

Yoshinori Horie, M.D., Ph.D.

Specially-appointed Professor of Keio University, Graduate School of Media and

Governance

Assistant Director of Shonan Keiiku Hospital

Visiting professor of Keio University

Specialty

Therapeutic strategy for severe alcoholic hepatitis

Epidemiology and prognosis of Hepatocellular carcinoma, alcohol liver disease and nonalcoholic fatty liver disease in Japan

Oxidative stress and microvascular dysfunction in alcohol liver disease

Education

Year	Degree	Field of Study	Institution
2003	PhD	Role of ICAM-1 in chronic ethanol consumption-enhanced liver injury after gut ischemia/reperfusion in rats.	Keio University School of Medicine

Appointments at Hospitals

Year	Position title	Division	Institution
2017-present	Professor	Graduate School of Media and Governance	Keio University
	Assistant Director		Shonan Keiiku Hospital
2010-2017	Professor	Research Center of Clinical Medicine	International University of Health and Welfare
	Director	Internal medicine	Sanno Hospital
2004-2010	Director	Internal medicine	EIJU General Hospital
2003-present	Assistant Professor	Gastroenterology and Hepatology	Keio University School of Medicine
1994-1997		Physiology	Louisiana State University Shreveport
1992-2003		Gastroenterology and Hepatology	Keio University School of Medicine

1990-1992	Internal Medicine	National Hospital Organization Kurihama Alcoholism Center
1988-1990	Internal Medicine	Keio University School of Medicine

Professional Societies

Title of role	Society Name
Member	International Society for Biomedical Research on Alcoholism
Member	Annual Research Society on Alcoholism Scientific Meeting
Director	Japanese Medical Society of Alcohol and Drug Studies
Auditor	Japanese Society of Biomedical Research on Alcohol
Councilor	Japanese Society of Gastroenterology
Councilor	Japanese Society of Hepatology
Member	Japan Gastroenterological Endoscopy Society
Member	Japanese Society of Internal Medicine
Member	Japanese Society of Microcirculation

Publications

1. Moriya S, Nagata S, Yokoyama H, Kato S, Horie Y, Ito T, Ebihara Y, Ishii H.

Expression of gamma-glutamyl transpeptidase mRNA after depletion of glutathione in rat liver. Alcohol Alcohol 1994; 29 Suppl 1: 107-111.

2. Horie Y, Wolf R, Miyasaka M, Anderson DC, Granger DN. Leukocyte adhesion and the hepatic microvascular responses to intestinal ischemia-reperfusion. Gastroenterology 1996; 111: 666-673.

3. Ohki E, Kato S, Horie Y, Mizukami T, Tamai H, Yokoyama H, Ito D, Fukuda M, Suzuki H, Kurose I, Ishii H. Chronic ethanol consumption enhances endotoxin induced hepatic sinusoidal leukocyte adhesion. *Alcohol. Clin. Exp. Res.* 1996; 20: 350A-355A.

4. Kurose I, Higuchi H, Kato S, Miura S, Watanabe N, Kamegaya Y, Tomita K, Takaishi M, Horie Y, Fukuda M, Mizukami K, Ishii H. Oxidative stress on mitochondria and cell membrane of cultured rat hepatocytes and perfused liver exposed to ethanol. *Gastroenterology* 1997; 112:1331-1343.

5. Horie Y, Wolf R, Anderson DC, Granger DN. Hepatic leukostasis and hypoxic stress in adhesion molecule-deficient mice after gut ischemia-reperfusion. *J. Clin. Invest.* 1997; 99: 781-788.

6. Horie Y, Chervenak RP, Wolf R, Gerritsen ME, Anderson DC, Komatsu S, Granger DN. Lymphocytes mediate TNF- α induced endothelial cell adhesion molecule expression: Studies on severe combined immunodeficient and RAG-1 mutant mice. *J. Immunol.* 1997; 159:5053-5062.

7. Horie Y, Wolf R, Granger DN. Role of nitric oxide in gut ischemia-reperfusion-induced hepatic microvascular dysfunction. *Am. J. Physiol.* 1997; 273; G1007-G1013.

8. Horie Y, Wolf R, Russell J, Shanley TP, Granger DN. Role of Kupffer cells in gut ischemia-reperfusion-induced hepatic microvascular dysfunction in mice. *Hepatology.* 1997; 26: 1499-1505.

