

only 5.5% documented their responses. From non-documented vaccinees, 9% were susceptible to HBV infection. It seems that a voluntary vaccination policy may not be as effective, as shown in another study⁵ where between 25% and 55% of HCW were not vaccinated under a voluntary system.

Therefore, optimal vaccine coverage would be best achieved by mandatory vaccination of all HCW while being trained. In addition all vaccinated HCW should have their response documented.

M J Saffar, A R Jooyan,
M R Mahdavi, A R Khalilian

Department of Pediatrics, Mazandaran University of
Medical Sciences, Bouali - Cina Hospital, Sari, Iran

References

1. American Academy of Pediatrics. *Hepatitis B. In: Pickering LK, Ed. Red Book: 2003 Report of the Committee on Infectious Diseases*, 26th ed. EIK Grove Village, IL: Academy of Pediatrics. 2003: p. 318-36.
2. Gunson RN, Shouval D, Rogendorf M, Zaaijer H, Nicholas S, Holzmann H, *et al.* Hepatitis B virus (HBV) and hepatitis C virus (HCV) infection in health care workers (HCWs): guidelines for prevention of transmission of HBV and HCV from HCWs to patients. *J Clin Virol* 2003;27:213-30.
3. Merat SH, Malekzadeh R, Rezvan M. Hepatitis in Iran. *Arch Iranian Med* 2000;3:192-201.
4. Lewis TL, Alter MJ, Chalmer TC, Holland PV, Purcell RH, Alling DW, *et al.* A comparison of the frequency of hepatitis B antigen and antibody in hospital and non-hospital personnel. *New Engl J Med* 1973;289:647-51.
5. Mahoney FJ, Stewart K, Hu H, Coleman P, Alter MJ. Progress toward the elimination of hepatitis B virus transmission among health care workers in the United States. *Arch Intern Med* 1997;157:2601-5.

Correspondence to: Dr Saffar. Fax: +98 (151) 223 4507. E-mail: saffar@softhome.net

Hepatitis C infection correlates with alteration of serum immunoglobulins pattern in chronic liver disease

Hyperglobulinemia affecting the three main immunoglobulin classes was considered a hallmark of chronic active hepatitis,¹ but studies before 1989 probably contained patients with both autoimmune hepatitis and chronic hepatitis C virus (HCV) infection.

We assayed serum levels of total IgG, IgM, IgA and IgG subclasses (IgG 1-4) in 50 patients (40 men; median age 35 years) with chronic hepatitis C and 25 healthy control subjects. All patients had positive serum anti-HCV antibody, positive serum HCV RNA, and histologically-proven chronic hepatitis. IgG, IgA and IgM were assayed by nephelometry (*BN-II* Analyzer; Behring Diagnostics, Marburg, Germany). IgG subclasses

were assayed using human IgG subclasses enzyme immunoassay kit (*Binding Site*, Birmingham, UK). Median values were compared by using the Mann-Whitney *U* test.

IGM, total IgG, IgG1, IgG2, IgG3 and IgG4 levels were increased in patients with HCV infection when compared with the control subjects (Table).

Table: Concentrations of serum immunoglobulins (mg/dL) in healthy subjects and in chronic HCV patients

Variable	Chronic HCV patients	Healthy controls	p value
IgA	400 (375, 421)	387.5 (350, 450)	0.4
IgM	173 (160, 190)	127 (110, 150)	<0.001
IgG	1395 (1350, 1448.5)	1111 (1065, 1150)	<0.001
IgG1	906.8 (836.7, 941.5)	722 (692, 747.5)	<0.001
IgG2	365.5 (353.7, 379.5)	291 (279, 301)	<0.001
IgG3	59.99 (58.1, 62.3)	47.8 (45.8, 49.5)	<0.001
IgG4	62.8 (60.8, 65.2)	50 (47.9, 51.8)	<0.001

Values as median (5th, 95th percentiles)

HCV infection is associated with cryoglobulinemia and occasionally with B-cell lymphoproliferative disorders.² Andre and McQuilkan³ reported that the increase in gamma globulin is due to stimulation of numerous plasma cell clones by exogenous or endogenous antigens. A specific cytokine imbalance could prompt B cells to increase IgG production in patients with HCV infection, independently from liver damage.

