

43. Iijima T, Nambu M: Changes in ICG plasma clearance and excretion rate into bile and urine of ICG before and after exercise in patients with chronic liver diseases. *Gastroenterol Jpn* 1989;24:338.
44. Cales P, Grasset D, Ravaud A, Meskens C, Blanc M, Vinel JP, Cottonat J, Pascal JP: Pharmacodynamic and pharmacokinetic study of propranolol in patients with cirrhosis and portal hypertension. *Br J Clin Pharmacol* 1989;27:763-70.
45. Takiguchi F: [The effects of exercise on liver function in patients with chronic liver disease] *Nippon Ika Daigaku Zasshi* 1989;56:132-43.
46. Cales P, Pierre-Nicolas M, Guell A, Mauroux JL, Franco-Sempe A, Vinel JP, Geraud G, Pascal JP: Propranolol does not alter cerebral blood flow and functions in cirrhotic patients without previous hepatic encephalopathy. *Hepatology* 1989;9:439-42.
47. Agusti AG, Roca J, Rodriguez-Roisin R, Mastai R, Wagner PD, Bosch J: Pulmonary hemodynamics and gas exchange during exercise in liver cirrhosis. *Am Rev Respir Dis* 1989;139:485-91.
48. Kelbaek H, Rabol A, Brynjolf I, Eriksen J, Bonnevie O, Godtfredsen J, Munck O, Lund JO: Haemodynamic response to exercise in patients with alcoholic liver cirrhosis. *Clin Physiol* 1987;7:35-41.
49. Pitts TO, Van Thiel DH: Urinary tract infections and renal papillary necrosis in alcoholism. *Recent Dev Alcohol* 1986;4:341-55.
50. Ratge D, Brugger G, Wehr M, Bode JC, Wisser H: Catecholamines in the plasma and urine of patients with alcoholic liver damage under resting and exercise conditions. *J Clin Chem Clin Biochem* 1985;23:447-52.
51. Ohnishi K, Saito M, Nakayama T, Iida S, Nomura F, Koen H, Okuda K: Portal venous hemodynamics in chronic liver disease: effects of posture change and exercise. *Radiology* 1985;155:757-61.
52. Kelbaek H, Eriksen J, Brynjolf I, Raboel A, Lund JO, Munck O, Bonnevie O, Godtfredsen J: Cardiac performance in patients with asymptomatic alcoholic cirrhosis of the liver. *Am J Cardiol* 1984;54:852-5.
53. Mills PR, Rae AP, Farah DA, Russell RI, Lorimer AR, Carter DC: Comparison of three adrenoceptor blocking agents in patients with cirrhosis and portal hypertension. *Gut* 1984;25:73-8.
54. Kennedy TC, Knudson RJ: Exercise-aggravated hypoxemia and orthodeoxia in cirrhosis. *Chest* 1977;72:305-9.
55. Sinniah D, Fulton TT, McCullough H: The effect of exercise on the venous blood ammonium concentration in man. *J Clin Pathol* 1970;23:715-9.
56. Jaros Z: [Edecrin] *Cas Lek Cesk* 1970;109:298-9.
57. Das PC, Cash JD: Fibrinolysis at rest and after exercise in hepatic cirrhosis. *Br J Haematol* 1969;17:431-43.
58. Secchi GC, Rezzonico A, Gervasini N, Azzollini F, Cocchi A: [On the possibility of using the hyperammonemia test after exercise for evaluation of the anti-ammonemic effectiveness of drugs] *Arch Ital Mal Appar Dig* 1966;33:522-8.
59. Chiesa A, Ciappi G, Chiandussi L, Balbi L, Vaccarino A, Sardi G, Motta PE, Agostoni A: [Study of the causes of the hypoxemia in hepatic cirrhosis. Arteriovenous shunts during muscular exercise of moderate intensity] *Minerva Med* 1966;57:3536-9.
60. Secchi GC, Rezzonico A, Azzolini F, Gervasini N: [Observations on the increase of blood ammonia after muscular exercise in patients with hepatic cirrhosis] *Arch Ital Mal Appar Dig* 1966;33:215-9.
61. Bergasa NV, Talbot TL, Alling DW, Schmitt JM, Walker EC, Baker BL, Korenman JC, Park Y, Hoofnagle JH, Jones EA: A controlled trial of naloxone infusions for the pruritus of chronic cholestasis. *Gastroenterology* 1992;102:544-9.

2. アンジオテンシン変換酵素阻害薬 (ACE) あるいはアンジオテンシン II 受容体拮抗薬 (ARB) は肝線維化進展を抑制するか

1. Wang WW, Yang XS, Wang J, Li X: [Expression of angiotensin II type 1 receptor in the procession of hepatic fibrosis] *Zhonghua Gan Zang Bing Za Zhi* 2004;12:91.
2. Bataller R, Schwabe RF, Choi YH, Yang L, Paik YH, Lindquist J, Qian T, Schoonhoven R, Hagedorn CH, Lemasters JJ, Brenner DA: NADPH oxidase signal transduces angiotensin II in hepatic stellate cells and is critical in hepatic fibrosis. *J Clin Invest* 2003;112:1383-94.
3. Shen FJ, Yin CH, Wang BE: [Renin angiotensin system and liver fibrosis or cirrhosis] *Zhonghua Gan Zang Bing Za Zhi* 2003;11:447-8.
4. Wang WW, Yang XS, Wu PS, Wang J, Zhang HB, Li X, Zheng WL: [Expressions of angiotensin II type 1 receptor mRNA in fibrotic and normal liver tissues] *Di Yi Jun Yi Da Xue Xue Bao* 2003;23:477-8, 482.
5. Yoshiji H, Kuriyama S, Fukui H: Angiotensin-I-converting enzyme inhibitors may be an alternative anti-angiogenic strategy in the treatment of liver fibrosis and hepatocellular carcinoma. Possible role of vascular endothelial growth factor. *Tumour Biol* 2002;23:348-56.
6. Schuppan D, Krebs A, Bauer M, Hahn EG: Hepatitis C and liver fibrosis. *Cell Death Differ* 2003;10 Suppl 1:S59-67.
7. Terui Y, Saito T, Watanabe H, Togashi H, Kawata S, Kamada Y, Sakuta S: Effect of angiotensin receptor antagonist on liver fibrosis in early stages of chronic hepatitis C. *Hepatology* 2002;36:1022.
8. Tabak F, Mert A, Ozaras R, Biyikli M, Ozturk R, Ozbay G, Senturk H, Aktuglu Y: Losartan-induced hepatic injury. *J Clin Gastroenterol* 2002;34:585-6.

3. 強力ミノファージェン C による肝庇護療法により線維化進展を遅らせることが出来るか

1. Zhang YF, Wang LL, Yin WH: [Clinical observation on the anti-liver fibrosis treatment by diammonion glycyrrhizinate injection combined with saliva] *Zhongguo Zhong Xi Yi Jie He Za Zhi* 2002;22:538-9.
2. Ueno T, Sata M: [Forefront of therapy for hepatic fibrosis] *Nippon Shokakibyō Gakkai Zasshi* 2002;99:365-78.
3. Kumada H: Long-term treatment of chronic hepatitis C with glycyrrhizin [stronger neominophagen C (SNMC)] for preventing liver cirrhosis and hepatocellular carcinoma. *Oncology* 2002;62 Suppl 1:94-100.
4. van Rossum TG, Vulto AG, Hop WC, Schalm SW: Pharmacokinetics of intravenous glycyrrhizin after single and multiple doses in patients with chronic hepatitis C infection. *Clin Ther* 1999;21:2080-90.
5. Takahashi M, Nakano S, Takeda I, Kumada T, Sugiyama K, Osada T, Kiriya S, Toyoda H, Shimada S, Samori T: [The pharmacokinetics of the glycyrrhizin and glycyrrhetic acid after intravenous administration of glycyrrhizin for the patients with chronic liver disease caused by type C hepatitis virus] *Nippon Shokakibyō Gakkai Zasshi* 1995;92:1929-36.
6. Yamamura Y, Tanaka N, Santa T, Kotaki H, Aikawa T, Uchino K, Osuga T, Sawada Y, Iga T: The relationship between pharmacokinetic behaviour of glycyrrhizin and hepatic function in patients with acute hepatitis and liver cirrhosis. *Biopharm Drug Dispos* 1995;16:13-21.
7. Wada T, Arima T, Nagashima H: Natural killer activity in patients with chronic hepatitis treated with OK432, interferon, adenine arabinoside and glycyrrhizin. *Gastroenterol Jpn* 1987;22:312-21.
8. Su XS, Chen HM, Wang LH, Jiang CF, Liu JH, Zhao MQ, Ma XH, Zhao YC, Han DW: Clinical and laboratory observation on the effect of glycyrrhizin in acute and chronic viral hepatitis. *J Tradit Chin Med* 1984;4:127-32.

4. UDCA による肝庇護療法により線維化進展を遅らせることが出来るか

1. Van Den Bogaert E, Francque S, Pelckmans P, Michielsen P: The use of ursodeoxycholic acid in patients with primary biliary cirrhosis: sense or nonsense. *Acta Gastroenterol Belg* 2003;66:283-7.
2. Talwalkar JA, Lindor KD: Primary biliary cirrhosis. *Lancet* 2003;362:53-61.