9. Horie Y, Kato S, Ohki E, Hamamatsu S, Fukumura D, Kurose I, Suzuki H, Suematsu M, Miura S, Ishii H. Effect of lipopolysaccharides on erythrocyte velocity in rat liver. *J. Gastroenterol.* 1997; 32: 783-790.

10. Horie Y, Wolf R, Anderson DC, Granger DN. Nitric oxide modulates gut ischemia/reperfusion-induced P-selectin expression in murine liver. *Am. J. Physiol.* 1998; 275: H520-H526.

11. Horie Y, Wolf R, Flores SC, McCord JM, Epstein CJ, Granger DN. Transgenic mice with increased Copper/Zinc-superoxide dismutase activity are resistant to hepatic

leukostasis and capillary No-reflow after gut Ischemia/Reperfusion. *Circ. Res.* 1998; 83: 691-696.

12. Mori N, Horie Y, Gerritsen ME, Anderson DC, Granger DN. Anti-inflammatory drugs and endothelial cell adhesion molecule expression in murine vascular beds. *Gut* 1999; 44: 186-195.

13. Mori N, Horie Y, Gerritsen ME, Granger DN. Ischemia-reperfusion induced microvascular responses in LDL-receptor $-/-$ mice. *Am. J. Physiol.* 1999; 276:H1647-1654.

14. Horie Y, Wolf R, Chervenak RP, Jennings SR, Granger DN. T-lymphocytes contribute to hepatic leukostasis and hypoxic stress induced by gut ischemia reperfusion. *Microcirculation* 1999; 6: 267-280.

15. Nakamura Y, Yokoyama H, Okamura Y, Ohgo H, Fukuda M, Horie Y, Kato S, Ishii H. Evidence for ethanol oxidation by Kupffer cells. *Alcohol Clin Exp Res* 1999; 23(4 Suppl): 92S-95S.

16. Tamai H, Kato S, Horie Y, Ohki E, Yokoyama H, Ishii H. Effect of acute ethanol administration on the intestinal absorption of endotoxin in rats. *Alcohol Clin Exp Res* 2000; 24: 390-394.

17. Horie Y, Kato S, Ohki E, Tamai H, Yamagishi Y, Ishii H. Hepatic microvascular dysfunction in endotoxemic rats after acute ethanol administration. *Alcohol Clin Exp Res* 2000; 24: 691-698.

18. Horie Y, Kimura H, Kato S, Ohki E, Tamai H, Yamagishi Y, Ishii H. Role of nitric oxide in endotoxin-induced hepatic microvascular dysfunction in rats chronically fed ethanol. *Alcohol Clin Exp Res* 2000; 24: 845-851.

19. Horie Y, Kato S, Ohki E, Tamai H, Ishii H. Role of Endothelin in Endotoxin induced Hepatic Microvascular Dysfunction in Rats Fed Ethanol Chronically. *J. Gastroenterol. Hepatol.* 2001; 16: 916-922.

20. Mori N, Horie Y, Nimura Y, Wolf R, Granger DN. Hepatic microvascular responses to ischemia-reperfusion in low-density lipoprotein receptor knockout mice. *Am J Physiol* 2000; 279: G1257-1264.

21. Horie Y, Kajihara M, Yamagishi Y, Kimura H, Tamai H, Kato S, Ishii H. A Japanese herbal medicine, Sho-Saiko-To, prevents ischemia/reperfusion-induced hepatic microvascular dysfunction in rats. *J Gastroenterol Hepatol* 2001; 16: 1260-1266.

22. Yamagishi Y, Horie Y, Kato S, Kajihara M, Tamai H, Granger DN, Ishii H. Ethanol modulates gut ischemia/reperfusion-induced liver injury in rats. *Am J Physiol* 2002; 282: G640-G646.

23. Zeki S, Miura S, Suzuki H, Watanabe N, Adachi M, Yokoyama H, Horie Y, Saito H, Kato S, Ishii H. Xanthine oxidase-derived oxygen radicals play significant roles in the development of chronic pancreatitis in WBN/Kob rats. *J Gastroenterol Hepatol* 2002; 17: 606-616.