Gonzalez-Quintela *et al*⁴ reported elevated IgG in these patients. Elevation of IgG1 and IgG2 level may be due to higher humoral response, and the lymphocytotoxic activity has been found mainly in these subclasses. These findings are similar to those in models of generalized enhanced B-cell responses. In many of these models elevated serum IgG subclass levels have been noticed to exist along with elevated specific antibody levels.⁵

Serum IgM levels were higher in patients with chronic hepatitis C than in healthy controls, corroborating earlier findings.^{6,7} The elevated levels of IgM and IgG in HCV infection could be due to dysfunction of T cells, currently taken as responsible for virus persistence.⁸

IgA levels were similar in patients and control subjects. Elevated IgA level has been reported in alcoholic liver disease.^{5,6,7} Watt *et al*⁹ reported elevated IgA in chronic HCV infection.

In conclusion, serum immunoglobulin pattern is altered in chronic hepatitis C infection. This may be useful in differentiation of these patients.

Ibrahim M El-Kady, Mahmoud Lotfy, Wesam A Nasif,
Aymen El-Kenawy, Gamal A Badra*

Genetic Engineering and Biotechnology Research
Institute, and *National Liver Institute, Minufiya
University, Sadat City, Minufiya, Egypt

References

1. Martin DM, Vroom DH, Nasrallah SM. Value of serum

- immunoglobulins in the diagnosis of liver disease. *Liver* 1984;4:214-8.
2. Zignego AL, Gianelli F, Marrochi ME, Mazzocca A, Ferri C, Giannini C, *et al.* T (14; 18) translocation in chronic hepatitis C virus infection. *Hepatology* 2000;31:474-9.
 3. Andre CM, McQuilkan SM. *Plasma proteins*. In: McGiven AR, Ed. Immunological Investigation of Renal Disease. Edinburgh, etc: Churchill Livingstone. 1980: p. 4.
 4. Gonnzalez-Quintela A, Alende MR, Gamallo R, Gonzalez-Gil P, Lopez-Ben S, Tome S, *et al.* Serum immunoglobulins (IgG, IgA, IgM) in chronic hepatitis C. A comparison with non-cirrhotic alcoholic liver disease. *Hepatogastroenterology* 2003;50:2121-6.
 5. Aceti A, Pennica A, Teggi A, Fondacaro LM, Caferro M, Leri O, *et al.* IgG subclasses in human hydatid disease: prominence of the IgG4 response. *Int Arch Allergy Immunol* 1993;102:347-51.
 6. Sarin AK, Dhingra N, Bansal A, Malhotra S, Guptan RC. Dietary and nutritional abnormalities in alcoholic liver disease: a comparison with chronic alcoholics without liver disease. *Am J Gastroenterol* 1997;92:777-83.
 7. Caly WR, Strauss E, Carrilho FJ, Laudanna AA. Different degrees of malnutrition and immunological alterations according to the etiology of cirrhosis: a prospective and sequential study. *Nutrition J* 2003;2:10-9.
 8. Yao Z-Q, Nguyen DT, Hiotellis AI, Hahn YS. Hepatitis C virus core protein inhibits human T lymphocyte responses by a complement-dependent regulatory pathway. *J Immunol* 2001;167:5264-72.
 9. Watt K, Uhanova J, Gong Y, Kaita K, Doucette K, Pettigrew N, *et al.* Serum immunoglobulins predict the extent of hepatic fibrosis in patients with chronic hepatitis C virus infection. *J Viral Hepat* 2004;11:251-6.

