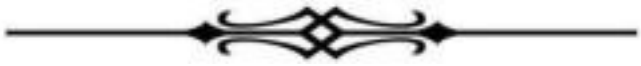

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