24. Horie Y, Yamagishi Y, Kato S, Kajihara M, Tamai H, Granger DN, Ishii H. Role of ICAM-1 in chronic ethanol consumption-enhanced liver injury after gut ischemia-reperfusion in rats. *Am J Physiol Gastrointest Liver Physiol* 2002; 283: G537-543.

25. Tamai H, Horie Y, Kato S, Yokoyama H, Ishii H. Long-term ethanol feeding enhances susceptibility of the liver to orally administered lipopolysaccharides in rats. *Alcohol Clin Exp Res* 2002; 26: 75S-80S.

26. Horie Y, Ishii H. National survey of alcoholic liver diseases in Japan. Proceeding in Asian Pacific Association for the Study of the Liver Meeting 2002. 2002; 109-112..

27. Horie Y, Yamagishi Y, Kato S, Kajihara M, Kimura H, Ishii H. Low-dose ethanol attenuates gut ischemia/reperfusion-induced liver injury in rats via nitric oxide production. *J Gastroenterol Hepatol* 2003; 18: 211-217.

28. Horie Y, Han JY, Kajihara M, Tamai H, Shinzo Kato S, and Ishii H. A herbal medicine, Cardiotonic Pills, prevents gut ischemia-reperfusion-induced hepatic microvascular dysfunction in rats. *Microcirculation Ann* 2003; 19: 31-32.

29. Adachi M, Saito H, Kobayashi H, Horie Y, Kato S, Yoshioka M, Ishii H. Hepatic injury in 12 patients taking the herbal weight loss AIDS Chaso or Onshido. *Ann Intern Med.* 2003; 139: 488-492.
30. Horie Y, Yamagishi Y, Kajihara M, Kato S, Ishii H. National Survey of Hepatocellular Carcinoma in Heavy Drinkers in Japan. *Alcohol Clin Exp Res* 2003; 27 (Suppl): 32S-36S.
31. Yamagishi Y, Horie Y., Kajihara M, Konishi M, Ebinuma H, Saito H, Kato S, Yokoyama A, Maruyama K, Ishii H. Hepatocellular carcinoma in heavy drinkers with negative markers for viral hepatitis. *Hepatol Res.* 2004; 28: 177-183.
32. Horie Y, Kajihara M, Mori S, Yamagishi Y, Kimura H, Tamai H, Kato S, Ishii H. A Japanese herbal medicine, "Saiko-Keishi-To", prevents ischemia/reperfusion-induced hepatic microvascular dysfunction in rats. *World J Gastroenterol* 2004; 10; 2241-2244.
33. Fukuda M, Yokoyama H, Mizukami T, Ohgo H, Okamura Y, Kamegaya Y, Horie Y, Kato S and Ishii H. Kupffer cell depletion attenuates superoxide anion release into the hepatic

sinusoids after lipopolysaccharide treatment. J Gastroenterol Hepatol 2004;
19:1155-1162, 2004.

34. Han JY, Akiba Y, Miura S, Horie Y, Suzuki H, Kato S, Nagata H, Oda M, Ishii H,
and Hibi T. Cardiotonic Pills, improves the aggregation of the mesenteric microvasculature
disturbances following reperfusion in chronically ethanol-fed rats. Microcirculation Ann
2004; 20: 23-24.

35. Horie Y, Han JY, and Ishii H. Herbal Cardiotonic Pills prevent gut
ischemia-reperfusion-induced hepatic microvascular dysfunction in rats fed ethanol
chronically. Microcirculation Ann 2004; 20: 31-32.

36. Horie Y, Han JY, Kajihara M, Mori S, Konishi M, Kajihara M, Kaneko T, Yamagishi Y,
Shinzo Kato S, and Ishii H. Herbal Cardiotonic Pills prevents gut
ischemia-reperfusion-induced hepatic microvascular dysfunction in rats fed ethanol
chronically. World J Gastroenterol 2005; 11(4):511-515.

37. Tomita K, Tamiya G, Ando S, Ohsumi K, Chiyo T, Mizutani A, Kitamura N, Toda K, Kaneko T, Horie Y, Han JY, Kato S, Shimoda M, Oike Y, Tomizawa M, Makino S, Ohkura T, Saito H, Kumagai N, Nagata H, Ishii H, Hibi T. Tumor necrosis factor- α signalling through activation of Kupffer cells plays an essential role in liver fibrosis of nonalcoholic steatohepatitis in mice. *Gut* 2006; 55: 415-424.