3. Gunsar F, Akarca US, Ersoz G, Karasu Z, Yuce G, Batur Y: Clinical and biochemical features and therapy responses in primary biliary cirrhosis and primary biliary cirrhosis-autoimmune hepatitis overlap syndrome. *Hepatogastroenterology* 2002;49:1195-200.
4. Neuman MG, Cameron RG, Haber JA, Katz GG, Blendis LM: An electron microscopic and morphometric study of ursodeoxycholic effect in primary biliary cirrhosis. *Liver* 2002;22:235-44.
5. Ursodeoxycholic acid: a second look. Primary biliary cirrhosis: dashed hopes. *Prescrire Int* 2002;11:67-9.
6. Szalay F: Treatment of primary biliary cirrhosis. *J Physiol Paris* 2001;95:407-12.
7. Nishio A, Bass NM, Luketic VA, Coppel RL, Gershwin ME: Primary biliary cirrhosis: from induction to destruction. *Semin Gastrointest Dis* 2001;12:89-102.
8. Nishio A, Keefe EB, Ishibashi H, Gershwin EM: Diagnosis and treatment of primary biliary cirrhosis. *Med Sci Monit* 2000;6:181-93.
9. Corpechot C, Carrat F, Bonnard AM, Poupon RE, Poupon R: The effect of ursodeoxycholic acid therapy on liver fibrosis progression in primary biliary cirrhosis. *Hepatology* 2000;32:1196-9.
10. Neuberger J: Recurrent primary biliary cirrhosis. *Baillieres Best Pract Res Clin Gastroenterol* 2000;14:669-80.
11. Poupon R, Poupon RE: Treatment of primary biliary cirrhosis. *Baillieres Best Pract Res Clin Gastroenterol* 2000;14:615-28.
12. Kowdley KV: Ursodeoxycholic acid therapy in hepatobiliary disease. *Am J Med* 2000;108:481-6.
13. Ramakrishna B, Eapen CE, Kang G, Kurian G, Chandy GM: Familial intrahepatic cholestatic cirrhosis with positive antimitochondrial antibody: familial primary biliary cirrhosis. *J Clin Gastroenterol* 2000;30:255-8.
14. Czaja AJ, Carpenter HA, Lindor KD: Ursodeoxycholic acid as adjunctive therapy for problematic type 1 autoimmune hepatitis: a randomized placebo-controlled treatment trial. *Hepatology* 1999;30:1381-6.
15. Skulina D, Owczarek D, Ciecko-Michalska I, Szczepanski W, Tetnowski J, Garlicka M, Janas-Skulina U: [The influence of ursodeoxycholic acid on some biochemical, immunologic and histopathologic parameters in patients with primary biliary cirrhosis] *Przegl Lek* 1999;56:201-4.
16. Poupon R, Chazouilleres O, Balkau B, Poupon RE: Clinical and biochemical expression of the histopathological lesions of primary biliary cirrhosis. UDCA-PBC Group. *J Hepatol* 1999;30:408-12.
17. Degott C, Zafrani ES, Callard P, Balkau B, Poupon RE, Poupon R: Histopathological study of primary biliary cirrhosis and the effect of ursodeoxycholic acid treatment on histology progression. *Hepatology* 1999;29:1007-12.
18. Kisand KE, Kisand KV, Karvonen AL, Vuoristo M, Mattila J, Makinen J, Uiho R: Antibodies to pyruvate dehydrogenase in primary biliary cirrhosis: correlation with histology. *APMIS* 1998;106:884-92.
19. Chazouilleres O, Wendum D, Serfaty L, Montembault S, Rosmorduc O, Poupon R: Primary biliary cirrhosis-autoimmune hepatitis overlap syndrome: clinical features and response to therapy. *Hepatology* 1998;28:296-301.
20. Schuppan D, Strobel D, Hahn EG: Hepatic fibrosis - therapeutic strategies. *Digestion* 1998;59:385-90.
21. Beuers U, Oswald M: [Cholestasis: therapeutic options] *Ther Umsch* 1998;55:97-103.
22. Poupon RE, Huet PM, Poupon R, Bonnard AM, Nhieu JT, Zafrani ES: A randomized trial comparing colchicine and ursodeoxycholic acid combination to ursodeoxycholic acid in primary biliary cirrhosis. UDCA-PBC Study Group. *Hepatology* 1996;24:1098-103.
23. Sipos P, Guldutuna S, Leuschner U, Vallent K: [Comparative study of superoxide production of monocytes in primary biliary cirrhosis] *Orv Hetil* 1995;136:2389-92.
24. Stiehl A: [Bile acids in liver diseases--current indications] *Ther Umsch* 1995;52:682-6.
25. Luketic VA, Sanyal AJ: The current status of ursodeoxycholate in the treatment of chronic cholestatic liver disease. *Gastroenterologist* 1994;2:74-9.
26. Floreani A, Zappala F, Mazzetto M, Naccarato R, Plebani M, Chiaramonte M: Different response to ursodeoxycholic acid (UDCA) in primary biliary cirrhosis according to severity of disease. *Dig Dis Sci* 1994;39:9-14.
27. Matsuzaki Y, Doy M, Tanaka N, Shoda J, Osuga T, Nakano M, Aikawa T: Biochemical and

- histological changes after more than four years of treatment of ursodeoxycholic acid in primary biliary cirrhosis. *J Clin Gastroenterol* 1994;18:36-41.
28. Kowdley KV, Kaplan MM: Treatment of primary biliary cirrhosis. *Gastroenterologist* 1993;1:199-210.
 29. Arrese M, Accatino L: [Ursodeoxycholic acid in the treatment of cholestatic liver diseases] *Rev Med Chil* 1993;121:439-46.
 30. Van de Meeberg PC, van Erpecum KJ, van Berge-Henegouwen GP: Therapy with ursodeoxycholic acid in cholestatic liver disease. *Scand J Gastroenterol Suppl* 1993;200:15-20.
 31. Leuschner U: [Drug therapy of cholestatic hepatopathies] *Schweiz Rundsch Med Prax* 1992;81:983-4.
 32. Rojkind M: Fibrogenesis in cirrhosis. Potential for therapeutic intervention. *Pharmacol Ther* 1992;53:81-104.
 33. Poupon RE, Poupon R: Ursodeoxycholic acid for the treatment of cholestatic diseases. *Prog Liver Dis* 1992;10:219-38.
 34. de Caestecker JS, Jazrawi RP, Petroni ML, Northfield TC: Ursodeoxycholic acid in chronic liver disease. *Gut* 1991;32:1061-5.
 35. Poupon RE, Balkau B, Eschwege E, Poupon R: A multicenter, controlled trial of ursodiol for the treatment of primary biliary cirrhosis. UDCA-PBC Study Group. *N Engl J Med* 1991;324:1548-54.
 36. Poupon R: [Primary biliary cirrhosis] *Rev Prat* 1991;41:1161-5.
 37. Stiehl A: [Therapy of cholestatic liver diseases with ursodeoxycholic acid: a new treatment principle] *Z Gastroenterol Verh* 1991;26:142-3.
 38. Matsuzaki Y, Tanaka N, Osuga T, Aikawa T, Shoda J, Doi M, Nakano M: Improvement of biliary enzyme levels and itching as a result of long-term administration of ursodeoxycholic acid in primary biliary cirrhosis. *Am J Gastroenterol* 1990;85:15-23.

5. 小柴胡湯による肝庇護療法により線維化進展を遅らせることが出来るか

1. Schuppan D, Krebs A, Bauer M, Hahn EG: Hepatitis C and liver fibrosis. *Cell Death Differ* 2003;10 Suppl 1:S59-67.
2. Shimizu I: Antifibrogenic therapies in chronic HCV infection. *Curr Drug Targets Infect Disord* 2001;1:227-40.
3. Oka H: [Sho-saiko-to] *Nippon Rinsho* 2001;59 Suppl 6:774-8.
4. Shimizu I: Sho-saiko-to: Japanese herbal medicine for protection against hepatic fibrosis and carcinoma. *J Gastroenterol Hepatol* 2000;15 Suppl:D84-90.
5. Yagura M, Murai S, Kojima H, Tokita H, Kamitsukasa H, Harada H: Changes of liver fibrosis in chronic hepatitis C patients with no response to interferon-alpha therapy: including quantitative assessment by a morphometric method. *J Gastroenterol* 2000;35:105-11.
6. Yamashiki M, Nishimura A, Huang XX, Nobori T, Sakaguchi S, Suzuki H: Effects of the Japanese herbal medicine "Sho-saiko-to" (TJ-9) on interleukin-12 production in patients with HCV-positive liver cirrhosis. *Dev Immunol* 1999;7:17-22.
7. Geerts A, Rogiers V: Sho-saiko-To: the right blend of traditional Oriental medicine and liver cell biology. *Hepatology* 1999;29:282-4.
8. Tojima H, Yamazaki T, Tokudome T: [Two cases of pneumonia caused by Sho-saiko-to] *Nihon Kyobu Shikkan Gakkai Zasshi* 1996;34:904-10.
9. Nakagawa A, Yamaguchi T, Takao T, Amano H: [Five cases of drug-induced pneumonitis due to Sho-saiko-to or interferon-alpha or both] *Nihon Kyobu Shikkan Gakkai Zasshi* 1995;33:1361-1366.
10. Oka H, Yamamoto S, Kuroki T, Harihara S, Marumo T, Kim SR, Monna T, Kobayashi K, Tango T: Prospective study of chemoprevention of hepatocellular carcinoma with Sho-saiko-to (TJ-9). *Cancer* 1995;76:743-9.