Correspondence to: Dr Lotfy, Molecular and Cellular Biology Department, Genetic Engineering and Biotechnology Research Institute, Minufiya University, Sadat City, P.O. 79, Minufiya, Egypt. E-mail: mlotfy2000@yahoo.com

Gastric cancer in southern Croatia during 2002-2003

Despite an overall declining incidence, gastric adenocarcinoma remains the second most common cause of death from malignant disease worldwide.¹ About 85 percent of stomach cancers are adenocarcinomas, with 15 percent due to lymphomas and gastrointestinal stromal tumors. High rates are observed in Japan, China, Finland, and Eastern Europe, and low incidence is observed in Western Europe and USA.¹ The annual incidence of gastric cancer in Croatia in the last thirty years is in decline, though it is still rather high at approximately 30 cases per 100,000 in the male population and 23 cases per 100,000 in females.²

We retrospectively analyzed the data on 86 cases of histologically diagnosed and surgically resected gastric adenocarcinoma seen in our hospital during 2002-2003. Adenocarcinoma was classified according to his-

tologic subtype, depth of invasion, site, presence of *Helicobacter pylori*, and age and gender ratio.

The mean (SD) age of the patients was 60 (20) years, and male / female ratio was 2.5:1 (62/24) which is in congruence with other studies.¹ Approximately 37 percent of gastric carcinomas in Western Europe and the United States originate in the upper third of the stomach, whereas 20 percent originate in the middle third, and 30 percent in the lower third; 12 percent of gastric carcinomas involve the entire stomach.^{1,3} In our patients the most frequent location was antrum (48 percent), followed by corpus (31.4 percent). The proximal stomach was involved in 19.8 percent (cardia 15.1 percent, fundus 4.7 percent). Several studies have shown sharp decrease in the incidence of the intestinal type of gastric adenocarcinoma^{4,5} but in our population the incidence is still 84.9 percent. In Western countries the incidence of early cancer exceeds 16 percent; in Japan it ranges from 40 percent to 60 percent.^{1,6} In our study the figure was about 16 percent. Epidemiologic studies have demonstrated an association between *Helicobacter pylori* infection and risk of gastric cancer.^{7,8} In our study 65.1 percent of patients were infected by *H. pylori*, which is similar to the prevalence in our general population (68 percent).⁹

We intend to initiate a program of screening endoscopy for persons 50 years of age or older in order to identify early gastric carcinoma. We also believe that control of *H. pylori* infection has the potential for prevention of gastric cancer.

Stjepan Mise, Ante Tonkic, Ivana Jukic, Marina Titlic, Valdi Pesutic-Pisac,* Darko Alfirevic*
Divisions of Gastroenterology and *Histopathology, Clinical Hospital Split, Split, Croatia

References

1. Fuchs CS, Mayer RJ. Gastric carcinoma. *N Engl J Med* 1995;333:32-41.
2. Roth A. *Gastric cancer*. In: Vucelic B, Ed. Gastroenterology and Hepatology. Zagreb: Medicinska Naklada. 2002: p. 548-50.
3. Blot WJ, Devesa SS, Kneller RW, Fraumeni JF Jr. Rising incidence of adenocarcinoma of the esophagus and gastric cardia. *JAMA* 1991;265:1287-9.
4. Craanen ME, Dekker W, Bolk P, Ferwerda J, Tytgat GN. Time trends in gastric carcinoma: changing patterns of type and location. *Am J Gastroentrol* 1992;87:572-9.
5. Henson DE, Dittus C, Younes M, Nguyen H, Albores-Saavedra J. Differential trends in the intestinal and diffuse types of gastric carcinoma in the United States, 1973-2000; increase in the signet ring cell type. *Arch Pathol Lab Med* 2004;128:765-70.
6. Lauwers GY, Shimizu M, Correa P, Riddell RH, Kato Y, Lewin KJ, *et al.* Evaluation of gastric biopsies for neoplasia – differences between Japanese and Western pathologists. *Am J Surg Pathol* 1999;23:511-8.