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# Treatment of *Helicobacter pylori*-associated lymphomas

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The regression of gastric MALT lymphoma after antibiotic eradication of *H. pylori* was first reported in 1993 by Wotherspoon and colleagues, who described the efficacy of antibiotic therapy in six patients with superficially invasive gastric MALT lymphoma.[1] Our and other groups thereafter confirmed the efficacy of antibiotics in inducing apparently durable lymphoma remissions: in 60-100% of patients with localized *H. pylori*-positive gastric MALT lymphoma.[2-9] The histologic remission can usually be documented within 6 months from the *H. pylori* eradication but sometimes the period required is more prolonged and the therapeutic response may be delayed up to more than 1 year.[10]

It is generally accepted that eradication of *H. pylori* with antibotics should be employed as the sole initial treatment of localized (i.e., confined to the gastric wall) MALT lymphoma. This nowadays is indeed the best studied therapeutic approach with more than 20 reported studies.[11-12] Any of the highly effective antibiotic regimens proposed[13-14] can be used. A strict endoscopic follow-up is recommended, with multiple biopsies taken 2-3 months after treatment to document H pylori eradication and, subsequently, at least twice per year for 2 years to monitor the histologic regression of the lymphoma. In case of unsuccessful *H. pylori* eradication, a second-line anti-*Helicobacter* therapy should be attempted with alternative triple- or quadruple-therapy regimens of proton-pump inhibitor plus antibiotics. However, it is still unknown whether *H. pylori* eradication will definitely cure the lymphoma; therefore, long-term follow-up of antibiotic-treated patients is mandatory. Cases of tumour recurrence following *H. pylori* reinfection have been reported, suggesting that residual dormant tumour cells can be present despite clinical and histologic remission. Relapses have also been documented in the absence of *H. pylori* reinfection, suggesting the emergence of B-cell lymphoma clones that are no longer antigen dependent.[8-9]

Several studies of post-antibiotic molecular follow-up showed that histological and endoscopic remission does not necessarily mean a cure. The long term persistence of monoclonal B-cells after histologic regression of the lymphoma has been detected by polymerase-chain reaction analysis in about half of the cases, suggesting that *H. pylori* eradication suppresses but does not eradicate the lymphoma clones.[8,15] Therefore, histological evaluation of repeat biopsies remains a fundamental follow-up procedure. Unfortunately, the interpretation of residual lymphoid infiltrate in post-treatment gastric biopsies can be very difficult and there are no uniform criteria for the definition of histologic remission. Wotherspoon in 1993 proposed a simple score to indicate the degree of confidence in the diagnosis of MALT lymphoma on small gastric biopsies1, this scoring system has been used to evaluate the response to therapy in some trials but many investigators found it difficult to apply in this setting and other criteria have been proposed.[8] Very recently a novel histological grading system has been proposed by Copie-Berman and colleagues16. This system, classifies the histological features in post-treatment gastric biopsies as "complete histological remission", "probable minimal residual disease", "responding residual disease", and "no change". It may become a useful tool but its reproducibility still needs to be confirmed on larger series.

The efficacy of antibiotic therapy is reduced in locally advanced disease, and as mentioned before, endoscopic ultrasound can be useful to predict the lymphoma response to *H. pylori* eradication. The response rate 70-90% for the mucosa-confined lymphomas but then decreases markedly and progressively for the tumors infiltrating the submucosa, the muscularis propria, and the serosa. In the cases with documented nodal involvement, a response is unlikely.[5,6] The t(11;18) translocation is absent in gastric MALT lymphomas showing complete regression,[17] but present in 77%

of non-responsive tumours, including 68% of those with the disease confined to the gastric wall.[18] Therefore, this translocation can be a valuable molecular marker to predict the therapeutic response of gastric MALT lymphoma to *H. pylori* eradication.[18,19]

### *References*


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