6. 肝硬変患者にコルヒチンを投与することで線維化は改善するか

1. Lieber CS: New concepts of the pathogenesis of alcoholic liver disease lead to novel treatments. *Curr Gastroenterol Rep* 2004;6:60-5.
2. Li W, Wang C, Zhang J: Effects of da ding feng zhu decoction in 30 cases of liver fibrosis. *J Tradit Chin Med* 2003;23:251-4.
3. Lonardo A, Loria P: Of liver, whisky and plants: a requiem for colchicine in alcoholic cirrhosis? *Eur J Gastroenterol Hepatol* 2002;14:355-8.
4. Weng HL, Cai WM, Liu RH: Animal experiment and clinical study of effect of gamma-interferon on hepatic fibrosis. *World J Gastroenterol* 2001;7:42-8.
5. Rambaldi A, Gluud C: Colchicine for alcoholic and non-alcoholic liver fibrosis and cirrhosis. *Cochrane Database Syst Rev* 2001;:CD002148.
6. Rambaldi A, Gluud C: Colchicine for alcoholic and non-alcoholic liver fibrosis or cirrhosis. *Liver* 2001;21:129-36.
7. Poupon R, Poupon RE: Treatment of primary biliary cirrhosis. *Baillieres Best Pract Res Clin Gastroenterol* 2000;14:615-28.
8. Rambaldi A, Gluud C: Colchicine for alcoholic and non-alcoholic liver fibrosis and cirrhosis. *Liver* 2000;20:262-6.
9. Rockey DC: Hepatic fibrogenesis and hepatitis C. *Semin Gastrointest Dis* 2000;11:69-83.
10. Heathcote EJ: Evidence-based therapy of primary biliary cirrhosis. *Eur J Gastroenterol Hepatol* 1999;11:607-15.
11. Kisand KE, Kisand KV, Karvonen AL, Vuoristo M, Mattila J, Makinen J, Uibo R: Antibodies to pyruvate dehydrogenase in primary biliary cirrhosis: correlation with histology. *APMIS* 1998;106:884-92.
12. Lieber CS: Pathogenesis and treatment of liver fibrosis in alcoholics: 1996 update. *Dig Dis* 1997;15:42-66.
13. Poupon RE, Huet PM, Poupon R, Bonnand AM, Nhieu JT, Zafrani ES: A randomized trial comparing colchicine and ursodeoxycholic acid combination to ursodeoxycholic acid in primary biliary cirrhosis. UDCA-PBC Study Group. *Hepatology* 1996;24:1098-103.
14. Kocak N, Yuce A, Gurakan F, Ozen H, Gogus S, Kale G, Caglar M: Colchicine in the treatment of hepatic fibrosis in children. *Am J Gastroenterol* 1996;91:179-80.
15. Miller LC, Sharma A, McKusick AF, Tassoni JP, Dinarello CA, Kaplan MM: Synthesis of interleukin-1 beta in primary biliary cirrhosis: relationship to treatment with methotrexate or colchicine and disease progression. *Hepatology* 1995;22:518-24.
16. Mancinella A: [The use of colchicine in the treatment of alcoholic liver fibrosis in the elderly. Report of 80 cases] *Clin Ter* 1995;146:191-201.
17. Wu J, Danielsson A: Inhibition of hepatic fibrogenesis: a review of pharmacologic candidates. *Scand J Gastroenterol* 1994;29:385-91.
18. Kowdley KV, Kaplan MM: Treatment of primary biliary cirrhosis. *Gastroenterologist* 1993;1:199-210.
19. Leveille CR, Arias IM: Pathophysiology and pharmacologic modulation of hepatic fibrosis. *J Vet Intern Med* 1993;7:73-84.
20. Crabb DW: Recent developments in alcoholism:the liver. *Recent Dev Alcohol* 1993;11:207-30.
21. Michel H, Larrey D, Blanc P: [Treatment of acute alcoholic alcoholism] *Ann Gastroenterol Hepatol (Paris)* 1993;29:29-39.
22. Jorens PG, Michielsen PP, Pelckmans PA, Fevery J, Desmet VJ, Geubel AP, Rahier J, Van Maercke YM: Vitamin A abuse: development of cirrhosis despite cessation of vitamin A. A six-year clinical and histopathologic follow-up. *Liver* 1992;12:381-6.
23. Shibata J, Fujiyama S, Honda Y, Sato T: Combination therapy with ursodeoxycholic acid and colchicine for primary biliary cirrhosis. *J Gastroenterol Hepatol* 1992;7:277-82.
24. Hogemann B: [What is reliable in therapy of liver fibrosis?] *Z Gastroenterol* 1992;30:333-6.
25. Mancinella A: [Steatosis and fibrosis: first stage of liver damage induced by chronic alcoholism. Our experience in 100 cases] *Clin Ter* 1991;137:29-38.
26. Mezey E: Approaches to treatment of fibrogenesis in alcoholic liver disease. *Alcohol Alcohol Suppl* 1991;1:363-7.
27. Brenner DA, Alcorn JM: Therapy for hepatic fibrosis. *Semin Liver Dis* 1990;10:75-83.
28. Kershenobich D, Rojkind M, Quiroga A, Alcocer-Varela J: Effect of colchicine on lymphocyte and

- monocyte function and its relation to fibroblast proliferation in primary biliary cirrhosis. *Hepatology* 1990;11:205-9.
29. Trinchet JC, Beaugrand M, Callard P, Hartmann DJ, Gotheil C, Nusgens BV, Lapiere CM, Ferrier JP: Treatment of alcoholic hepatitis with colchicine. Results of a randomized double blind trial. *Gastroenterol Clin Biol* 1989;13:551-5.
 30. Kershenovich D, Vargas F, Garcia-Tsao G, Perez Tamayo R, Gent M, Rojkind M: Colchicine in the treatment of cirrhosis of the liver. *N Engl J Med* 1988;318:1709-13.
 31. Wiesner RH, Grambsch PM, Lindor KD, Ludwig J, Dickson ER: Clinical and statistical analyses of new and evolving therapies for primary biliary cirrhosis. *Hepatology* 1988;8:668-76.
 32. Kaplan MM, Alling DW, Zimmerman HJ, Wolfe HJ, Sepersky RA, Hirsch GS, Elta GH, Glick KA, Eagen KA: A prospective trial of colchicine for primary biliary cirrhosis. *N Engl J Med* 1986;315:1448-54.
 33. Tapalaga D, Dumitrascu D, Cotul S, Stanciu L, Tamas S: Colchicine treatment effects on liver cirrhosis assessed by liver blood flow measurements. *Med Interne* 1986;24:69-73.
 34. Reinhardt M, Jorke D, Jahn G, Krombholz B, Muller A, Machnik G, Kunath H: [Colchicine therapy of fibrosing liver diseases--report of a randomized double-blind study] *Dtsch Z Verdau Stoffwechselkr* 1986;46:257-75.
 35. Last JA: Changes in the collagen pathway in fibrosis. *Fundam Appl Toxicol* 1985;5:210-8.
 36. Chaldukov G, Vankov V: [Colchicine: new therapeutic possibilities] *Vutr Boles* 1985;24:34-8.
 37. Juszczak J: [Hepatology news (5). Is it possible to control liver fibrosis?] *Pol Tyg Lek* 1984;39:475-8.
 38. Kershenovich D, Uribe M, Suarez GI, Mata JM, Perez-Tamayo R, Rojkind M: Treatment of cirrhosis with colchicine. A double-blind randomized trial. *Gastroenterology* 1979;77:532-6.
 39. Cunnane SC, Manku MS, Horrobin DF: The pineal and regulation of fibrosis: pinealectomy as a model of primary biliary cirrhosis: roles of melatonin and prostaglandins in fibrosis and regulation of T lymphocytes. *Med Hypotheses* 1979;5:403-14.
 40. Poupon RE, Huet PM, Poupon R, Bonnand AM, Nhieu JT, Zafrani ES: A randomized trial comparing colchicine and ursodeoxycholic acid combination to ursodeoxycholic acid in primary biliary cirrhosis. UDCA-PBC Study Group. *Hepatology* 1996;24:1098-103.

栄養療法

7. 代償性肝硬変に対する高蛋白食は予後を改善するか

1. Amodio P, Caregaro L, Patteno E, Marcon M, Del Piccolo F, Gatta A: Vegetarian diets in hepatic encephalopathy: facts or fantasies? *Dig Liver Dis* 2001;33:492-500.
2. Tozun N: Influence of the metabolic complications of liver cirrhosis on dietary intake. *Med Sci Monit* 2000;6:1223-6.
3. Tangkijvanich P, Mahachai V, Wittayalertpanya S, Ariyawongsopon V, Isarasena S: Short-term effects of branched-chain amino acids on liver function tests in cirrhotic patients. *Southeast Asian J Trop Med Public Health* 2000;31:152-7.
4. Kawamura-Yasui N, Kaito M, Nakagawa N, Fujita N, Ikoma J, Gabazza EC, Watanabe S, Adachi Y: Evaluating response to nutritional therapy using the branched-chain amino acid/tyrosine ratio in patients with chronic liver disease. *J Clin Lab Anal* 1999;13:31-4.
5. Campillo B, Bories PN, Pornin B, Devanlay M: Influence of liver failure, ascites, and energy expenditure on the response to oral nutrition in alcoholic liver cirrhosis. *Nutrition* 1997;13:613-21.
6. Nielsen K, Kondrup J, Martinsen L, Dossing H, Larsson B, Stilling B, Jensen MG: Long-term oral refeeding of patients with cirrhosis of the liver. *Br J Nutr* 1995;74:557-67.
7. Watanabe A, Kuwabara Y, Hioki O, Yago K, Kugu K, Akira M: Tentative diet for liver failure containing well-polished rice. *Nutrition* 1995;11:355-9.
8. Campillo B, Bories PN, Leluan M, Pornin B, Devanlay M, Fouet P: Short-term changes in energy metabolism after 1 month of a regular oral diet in severely malnourished cirrhotic patients. *Metabolism* 1995;44:765-70.
9. Bories PN, Campillo B: One-month regular oral nutrition in alcoholic cirrhotic patients. Changes of

