



**San Jose Gastroenterology**

2340 Montpelier Drive  
San Jose, CA 95116

231 O'Connor Drive  
San Jose, CA 95128

Phone: (408) 347-9001  
Fax: (408) 347-9004  
www.sjgi.com

Ruel T. Garcia, M.D.  
Brian S. Levitt, M.D.  
Huy A. Nguyen, M.D.  
Khanh K. Nguyen, M.D.  
Huy N. Trinh, M.D.

San Jose Gastroenterology Newsletter is a professional letter focusing on the topics that physicians encounter in daily practice. This letter is printed periodically by San Jose Gastroenterology. The sources of this letter were adapted from Gastroenterology Journals for informational purposes and for communication with our colleagues. We will provide references for our sources if requested.

To sign up for email of GI Focus or to provide comments, support or requests, please email us at GIfocus@sjgi.com.

**Hepatitis B and "Normal" ALT: Not Always a Safe Place to Be**

It is estimated that about 350 million people worldwide have chronic hepatitis B infection (CHB). This disease is particularly prevalent in the Asian/Pacific Island (API) community including in the US<sup>1,2</sup>. Since the vast majority of patients with CHB are asymptomatic, assessing disease severity usually relies on laboratory tests. This will predict prognosis and help determine if long-term antiviral treatment should be initiated. By far, the simplest and most commonly used method is to check and follow liver function tests especially the serum alanine aminotransferase (ALT) level. Many clinicians rely on elevations of ALT above the upper limit of normal (>ULN) to determine if a patient should be referred for further evaluation and possible treatment.

New data suggests that relying on ALT >ULN as a marker for significant liver disease in CHB is inadequate. The commonly used ULN for ALT (for example: <40 U/L for Quest, and <60 U/L Stanford Lab) is too high. Based on recent studies, the true normal ALT level should be <30 U/L for men and <19 U/L for women<sup>3,4</sup>. Therefore, clinicians should be conscious of this and specifically look at the actual ALT rather than relying on what the lab report flags as "abnormal". Even when the ALT is just slightly above normal (1-2X ULN), which translates to ALT 30-60 for men and 20-40 for women, there is still a high prevalence of significant liver disease in this population.

San Jose Gastroenterology in collaboration with Pacific Health Foundation and Stanford University recently published a study in the journal Clinical Gastroenterology and Hepatology, on the prevalence of significant liver disease in CHB patients with only slightly elevated ALT<sup>5</sup>. A total of 193 patients with ALT 1-2X ULN based on new criteria <30 for men, <19 for women, underwent liver biopsy. Patients were considered to have significant

liver histology if the fibrosis stage was  $\geq 2$ , or stage 1 and at least grade 2 inflammation. Significant liver histology was found in 20-27% and 44-53% of patients with ALT 1-1.5X ULN, and 1.5-2X ULN respectively. On multivariate analysis, independent predictors for significant histology were age  $\geq 35$ , male gender, and increasing ALT level. In fact, in patients with age  $\geq 35$ , the prevalence of significant liver disease was 54%, and with age  $\geq 50$ , this rose to 57-75%.

Patients with significant liver histology generally should be treated with long-term antiviral medication<sup>4</sup>. Therefore, it is important to recognize that even patients with normal and mildly elevated ALT are still at risk for significant liver disease especially as they get older (age >35).

The true upper limit of normal ALT should be  $\leq 30$  U/L for men and  $\leq 19$  U/L for women.

Significant liver disease was found in 54% of patients with age  $\geq 35$ , and 57-75% of patients  $\geq 50$ , even when ALT was only slightly elevated (30-60 U/L for men, and 20-40 U/L for women).

Most patients with significant liver disease on liver biopsy should be treated with long-term antiviral drugs, regardless of ALT level.

1. Lok, ASF. AASLD Guidelines. Chronic Hepatitis B. Hepatology 2007; 45: 507-539.
2. Lin, SY, et al. Why we should routinely screen Asian American adults for hepatitis B: A cross-sectional study of Asians in California. Hepatology 2007; 46: 1034-1040.
3. Kim, HC, et al. Normal serum aminotransferase concentration and risk of mortality from liver disease: prospective cohort study. BMJ 2004; 328: 983-989.
4. Keeffe, E, et al. A Treatment Algorithm for the Management of Chronic Hepatitis B Infection in the United States: An Update. Clinical Gastroenterology and Hepatology 2006; 4: 936-962.
5. Tsang, PSY, et al. Significant Prevalence of Histologic Disease in Patients with Chronic Hepatitis B and Mildly Elevated Alanine Aminotransferase Levels. Clinical Gastroenterology and Hepatology 2008; 6: 569-574.