38. Horie Y, Ishii H, Hibi T. Severe alcoholic hepatitis in Japan: prognosis and therapy. *Alcohol Clin Exp Res.* 2005; 29(12 Suppl):251S-258S.

39. Tomita K, Tamiya G, Ando S, Kitamura N, Koizumi H, Kato S, Horie Y, Kaneko T, Azuma T, Nagata H, Ishii H, Hibi T. AICAR, an AMPK activator, has protective effects on alcohol-induced fatty liver in rats. *Alcohol Clin Exp Res.* 2005; 29(12 Suppl):240S-245S.

40. Yamagishi Y, Saito H, Tada S, Horie Y, Kato S, Ishii H, Shimojima N, Haga J, Shimazu M, Kitajima M, Hibi T. Value of computed tomography-derived estimated liver volume/standard liver volume ratio for predicting the prognosis of adult fulminant hepatic failure in Japan. *J Gastroenterol Hepatol.* 2005; 20:1843-1849.

41. Horie Y, Ishii H, Hibi T. Oxidative stress and liver disease. Nippon Shokakibyō Gakkai Zasshi. 2006; 103:789-96.

42. Han JY, Horie Y, Li D, Akiba Y, Nagata H, Miura S, Oda M, Ishii H, Hibi T. Attenuating effect of Myakuryu on mesenteric microcirculatory disorders induced by ischemia and reperfusion. Clin Hemorheol Microcirc. 2006; 34:145-50.

43. Sun K, Wang CS, Guo J, Horie Y, Fang SP, Wang F, Liu YY, Liu LY, Yang JY, Fan JY, Han JY. Protective effects of ginsenoside Rb1, ginsenoside Rg1, and notoginsenoside R1 on lipopolysaccharide-induced microcirculatory disturbance in rat mesentery. Life Sci. 2007; 81:509-18.

44. Guo J, Sun K, Wang CS, Fang SP, Horie Y, Yang JY, Liu YY, Wang F, Liu LY, Fan JY, Hibi T, Han JY. Protective effects of dihydroxyphenyl lactic acid and salvianolic acid B on LPS-induced mesenteric microcirculatory disturbance in rats. Shock. 2008; 29: 205-211

45. Han JY, Horie Y, Miura S, Akiba Y, Guo J, Li D, Fan JY, Liu YY, Hu BH, An LH, Chang X, Xu M, Guo DA, Sun K, Yang JY, Fang SP, Xian MJ, Kizaki M, Nagata H, Hibi T. Compound Danshen injection improves endotoxin-induced microcirculatory disturbance in rat mesentery. *World J Gastroenterol.* 2007; 13: 3581-3591.

46. Ishii H, Horie Y, Yamagishi Y: Alcoholic liver disease with particular emphasis on alcoholic hepatitis: A clinical perspective. *Gut and Liver* 2007; 1(Suppl. 2):37-41.

47. Kajihara M, Horie Y, Ishii H. Non-alcoholic fatty liver disease (NAFLD) and non-alcoholic steatohepatitis (NASH) in Asian-Pacific region. *Gut and Liver* 2007; 1(Suppl. 2): 119-124.

48. Han JY, Horie Y, Fan JY, Sun K, Guo J, Miura S, Hibi T.. Potential of 3, 4-Dihydroxy-phenyl Lactic Acid for Ameliorating Ischemia-Reperfusion-Induced Microvascular Disturbance in Rat Mesentery. *Am J Physiol Gastrointest Liver Physiol* 2009; 296: G36-44

49. Han J-Y, Fan J-Y, Horie Y, Miura S, Cui D-H, Ishii H, Hibi T, Tsuneke H, Kimura I.

Ameliorating effects of compounds derived from salvia miltiorrhiza root extract on microcirculatory disturbance and target-organ injury by ischemia-reperfusion.

Pharmacology and Therapeutics 2008; 117: 280-295.

50. Yamagishi Y, Saito H, Ebinuma H, Kikuchi M, Ojiro K, Kanamori H, Tada S, Horie Y,

Kato S, Hibi T. A new prognostic formula for adult acute liver failure using computer

tomography-derived hepatic volumetric analysis. J Gastroenterol. 2009; 44: 615-623.

51. Horie Y, Kikuchi M, Yamagishi Y, Rumiko R, Ebinuma H, Saito H, Kato S, Ishii H, Hibi

T, and Han JY. Effect of a herbal medicine on fatty liver in rats fed ethanol chronically.