- nutritional status, hepatic function and serum lipid pattern. *Br J Nutr* 1994;72:937-46.
10. Kuroki T, Nishiguchi S, Nakajima S, Shiomi S, Oka H, Harihara S: [The managements of nutrition for hepatic cirrhosis] *Nippon Rinsho* 1994;52:197-202.
 11. Bianchi GP, Marchesini G, Fabbri A, Rondelli A, Bugianesi E, Zoli M, Pisi E: Vegetable versus animal protein diet in cirrhotic patients with chronic encephalopathy. A randomized cross-over comparison. *J Intern Med* 1993;233:385-92.
 12. Bunout D, Aicardi V, Hirsch S, Petermann M, Kelly M, Silva G, Garay P, Ugarte G, Iturriaga H: Nutritional support in hospitalized patients with alcoholic liver disease. *Eur J Clin Nutr* 1989;43:615-21.
 13. Christie ML, Sack DM, Pomposelli J, Horst D: Enriched branched-chain amino acid formula versus a casein-based supplement in the treatment of cirrhosis. *JPEN J Parenter Enteral Nutr* 1985;9:671-8.
 14. Okita M, Watanabe A, Nagashima H: Nutritional treatment of liver cirrhosis by branched-chain amino acid-enriched nutrient mixture. *J Nutr Sci Vitaminol (Tokyo)* 1985;31:291-303.
 15. Uribe M, Dibildox M, Malpica S, Guillermo E, Villalobos A, Nieto L, Vargas F, Garcia Ramos G: Beneficial effect of vegetable protein diet supplemented with psyllium plantago in patients with hepatic encephalopathy and diabetes mellitus. *Gastroenterology* 1985;88:901-7.
 16. Okita M, Watanabe A, Nagashima H: A vegetable protein-rich diet for the treatment of liver cirrhosis. *Acta Med Okayama* 1985;39:59-65.
 17. Calvey H, Davis M, Williams R: Controlled trial of nutritional supplementation, with and without branched chain amino acid enrichment, in treatment of acute alcoholic hepatitis. *J Hepatol* 1985;1:141-51.
 18. Sieg A, Walker S, Czygan P, Gartner U, Lanzinger-Rossnagel G, Stiehl A, Kommerell B: Branched-chain amino acid-enriched elemental diet in patients with cirrhosis of the liver. A double blind crossover trial. *Z Gastroenterol* 1983;21:644-50.
 19. McGhee A, Henderson JM, Millikan WJ Jr, Bleier JC, Vogel R, Kassouny M, Rudman D: Comparison of the effects of Hepatic-Aid and a Casein modular diet on encephalopathy, plasma amino acids, and nitrogen balance in cirrhotic patients. *Ann Surg* 1983;197:288-93.
 20. Millikan WJ Jr, Henderson JM, Warren WD, Riepe SP, Kutner MH, Wright-Bacon L, Epstein C, Parks RB: Total parenteral nutrition with F080 in cirrhotics with subclinical encephalopathy. *Ann Surg* 1983;197:294-304.
 21. Uribe M, Marquez MA, Garcia Ramos G, Ramos-Uribe MH, Vargas F, Villalobos A, Ramos C: Treatment of chronic portal--systemic encephalopathy with vegetable and animal protein diets. A controlled crossover study. *Dig Dis Sci* 1982;27:1109-16.
 22. Schafer K, Winther MB, Ukida M, Leweling H, Reiter HJ, Bode JC: Influence of an orally administered protein mixture enriched in branched chain amino acids on the chronic hepatic encephalopathy (CHE) of patients with liver cirrhosis. *Z Gastroenterol* 1981;19:356-62.
 23. Okita M, Watanabe A, Nagashima H: Treatment of liver cirrhosis with branched chain amino acid-supplemented diet. *Gastroenterol Jpn* 1981;16:389-92.

8. BCAA 投与は肝硬変の予後を改善するか

1. Fukushima H, Miwa Y, Ida E, Kuriyama S, Toda K, Shimomura Y, Sugiyama A, Sugihara J, Tomita E, Moriwaki H: Nocturnal branched-chain amino acid administration improves protein metabolism in patients with liver cirrhosis: comparison with daytime administration. *JPEN J Parenter Enteral Nutr* 2003;27:315-22.
2. Iwasa M, Matsumura K, Watanabe Y, Yamamoto M, Kaito M, Ikoma J, Gabazza EC, Takeda K, Adachi Y: Improvement of regional cerebral blood flow after treatment with branched-chain amino acid solutions in patients with cirrhosis. *Eur J Gastroenterol Hepatol* 2003;15:733-7.
3. Marchesini G, Bianchi G, Merli M, Amodio P, Panella C, Loguercio C, Rossi Fanelli F, Abbiati R: Nutritional supplementation with branched-chain amino acids in advanced cirrhosis: a double-blind, randomized trial. *Gastroenterology* 2003;124:1792-801.
4. Tangkijvanich P, Mahachai V, Wittayalerpanya S, Ariyawongsopon V, Isarasena S: Short-term effects of branched-chain amino acids on liver function tests in cirrhotic patients. *Southeast Asian*

- J Trop Med Public Health 2000;31:152-7.
5. Takegoshi K, Nanasawa H, Itoh H, Yasuyama T, Ohmoto Y, Sugiyama K: Effects of branched-chain amino acid-enriched nutrient mixture on natural killer cell activity in viral cirrhosis. *Arzneimittelforschung* 1998;48:701-6.
 6. Ledesma Castana F, Casafont Morencos F, Martin Ramos L, Sanchez Hernandez E, Ordonez Gonzalez J, Pons Romero F: [Influence of the nutritional status on the characteristics of the ascitic fluid in alcoholic hepatic cirrhosis] *Nutr Hosp* 1996;11:238-44.
 7. Watanabe A, Wakabayashi H, Kuwabara Y: Nutrient-induced thermogenesis and protein-sparing effect by rapid infusion of a branched chain-enriched amino acid solution to cirrhotic patients. *J Med* 1996;27:176-82.
 8. Higuchi K, Shimizu Y, Nambu S, Miyabayashi C, Takahara T, Saito S, Hioki O, Kuwabara Y, Watanabe A: Effects of an infusion of branched-chain amino acids on neurophysiological and psychometric testings in cirrhotic patients with mild hepatic encephalopathy. *J Gastroenterol Hepatol* 1994;9:366-72.
 9. Bianchi GP, Marchesini G, Zoli M, Abbiati R, Ferrario E, Fabbri A, Pisi E: Oral BCAA supplementation in cirrhosis with chronic encephalopathy: effects on prolactin and estradiol levels. *Hepatogastroenterology* 1992;39:443-6.
 10. Marchesini G, Dioguardi FS, Bianchi GP, Zoli M, Bellati G, Roffi L, Martines D, Abbiati R: Long-term oral branched-chain amino acid treatment in chronic hepatic encephalopathy. A randomized double-blind casein-controlled trial. The Italian Multicenter Study Group. *J Hepatol* 1990;11:92-101.
 11. Vilstrup H, Gluud C, Hardt F, Kristensen M, Kohler O, Melgaard B, Dejgaard A, Hansen BA, Krintel JJ, Schutten HJ, et al.: Branched chain enriched amino acid versus glucose treatment of hepatic encephalopathy. A double-blind study of 65 patients with cirrhosis. *J Hepatol* 1990;10:291-6.
 12. Cabre E, Gonzalez-Huix F, Abad-Lacruz A, Esteve M, Acero D, Fernandez-Banares F, Xiol X, Gassull MA: Effect of total enteral nutrition on the short-term outcome of severely malnourished cirrhotics. A randomized controlled trial. *Gastroenterology* 1990;98:715-20.
 13. Kanematsu T, Koyanagi N, Matsumata T, Kitano S, Takenaka K, Sugimachi K: Lack of preventive effect of branched-chain amino acid solution on postoperative hepatic encephalopathy in patients with cirrhosis: a randomized, prospective trial. *Surgery* 1988;104:482-8.
 14. Doffoel M, Vetter D, Doffoel S, Bockel R: [Effects of discontinuous intravenous infusion of ramified amino acids on blood insulin, blood glucagon and protein metabolism in cirrhotic patients after 10 days. Results of a controlled comparative study with sorbitol] *Rev Med Interne* 1987;8:276-82.
 15. Wright PD, Holdsworth JD, Dionigi P, Clague MB, James OF: Effect of branched chain amino acid infusions on body protein metabolism in cirrhosis of liver. *Gut* 1986;27 Suppl 1:96-102.
 16. Egberts EH, Schomerus H, Hamster W, Jurgens P: [Branched-chain amino acids in the treatment of latent porto-systemic encephalopathy. A placebo-controlled double-blind cross-over study] *Z Ernahrungswiss* 1986;25:9-28.
 17. Christie ML, Sack DM, Pomposelli J, Horst D: Enriched branched-chain amino acid formula versus a casein-based supplement in the treatment of cirrhosis. *JPEN J Parenter Enteral Nutr* 1985;9:671-8.
 18. Michel H, Bories P, Aubin JP, Pomier-Layrargues G, Bauret P, Bellet-Herman H: Treatment of acute hepatic encephalopathy in cirrhotics with a branched-chain amino acids enriched versus a conventional amino acids mixture. A controlled study of 70 patients. *Liver* 1985;5:282-9.
 19. Rocchi E, Cassanelli M, Gibertini P, Pietrangelo A, Casalgrandi G, Ventura E: Standard or branched-chain amino acid infusions as short-term nutritional support in liver cirrhosis? *JPEN J Parenter Enteral Nutr* 1985;9:447-51.
 20. Cerra FB, Cheung NK, Fischer JE, Kaplowitz N, Schiff ER, Dienstag JL, Bower RH, Mabry CD, Leevy CM, Kiernan T: Disease-specific amino acid infusion (F080) in hepatic encephalopathy: a prospective, randomized, double-blind, controlled trial. *JPEN J Parenter Enteral Nutr* 1985;9:288-95.
 21. Egberts EH, Schomerus H, Hamster W, Jurgens P: Branched chain amino acids in the treatment of latent portosystemic encephalopathy. A double-blind placebo-controlled crossover study.