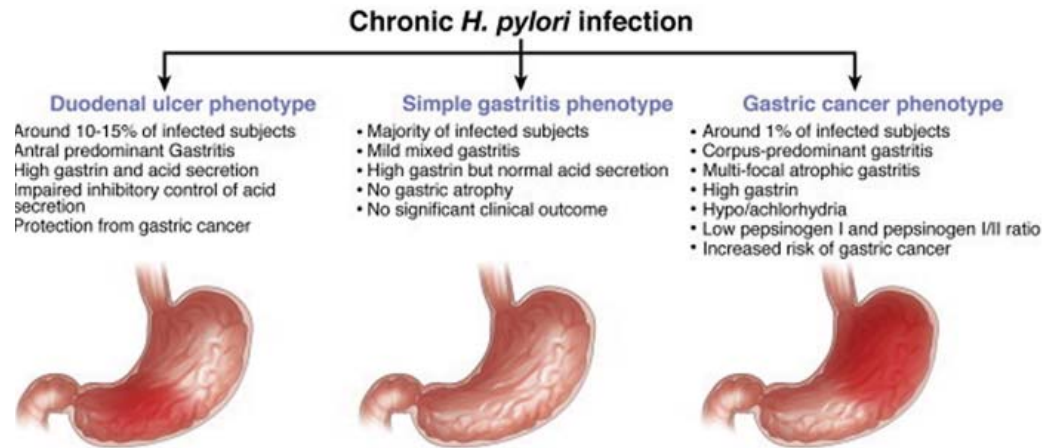


## Update in H pylori

*Helicobacter pylori* infection is usually acquired early in childhood and lasts for a lifetime. Though transmission occurs both from fecal-oral and oral routes, the predominant mechanism of transmission remains unclear<sup>1</sup>. Prevalence reaches 70-80% in Asia and 30-40% in the USA and Western Europe. The majority of those infected (80-90%) will carry and transmit the infection without any symptoms of disease. Therefore, some argue that *H. pylori* should be considered commensal, rather than a pathogen. However, it is the strongest risk factor for gastroduodenal ulcers, with infection present in 60-80% of gastric and 95% of duodenal ulcers<sup>2</sup>. It is also the first bacterium to be classified as a definite carcinogen by the World Health Organization, due to its association with gastric adenocarcinoma and gastric lymphoma.



There are three main outcomes of chronic infection, as illustrated below:



There is clear evidence for *H. pylori* eradication to prevent ulcer recurrence, and even as a stand-alone treatment for gastric MALT (50% remission in one study<sup>3</sup>). There is no clear data to support eradication to prevent progression to gastric cancer, however<sup>4</sup>. There have been two meta-analyses of *H. pylori* eradication in non-ulcer dyspepsia: one showed no improvement<sup>5</sup> and the other showed a small but statistically significant benefit<sup>6</sup>.



## Selected Regimens for Helicobacter pylori Eradication<sup>7</sup>

Treatment regimen	Duration	Eradication rate (%)
Proton pump inhibitor twice daily, plus amoxicillin, 1 g twice daily, plus clarithromycin 500 mg twice daily	10 to 14 days	86
Bismuth subsalicylate 525 mg four times daily, plus metronidazole 250 mg four times daily, plus tetracycline 500 mg four times daily, H2 blocker	14 days (then H2 blocker alone for 14 days more)	80



Recent studies show second line therapy with a levofloxacin-based regimen, along with amoxicillin and PPI, have an eradication rate of about 80%<sup>8</sup>.

### Refs:

1. Amieva MR and El-Omar EM, Host bacterial interactions in *Helicobacter pylori* infection. *Gastro* 2008;134:306-323.
2. Marshall BJ, *JAMA* 1995;274:1064-1066.
3. Steinbach G et al. *Ann Int Med* 1999;131:88.
4. Wong et al. *JAMA* 2004;291:187-194.
5. Laine et al. *Ann Intern Med* 2001;134:361.
6. Moayyedi P et al. *Am J Gastro* 2003;98:2621-2626.
7. Ables AZ et al. *Am Fam Physician* 2007;75:351-8.
8. Gisbert JP et al. *Am J Gastro* 2008;103:71-6.