Jpn. J. Alcohol & Drug Dependence 2009; 44: 636-648.

52. Tokushige K, Hashimoto E, Horie Y, Taniai M, Higuchi S. Hepatocellular carcinoma

in Japanese patients with nonalcoholic fatty liver disease, alcoholic liver disease, and

chronic liver disease of unknown etiology: report of the nationwide survey. J

Gastroenterol. 2011; 46:1230-1237

53. Horie Y, Yamagishi Y, Ebinuma H, Hibi T. Therapeutic strategies for severe alcoholic hepatitis. *Clin Res Hepatol Gastroenterol*. 2011; 35, 738-744.

54. Ebinuma H, Saito H, Tada S, Nakamoto N, Ohishi T, Tsunematsu S, Kumagai N, Tsuchimoto K, Tsukada N, Inagaki Y, Horie Y, Takahashi M, Atsukawa K, Okamura Y, Kanai T, Hibi T. Disadvantages of peginterferon and ribavirin treatment in older patients with chronic hepatitis C: an analysis using the propensity score. *Hepatol Int*. 2011 Sep 10. [Epub ahead of print] PMID: 22020828

55. Horie Y. Granulocytapheresis and plasma exchange for severe alcoholic hepatitis. *J Gastroenterol Hepatol*. 2012; 27 Suppl 2:99-103.

56. Horie Y, Yamagishi Y, Ebinuma H, Hibi T. Obesity, Type 2 Diabetes, Age and Female Gender Are Significant Risk Factors in the Development of Alcoholic Liver Cirrhosis. *Hepatol Int*. 2013; 7: 280-285.

57. Tokushige K, Hashimoto E, Horie Y, Tani M, Higuchi S. Hepatocellular carcinoma based on cryptogenic liver disease: The most common non-viral hepatocellular carcinoma in patients aged over 80 years. *Hepatol Res.* 2015; 45: 441-447.

58. Kagawa T, Hirose S, Arase Y, Oka A, Anzai K, Tsuruya K, Shiraishi K, Orii R, Ieda S, Nakazawa T, Tomita K, Hokari R, Miura S, Ebinuma H, Saito H, Kitamura T, Horie Y, Okuse C, Wasada M, Inoko H, Tohkin M, Saito Y, Maekawa K, Takikawa H, and Tetsuya Mine T. No Contribution of the ABCB11 p.444A Polymorphism in Japanese Patients with Drug-induced Cholestasis *Drug Metab Dispos* 2015; 43: 691-697.

59. Kikuchi M, Horie Y, Ebinuma H, Taniki N, Nakamoto N, Kanai T. Alcoholic liver cirrhosis and significant risk factors for the development of alcohol-related hepatocellular carcinoma—Japan, 2012. *Nihon Arukoru Yakubutsu Igakkai Zasshi*, 2015; 50, 222-234.

60. Osaki Y, Kinjo A, Higuchi S, Matsumoto H, Yuzuriha T, Horie Y, Kimura M, Kanda H and Yoshimoto H. Prevalence and Trends in Alcohol Dependence and Alcohol Use Disorders in Japanese Adults; Results from Periodical Nationwide Surveys. *Alcohol and Alcoholism*, 2016; 51, 465-473.

61. Horie Y, Kikuchi M, Ebinuma H, Taniki N, Umeda R, Shiba S, Taniki N, Chu P,
Nakamoto N, Kanai T. Current Status of Alcoholic Hepatitis in Japan (2011– 2013). *Nihon
Arukoru Yakubutsu Igakkai Zasshi*, 2017; 52, 177-192.

Review

1. Horie Y, Ishii H. Liver dysfunction elicited by gut ischemia-reperfusion. *Pathophysiology* 2001; 8: 11-20.
2. Horie Y, Ishii H. (Editorial) What factors play a crucial role in the pathogenesis of alcohol related chronic pancreatitis and liver cirrhosis? *J Gastroenterol* 2004; 39, 915-917.
3. Horie Y, Kikuchi M, Ebinuma H, Kanai T. Current Status of Alcoholic Liver Disease in Japan and Therapeutic Strategy. *Nihon Arukoru Yakubutsu Igakkai Zasshi*, 2016; 51, 71-90.