Gastroenterology 1985;88:887-95.

22. Sieg A, Walker S, Czygan P, Gartner U, Lanzinger-Rosnagel G, Stiehl A, Kommerell B: Branched-chain amino acid-enriched elemental diet in patients with cirrhosis of the liver. A double blind crossover trial. *Z Gastroenterol* 1983;21:644-50.
23. Cerra FB, McMillen M, Angelico R, Cline B, Lyons J, Faulkenbach L, Paysinger J: Cirrhosis, encephalopathy, and improved results with metabolic support. *Surgery* 1983;94:612-9.
24. Wahren J, Denis J, Desurmont P, Eriksson LS, Escoffier JM, Gauthier AP, Hagenfeldt L, Michel H, Opolon P, Paris JC, Veyrac M: Is intravenous administration of branched chain amino acids effective in the treatment of hepatic encephalopathy? A multicenter study. *Hepatology* 1983;3:475-80.
25. Uribe M, Marquez MA, Garcia Ramos G, Ramos-Urbe MH, Vargas F, Villalobos A, Ramos C: Treatment of chronic portal-systemic encephalopathy with vegetable and animal protein diets. A controlled crossover study. *Dig Dis Sci* 1982;27:1109-16.
26. Eriksson LS, Persson A, Wahren J: Branched-chain amino acids in the treatment of chronic hepatic encephalopathy. *Gut* 1982;23:801-6.
27. Rossi-Fanelli F, Riggio O, Cangiano C, Cascino A, De Conciliis D, Merli M, Stortoni M, Giunchi G: Branched-chain amino acids vs lactulose in the treatment of hepatic coma: a controlled study. *Dig Dis Sci* 1982;27:929-35.
28. Walker S, Gotz R, Czygan P, Stiehl A, Lanzinger G, Sieg A, Raedsch R, Kommerell B: Oral keto analogs of branched-chain amino acids in hyperammonemia in patients with cirrhosis of the liver. A double-blind crossover study. *Digestion* 1982;24:105-11.

9. 肝硬変に伴う低アルブミン血症に対して BCAA 製剤は有効か

1. Fukushima H, Miwa Y, Ida E, Kuriyama S, Toda K, Shimomura Y, Sugiyama A, Sugihara J, Tomita E, Moriwaki H: Nocturnal branched-chain amino acid administration improves protein metabolism in patients with liver cirrhosis: comparison with daytime administration. *JPEN J Parenter Enteral Nutr* 2003;27:315-22.
2. Takegoshi K, Nanasawa H, Itoh H, Yasuyama T, Ohmoto Y, Sugiyama K: Effects of branched-chain amino acid-enriched nutrient mixture on natural killer cell activity in viral cirrhosis. *Arzneimittelforschung* 1998;48:701-6.
3. Cabre E, Gonzalez-Huix F, Abad-Lacruz A, Esteve M, Acero D, Fernandez-Banares F, Xiol X, Gassull MA: Effect of total enteral nutrition on the short-term outcome of severely malnourished cirrhotics. A randomized controlled trial. *Gastroenterology* 1990;98:715-20.
4. McCullough AJ, Czaja AJ, Jones JD, Go VL: The nature and prognostic significance of serial amino acid determinations in severe chronic active liver disease. *Gastroenterology* 1981;81:645-52.

10. 低アルブミン血症に対してアルブミン製剤を投与することは予後の改善につながるか

1. Garcia-Compean D, Blanc P, Larrey D, Daures JP, Hirtz J, Mendoza E, Maldonado H, Michel H: Treatment of cirrhotic tense ascites with Dextran-40 versus albumin associated with large volume paracentesis: a randomized controlled trial. *Ann Hepatol* 2002;1:29-35.
2. Gines P, Uriz J, Calahorra B, Garcia-Tsao G, Kamath PS, Del Arbol LR, Planas R, Bosch J, Arroyo V, Rodes J: Transjugular intrahepatic portosystemic shunting versus paracentesis plus albumin for refractory ascites in cirrhosis. *Gastroenterology* 2002;123:1839-47.
3. Ortega R, Gines P, Uriz J, Cardenas A, Calahorra B, De Las Heras D, Guevara M, Bataller R, Jimenez W, Arroyo V, Rodes J: Terlipressin therapy with and without albumin for patients with hepatorenal syndrome: results of a prospective, nonrandomized study. *Hepatology* 2002;36:941-8.
4. Moreau R, Asselah T, Condat B, de Kerguenec C, Pessione F, Bernard B, Poynard T, Binn M, Grange JD, Valla D, Lebrec D: Comparison of the effect of terlipressin and albumin on arterial blood volume in patients with cirrhosis and tense ascites treated by paracentesis: a randomised pilot study. *Gut* 2002;50:90-4.

5. Zaak D, Paquet KJ, Kuhn R: Prospective study comparing human albumin vs. reinfusion of ultrafiltrate-ascitic fluid after total paracentesis in cirrhotic patients with tense ascites. *Z Gastroenterol* 2001;39:5-10.
6. Mitzner SR, Stange J, Klammt S, Risler T, Erley CM, Bader BD, Berger ED, Lauchart W, Peszynski P, Freytag J, Hickstein H, Looock J, Lohr JM, Liebe S, Emmrich J, Korten G, Schmidt R: Improvement of hepatorenal syndrome with extracorporeal albumin dialysis MARS: results of a prospective, randomized, controlled clinical trial. *Liver Transpl* 2000;6:277-86.
7. Sort P, Navasa M, Arroyo V, Aldeguer X, Planas R, Ruiz-del-Arbol L, Castells L, Vargas V, Soriano G, Guevara M, Gines P, Rodes J: Effect of intravenous albumin on renal impairment and mortality in patients with cirrhosis and spontaneous bacterial peritonitis. *N Engl J Med* 1999;341:403-9.
8. Gentilini P, Casini-Raggi V, Di Fiore G, Romanelli RG, Buzzelli G, Pinzani M, La Villa G, Laffi G: Albumin improves the response to diuretics in patients with cirrhosis and ascites: results of a randomized, controlled trial. *J Hepatol* 1999;30:639-45.
9. Graziotto A, Rossaro L, Inturri P, Salvagnini M: Reinfusion of concentrated ascitic fluid versus total paracentesis. A randomized prospective trial. *Dig Dis Sci* 1997;42:1708-14.
10. Gines A, Fernandez-Esparrach G, Monescillo A, Vila C, Domenech E, Abecasis R, Angeli P, Ruiz-Del-Arbol L, Planas R, Sola R, Gines P, Terg R, Inglada L, Vaque P, Salerno F, Vargas V, Clemente G, Quer JC, Jimenez W, Arroyo V, Rodes J: Randomized trial comparing albumin, dextran 70, and polygeline in cirrhotic patients with ascites treated by paracentesis. *Gastroenterology* 1996;111:1002-10.
11. Fassio E, Terg R, Landeira G, Abecasis R, Salemne M, Podesta A, Rodriguez P, Levi D, Kravetz D: Paracentesis with Dextran 70 vs. paracentesis with albumin in cirrhosis with tense ascites. Results of a randomized study. *J Hepatol* 1992;14:310-6.
12. Hagege H, Ink O, Ducreux M, Pelletier G, Buffet C, Etienne JP: [Treatment of ascites in patients with liver cirrhosis without neither hyponatremia nor renal insufficiency. Results of a randomized study comparing diuretics and punctures compensated by albumin] *Gastroenterol Clin Biol* 1992;16:751-5.
13. Gines P, Arroyo V, Vargas V, Planas R, Casafont F, Panes J, Hoyos M, Viladomiu L, Rimola A, Morillas R, et al.: Paracentesis with intravenous infusion of albumin as compared with peritoneovenous shunting in cirrhosis with refractory ascites. *N Engl J Med* 1991;325:829-35.
14. Salerno F, Badalamenti S, Lorenzano E, Moser P, Incerti P: Randomized comparative study of hemaccel vs. albumin infusion after total paracentesis in cirrhotic patients with refractory ascites. *Hepatology* 1991;13:707-13.
15. Planas R, Gines P, Arroyo V, Llach J, Panes J, Vargas V, Salmeron JM, Gines A, Toledo C, Rimola A, et al.: Dextran-70 versus albumin as plasma expanders in cirrhotic patients with tense ascites treated with total paracentesis. Results of a randomized study. *Gastroenterology* 1990;99:1736-44.
16. Gines P, Tito L, Arroyo V, Planas R, Panes J, Viver J, Torres M, Humbert P, Rimola A, Llach J, et al.: Randomized comparative study of therapeutic paracentesis with and without intravenous albumin in cirrhosis. *Gastroenterology* 1988;94:1493-502.
17. Gines P, Arroyo V, Quintero E, Planas R, Bory F, Cabrera J, Rimola A, Viver J, Camps J, Jimenez W, et al.: Comparison of paracentesis and diuretics in the treatment of cirrhotics with tense ascites. Results of a randomized study. *Gastroenterology* 1987;93:234-41.

1 1. 肝硬変患者に BCAA 製剤投与は患者の QOL を改善するか

1. Moriwaki H, Miwa Y, Tajika M, Kato M, Fukushima H, Shiraki M: Branched-chain amino acids as a protein- and energy-source in liver cirrhosis. *Biochem Biophys Res Commun* 2004;313:405-9.
2. Marchesini G, Bianchi G, Merli M, Amodio P, Panella C, Loguercio C, Rossi Fanelli F, Abbiati R: Nutritional supplementation with branched-chain amino acids in advanced cirrhosis: a double-blind, randomized trial. *Gastroenterology* 2003;124:1792-801.
3. Blei AT, Cordoba J: Hepatic Encephalopathy. *Am J Gastroenterol* 2001;96:1968-76.
4. Marchesini G, Bianchi G, Rossi B, Brizi M, Melchionda N: Nutritional treatment with branched-

- chain amino acids in advanced liver cirrhosis. *J Gastroenterol* 2000;35 Suppl 12:7-12.
5. Masuzawa M, Okuyama T, Kato M: [Parenteral and enteral nutritional support for patients with liver cirrhosis] *Nippon Rinsho* 1994;52:203-8.

1 2. 肝硬変患者の低栄養状態は予後に影響を与えるか

1. Campillo B, Richardet JP, Scherman E, Bories PN: Evaluation of nutritional practice in hospitalized cirrhotic patients: results of a prospective study. *Nutrition* 2003;19:515-21.
2. Tessari P: Protein metabolism in liver cirrhosis: from albumin to muscle myofibrils. *Curr Opin Clin Nutr Metab Care* 2003;6:79-85.
3. Tajika M, Kato M, Mohri H, Miwa Y, Kato T, Ohnishi H, Moriwaki H: Prognostic value of energy metabolism in patients with viral liver cirrhosis. *Nutrition* 2002;18:229-34.
4. Alberino F, Gatta A, Amodio P, Merkel C, Di Pascoli L, Boffo G, Caregaro L: Nutrition and survival in patients with liver cirrhosis. *Nutrition* 2001;17:445-50.
5. Caregaro L, Alberino F, Amodio P, Merkel C, Angeli P, Plebani M, Bolognesi M, Gatta A: Nutritional and prognostic significance of insulin-like growth factor 1 in patients with liver cirrhosis. *Nutrition* 1997;13:185-90.
6. Loguercio C, Sava E, Sicolo P, Castellano I, Narciso O: Nutritional status and survival of patients with liver cirrhosis: anthropometric evaluation. *Minerva Gastroenterol Dietol* 1996;42:57-60.
7. Merli M, Riggio O, Dally L: Does malnutrition affect survival in cirrhosis? PINC (Policentrica Italiana Nutrizione Cirrosi). *Hepatology* 1996;23:1041-6.
8. Caregaro L, Alberino F, Amodio P, Merkel C, Bolognesi M, Angeli P, Gatta A: Malnutrition in alcoholic and virus-related cirrhosis. *Am J Clin Nutr* 1996;63:602-9.
9. Nutritional status in cirrhosis. Italian Multicentre Cooperative Project on Nutrition in Liver Cirrhosis. *J Hepatol* 1994;21:317-25.
10. Kondrup J, Nielsen K, Hamberg O: [Nutritional therapy in patients with liver cirrhosis] *Ugeskr Laeger* 1993;155:2248-51.
11. Cabre E, Gonzalez-Huix F, Abad-Lacruz A, Esteve M, Acero D, Fernandez-Banares F, Xiol X, Gassull MA: Effect of total enteral nutrition on the short-term outcome of severely malnourished cirrhotics. A randomized controlled trial. *Gastroenterology* 1990;98:715-20.

1 3. 肝硬変患者に対する就寝前エネルギー投与(late evening snack ; L E S)は予後を改善するか

1. Moriwaki H, Miwa Y, Tajika M, Kato M, Fukushima H, Shiraki M: Branched-chain amino acids as a protein- and energy-source in liver cirrhosis. *Biochem Biophys Res Commun* 2004;313:405-9.
2. Okamoto M, Sakaida I, Tsuchiya M, Suzuki C, Okita K: Effect of a late evening snack on the blood glucose level and energy metabolism in patients with liver cirrhosis. *Hepatol Res* 2003;27:45-50.
3. Nakaya Y, Harada N, Kakui S, Okada K, Takahashi A, Inoi J, Ito S: Severe catabolic state after prolonged fasting in cirrhotic patients: effect of oral branched-chain amino-acid-enriched nutrient mixture. *J Gastroenterol* 2002;37:531-6.
4. Marchesini G, Bianchi G, Rossi B, Brizi M, Melchionda N: Nutritional treatment with branched-chain amino acids in advanced liver cirrhosis. *J Gastroenterol* 2000;35 Suppl 12:7-12.
5. Chang WK, Chao YC, Tang HS, Lang HF, Hsu CT: Effects of extra-carbohydrate supplementation in the late evening on energy expenditure and substrate oxidation in patients with liver cirrhosis. *JPEN J Parenter Enteral Nutr* 1997;21:96-9.
6. Zillikens MC, Swart GR, van den Berg JW, Wilson JH: Effects of the glucosidase inhibitor acarbose in patients with liver cirrhosis. *Aliment Pharmacol Ther* 1989;3:453-9. ID:2518858
7. Yamauchi M, Takeda K, Sakamoto K, Ohata M, Toda G: Effect of oral branched chain amino acid supplementation in the late evening on the nutritional state of patients with liver cirrhosis. *Hepatol Res* 2001;21:199-204.
8. Zillikens MC, van den Berg JW, Wattimena JL, Rietveld T, Swart GR: Nocturnal oral glucose

- supplementation. The effects on protein metabolism in cirrhotic patients and in healthy controls. *J Hepatol* 1993;17:377-83. ID:8315266
9. Donaghy A: Issues of malnutrition and bone disease in patients with cirrhosis. *J Gastroenterol Hepatol* 2002;17:462-6.
 10. Miwa Y, Shiraki M, Kato M, Tajika M, Mohri H, Murakami N, Kato T, Ohnishi H, Morioku T, Muto Y, Moriwaki H: Improvement of fuel metabolism by nocturnal energy supplementation in patients with liver cirrhosis. *Hepatol Res* 2000;18:184-189.
 11. Fukushima H, Miwa Y, Ida E, Kuriyama S, Toda K, Shimomura Y, Sugiyama A, Sugihara J, Tomita E, Moriwaki H: Nocturnal branched-chain amino acid administration improves protein metabolism in patients with liver cirrhosis: comparison with daytime administration. *JPEN J Parenter Enteral Nutr* 2003;27:315-22.
 12. Yamauchi M, Takeda K, Sakamoto K, Ohata M, Toda G: Effect of oral branched chain amino acid supplementation in the late evening on the nutritional state of patients with liver cirrhosis. *Hepatol Res* 2001;21:199-204.
 13. Lochs H, Plauth M: Liver cirrhosis: rationale and modalities for nutritional support—the European Society of Parenteral and Enteral Nutrition consensus and beyond. *Curr Opin Clin Nutr Metab Care* 1999;2:345-9.
 14. Verboeket-van de Venne WP, Westerterp KR, van Hoek B, Swart GR: Energy expenditure and substrate metabolism in patients with cirrhosis of the liver: effects of the pattern of food intake. *Gut* 1995;36:110-6.
 15. Swart GR, Zillikens MC, van Vuure JK, van den Berg JW: Effect of a late evening meal on nitrogen balance in patients with cirrhosis of the liver. *BMJ* 1989;299:1202-3.

原因療法（ウイルス C 型）

14. C 型肝炎における IFN 療法（IFN、リバビリン併用療法）の治療効果は慢性肝炎と同等か
 15. C 型肝炎患者に対してインターフェロン療法を行うことで HCV の持続陰性化が得られるか
1. Shiffman ML, Di Bisceglie AM, Lindsay KL, Morishima C, Wright EC, Everson GT, Lok AS, Morgan TR, Bonkovsky HL, Lee WM, Dienstag JL, Ghany MG, Goodman ZD, Everhart JE: Peginterferon alfa-2a and ribavirin in patients with chronic hepatitis C who have failed prior treatment. *Gastroenterology* 2004;126:1015-23; discussion 947.
 2. Camma C, Di Bona D, Schepis F, Heathcote EJ, Zeuzem S, Pockros PJ, Marcellin P, Balart L, Alberti A, Craxi A: Effect of peginterferon alfa-2a on liver histology in chronic hepatitis C: a meta-analysis of individual patient data. *Hepatology* 2004;39:333-42.
 3. Van Vlierberghe H, Leroux-Roels G, Adler M, Bourgeois N, Nevens F, Horsmans Y, Brouwer J, Colle I, Delwaide J, Brenard R, Bastens B, Henrion J, de Vries RA, de Galocsy C, Michielsen P, Robaey G, Bruckers L: Daily induction combination treatment with alpha 2b interferon and ribavirin or standard combination treatment in naive chronic hepatitis C patients. A multicentre randomized controlled trial. *J Viral Hepat* 2003;10:460-6.
 4. Poynard T, McHutchison J, Manns M, Myers RP, Albrecht J: Biochemical surrogate markers of liver fibrosis and activity in a randomized trial of peginterferon alfa-2b and ribavirin. *Hepatology* 2003;38:481-92.
 5. Adinolfi LE, Utili R, Tonziello A, Ruggiero G: Effects of alpha interferon induction plus ribavirin with or without amantadine in the treatment of interferon non-responsive chronic hepatitis C: a randomised trial. *Gut* 2003;52:701-5.
 6. Testino G: [Hepatocarcinoma in HCV compensated correlated liver cirrhosis: role of treatment with interferon] *Recenti Prog Med* 2002;93:302-7.
 7. de Ledinghen V, Trimoulet P, Winnock M, Bernard PH, Bourliere M, Portal I, Remy AJ, Szostak N, Levy S, Tran A, Abergel A, Chene G, Fleury H, Couzigou P: Daily or three times per week interferon alpha-2b in combination with ribavirin or interferon alone for the treatment of patients with chronic hepatitis C not responding to previous interferon alone. *J Hepatol*

2002;36:819-26.

8. Planas R, Quer JC, Enriquez J, Barrera JM, Dalmau B, Casanovas T, Viver JM, Torres M, Boadas J, Sola R, Durandez R, Richart C, Bruguera M: [Induction therapy with interferon alfa-2a in compensated hepatitis C virus-related cirrhosis. Randomized, multicenter study] *Med Clin (Barc)* 2002;118:641-4.
9. Poynard T, Imbert-Bismut F, Ratziu V, Chevret S, Jardel C, Moussalli J, Messous D, Degos F: Biochemical markers of liver fibrosis in patients infected by hepatitis C virus: longitudinal validation in a randomized trial. *J Viral Hepat* 2002;9:128-33.
10. Heathcote EJ, Shiffman ML, Cooksley WG, Dusheiko GM, Lee SS, Balart L, Reindollar R, Reddy RK, Wright TL, Lin A, Hoffman J, De Pamphilis J: Peginterferon alfa-2a in patients with chronic hepatitis C and cirrhosis. *N Engl J Med* 2000;343:1673-80.
11. Shinzawa H, Yoshida Y, Masamune O, Toyota T, Takahashi T, Kasukawa R, Sudo T, Ishikawa K, Komatsu M, Ishii M, Takagi T, Hisamichi S, Sato S, Ichida H: Analysis of biochemical and virological efficacy of human lymphoblastoid interferon (IFN) in patients with compensated type C liver cirrhosis: comparative study between increase in individual IFN dose and prolonging of treatment period, using a multicenter randomized controlled trial. *Dig Dis Sci* 2000;45:575-80.
12. Bernardinello E, Cavalletto L, Chemello L, Mezzocolli I, Donada C, Benvegna L, Merkel C, Gatta A, Alberti A: Long-term clinical outcome after beta-interferon therapy in cirrhotic patients with chronic hepatitis C. TVVH Study Group. *Hepatogastroenterology* 1999;46:3216-22.
13. Schalm SW, Weiland O, Hansen BE, Milella M, Lai MY, Hollander A, Michielsen PP, Bellobuono A, Chemello L, Pastore G, Chen DS, Brouwer JT: Interferon-ribavirin for chronic hepatitis C with and without cirrhosis: analysis of individual patient data of six controlled trials. Eurohep Study Group for Viral Hepatitis. *Gastroenterology* 1999;117:408-13.
14. Everson GT, Jensen DM, Craig JR, van Leeuwen DJ, Bain VG, Ehrinpreis MN, Albert D, Joh T, Witt K: Efficacy of interferon treatment for patients with chronic hepatitis C: comparison of response in cirrhotics, fibrotics, or nonfibrotics. *Hepatology* 1999;30:271-6.
15. Valla DC, Chevallier M, Marcellin P, Payen JL, Trepo C, Fonck M, Bourliere M, Boucher E, Miguet JP, Parlier D, Lemonnier C, Opolon P: Treatment of hepatitis C virus-related cirrhosis: a randomized, controlled trial of interferon alfa-2b versus no treatment. *Hepatology* 1999;29:1870-5.
16. Shiratori Y, Yokosuka O, Nakata R, Ihori M, Hirota K, Katamoto T, Unuma T, Okano K, Ikeda Y, Hirano M, Kawase T, Takano S, Matsumoto K, Ohashi Y, Omata M: Prospective study of interferon therapy for compensated cirrhotic patients with chronic hepatitis C by monitoring serum hepatitis C RNA. *Hepatology* 1999;29:1573-80.
17. Montalto G, Soresi M, Carroccio A, Anastasi G, Campagna P, Vasile F, Di Prima L, Cartabellotta A, Giannitrapani L, Fulco M: Comparative responses to three different types of interferon-alpha in patients with chronic hepatitis C. *Curr Med Res Opin* 1998;14:235-41.
18. Ascione A, De Luca M, Canestrini C, Di Costanzo GG, Raimondo G, Longo G, Manns MP, Tillmann HL, Forte GB, Rocco P, Biceglia O, Faleo D, Vinelli F, Cela EM, Amitrano L, Addario L, Gigliotti T: Efficacy of high dose of recombinant alpha 2b interferon on long term response in chronic hepatitis C and cirrhosis: prospective randomized multicentre study. *Ital J Gastroenterol Hepatol* 1998;30:517-23.
19. Brouwer JT, Nevens F, Kleter B, Elewaut A, Adler M, Brenard R, Chamuleau RA, Michielsen PP, Piroette J, Hautekeete ML, Weber J, Bourgeois N, Hansen BE, Bronkhorst CM, ten Kate FJ, Heijtkink RA, Fevery J, Schalm SW: Efficacy of interferon dose and prediction of response in chronic hepatitis C: Benelux study in 336 patients. *J Hepatol* 1998;28:951-9.
20. al-Faleh FZ, Sbeih F, al-Karawi M, al-Mofleh IA, al-Rashed RS, Ayoola A, al-Amri S, Mayet I, al-Habbal TM, al-Omair A, al-Sohaibani MO, Abdullah AO, Mohamed SA, el-Sheikh MA: Treatment of chronic hepatitis C genotype 4 with alpha-interferon in Saudi Arabia: a multicenter study. *Hepatogastroenterology* 1998;45:488-91.
21. Ouzan D, Babany G, Valla D, Opolon P: Comparison of high initial and fixed-dose regimens of interferon-alpha2a in chronic hepatitis C: a randomized controlled trial. French Multicenter Interferon Study Group. *J Viral Hepat* 1998;5:53-9.
22. Furusyo N, Hayashi J, Ueno K, Sawayama Y, Kawakami Y, Kishihara Y, Kashiwagi S: Human

- lymphoblastoid interferon treatment for patients with hepatitis C virus-related cirrhosis. *Clin Ther* 1997;19:1352-67.
23. Ziol M, Nhieu JT, Roudot-Thoraval F, Metreau JM, Deugnier Y, Dhumeaux D, Zafrani ES: A histopathological study of the effects of 6-month versus 12-month interferon alpha-2b therapy in chronic hepatitis C. *J Hepatol* 1996;25:833-41.
 24. Niederau C, Heintges T, Haussinger D: Treatment of chronic hepatitis C with a-interferon: an analysis of the literature. *Hepatology* 1996;43:1544-56.
 25. Magrin S, Craxi A, Fabiano C, Marino L, Fiorentino G, Lo Iacono O, Volpes R, Di Marco V, Almasio P, Vaccaro A, Urdea MS, Wilber JC, Bonura C, Gianguzza F, Capursi V, Filiberti S, Stuyver L, Pagliaro L: HCV viraemia is more important than genotype as a predictor of response to interferon in Sicily (southern Italy). *J Hepatol* 1996;25:583-90.
 26. Mazzella G, Accogli E, Sottili S, Festi D, Orsini M, Salzetta A, Novelli V, Cipolla A, Fabbri C, Pezzoli A, Roda E: Alpha interferon treatment may prevent hepatocellular carcinoma in HCV-related liver cirrhosis. *J Hepatol* 1996;24:141-7.
 27. Nishiguchi S, Kuroki T, Nakatani S, Morimoto H, Takeda T, Nakajima S, Shiomi S, Seki S, Kobayashi K, Otani S: Randomised trial of effects of interferon-alpha on incidence of hepatocellular carcinoma in chronic active hepatitis C with cirrhosis. *Lancet* 1995;346:1051-5.
 28. Pardo M, Castillo I, Navas S, Carreno V: Treatment of chronic hepatitis C with cirrhosis with recombinant human granulocyte colony-stimulating factor plus recombinant interferon-alpha. *J Med Virol* 1995;45:439-44.
 29. Saito T, Shinzawa H, Takahashi T: [Interferon therapy of compensated type C cirrhosis] *Nippon Rinsho* 1994;52:1875-9.
 30. Saito T, Shinzawa H, Kuboki M, Ishibashi M, Toda H, Okuyama Y, Nakamura T, Yamada N, Wakabayashi H, Togashi H, et al.: A randomized, controlled trial of human lymphoblastoid interferon in patients with compensated type C cirrhosis. *Am J Gastroenterol* 1994;89:681-6.
 31. Jouet P, Roudot-Thoraval F, Dhumeaux D, Metreau JM: Comparative efficacy of interferon alfa in cirrhotic and noncirrhotic patients with non-A, non-B, C hepatitis. *Le Groupe Francais pour l'Etude du Traitement des Hepatites Chroniques NANB/C. Gastroenterology* 1994;106:686-90.
 32. Caporaso N, Suozzo R, Morisco F, D'Antonio M, Romano M, Coltorti M: Recombinant human interferon alpha-2a therapy for chronic hepatitis C with or without cirrhosis: comparison of 3 or 6 MU for 1 year. *Ital J Gastroenterol* 1993;25:482-6.

1 6 . IFN 療法後 SVR が得られた C 型肝硬変では線維化が改善するか

1 7 . C 型肝硬変患者に対してインターフェロン療法は肝硬変の進展を抑制するか

1. Shiffman ML, Di Bisceglie AM, Lindsay KL, Morishima C, Wright EC, Everson GT, Lok AS, Morgan TR, Bonkovsky HL, Lee WM, Dienstag JL, Ghany MG, Goodman ZD, Everhart JE: Peginterferon alfa-2a and ribavirin in patients with chronic hepatitis C who have failed prior treatment. *Gastroenterology* 2004;126:1015-23; discussion 947.
2. Camma C, Di Bona D, Schepis F, Heathcote EJ, Zeuzem S, Pockros PJ, Marcellin P, Balart L, Alberti A, Craxi A: Effect of peginterferon alfa-2a on liver histology in chronic hepatitis C: a meta-analysis of individual patient data. *Hepatology* 2004;39:333-42.
3. Poynard T, McHutchison J, Manns M, Myers RP, Albrecht J: Biochemical surrogate markers of liver fibrosis and activity in a randomized trial of peginterferon alfa-2b and ribavirin. *Hepatology* 2003;38:481-92.
4. Heathcote EJ, Shiffman ML, Cooksley WG, Dusheiko GM, Lee SS, Balart L, Reindollar R, Reddy RK, Wright TL, Lin A, Hoffman J, De Pamphilis J: Peginterferon alfa-2a in patients with chronic hepatitis C and cirrhosis. *N Engl J Med* 2000;343:1673-80.
5. Poynard T, McHutchison J, Davis GL, Esteban-Mur R, Goodman Z, Bedossa P, Albrecht J: Impact of interferon alfa-2b and ribavirin on progression of liver fibrosis in patients with chronic hepatitis C. *Hepatology* 2000;32:1131-7.
6. Guerret S, Desmouliere A, Chossegros P, Costa AM, Badid C, Trepo C, Grimaud JA, Chevallier M: Long-term administration of interferon-alpha in non-responder patients with chronic hepatitis C:

follow-up of liver fibrosis over 5 years. *J Viral Hepat* 1999;6:125-33.

7. Everson GT, Jensen DM, Craig JR, van Leeuwen DJ, Bain VG, Ehrinpreis MN, Albert D, Joh T, Witt K: Efficacy of interferon treatment for patients with chronic hepatitis C: comparison of response in cirrhotics, fibrotics, or nonfibrotics. *Hepatology* 1999;30:271-6.

1 8 . C 型肝硬変に対する IFN 療法は合併症を誘発し予後に悪影響を与えないか

1. Shiffman ML, Di Bisceglie AM, Lindsay KL, Morishima C, Wright EC, Everson GT, Lok AS, Morgan TR, Bonkovsky HL, Lee WM, Dienstag JL, Ghany MG, Goodman ZD, Everhart JE: Peginterferon alfa-2a and ribavirin in patients with chronic hepatitis C who have failed prior treatment. *Gastroenterology* 2004;126:1015-23; discussion 947.
2. Moriyama M, Matsumura H, Aoki H, Shimizu T, Nakai K, Saito T, Yamagami H, Shioda A, Kaneko M, Goto I, Tanaka N, Arakawa Y: Long-term outcome, with monitoring of platelet counts, in patients with chronic hepatitis C and liver cirrhosis after interferon therapy. *Intervirol* 2003;46:296-307.
3. Adinolfi LE, Utili R, Tonziello A, Ruggiero G: Effects of alpha interferon induction plus ribavirin with or without amantadine in the treatment of interferon non-responsive chronic hepatitis C: a randomised trial. *Gut* 2003;52:701-5.
4. Rajan S, Liebman HA: Treatment of hepatitis C related thrombocytopenia with interferon alpha. *Am J Hematol* 2001;68:202-9.
5. Gramenzi A, Andreone P, Fiorino S, Camma C, Giunta M, Magalotti D, Cursaro C, Calabrese C, Arienti V, Rossi C, Di Febo G, Zoli M, Craxi A, Gasbarrini G, Bernardi M: Impact of interferon therapy on the natural history of hepatitis C virus related cirrhosis. *Gut* 2001;48:843-8.
6. Heathcote EJ, Shiffman ML, Cooksley WG, Dusheiko GM, Lee SS, Balart L, Reindollar R, Reddy RK, Wright TL, Lin A, Hoffman J, De Pamphilis J: Peginterferon alfa-2a in patients with chronic hepatitis C and cirrhosis. *N Engl J Med* 2000;343:1673-80.
7. Shiratori Y, Moriyama M, Imazeki F, Ohkubo H, Tanaka N, Arakawa Y, Yoshida H, Yokosuka O, Shibuya A, Matsuzaki K, Hashimoto E, Hayashi N, Hirata K, Ohashi Y, Omata M: A prospective study of interferon therapy modified by pre-treatment viral load in cirrhotic patients. *Tokyo-Chiba Hepatitis Research Group. Liver* 2000;20:271-80.
8. Lirussi F, Beccarello A, Bortolato L, Morselli-Labate AM, Crovatto M, Ceselli S, Santini G, Crepaldi G: Long-term treatment of chronic hepatitis C with ursodeoxycholic acid: influence of HCV genotypes and severity of liver disease. *Liver* 1999;19:381-8.
9. Valla DC, Chevallier M, Marcellin P, Payen JL, Trepo C, Fonck M, Bourliere M, Boucher E, Miguet JP, Parlier D, Lemonnier C, Opolon P: Treatment of hepatitis C virus-related cirrhosis: a randomized, controlled trial of interferon alfa-2b versus no treatment. *Hepatology* 1999;29:1870-5.
10. Shiratori Y, Yokosuka O, Nakata R, Ihori M, Hirota K, Katamoto T, Unuma T, Okano K, Ikeda Y, Hirano M, Kawase T, Takano S, Matsumoto K, Ohashi Y, Omata M: Prospective study of interferon therapy for compensated cirrhotic patients with chronic hepatitis C by monitoring serum hepatitis C RNA. *Hepatology* 1999;29:1573-80.
11. Simon K, Gladysz A, Rotter K, Glowacki A, Dobracki W, Knysz B, Ingot M, Mach G, Machaj A, Piszko P, Zalewska M: [Therapeutic efficacy of low-dose alpha interferon therapy in liver cirrhosis associated with HBV] *Pol Arch Med Wewn* 1998;99:487-92.
12. Ascione A, De Luca M, Canestrini C, Di Costanzo GG, Raimondo G, Longo G, Manns MP, Tillmann HL, Forte GB, Rocco P, Biceglia O, Faleo D, Vinelli F, Cela EM, Amitrano L, Addario L, Gigliotti T: Efficacy of high dose of recombinant alpha 2b interferon on long term response in chronic hepatitis C and cirrhosis: prospective randomized multicentre study. *Ital J Gastroenterol Hepatol* 1998;30:517-23.
13. Fattovich G, Giustina G, Realdi G, Corrocher R, Schalm SW: Long-term outcome of hepatitis B e antigen-positive patients with compensated cirrhosis treated with interferon alfa. *European Concerted Action on Viral Hepatitis (EUROHEP). Hepatology* 1997;26:1338-42.
14. Farrell G, Cooksley WG, Dudley FJ, Watson K: Efficacy and tolerance of a 6-month treatment course of daily interferon-alpha 2a for chronic hepatitis C with cirrhosis. *The Australian Hepatitis*

C Study Group. *J Viral Hepat* 1997;4:317-23.

15. Magrin S, Craxi A, Fabiano C, Marino L, Fiorentino G, Lo Iacono O, Volpes R, Di Marco V, Almasio P, Vaccaro A, Urdea MS, Wilber JC, Bonura C, Gianguzza F, Capursi V, Filiberti S, Stuyver L, Pagliaro L: HCV viraemia is more important than genotype as a predictor of response to interferon in Sicily (southern Italy). *J Hepatol* 1996;25:583-90.

原因療法 (ウイルス B 型)

19. ラミブジン内服により血清中 HBV の陰性化が得られると肝線維化は改善するか

1. Shindo M, Hamada K, Nishioji K, Muramatsu A, Oda Y, Okuno T: The predictive value of liver fibrosis in determining the effectiveness of interferon and lamivudine therapies for chronic hepatitis B. *J Gastroenterol* 2004;39:260-7.
2. Dienstag JL, Goldin RD, Heathcote EJ, Hann HW, Woessner M, Stephenson SL, Gardner S, Gray DF, Schiff ER: Histological outcome during long-term lamivudine therapy. *Gastroenterology* 2003;124:105-17.
3. Andreone P, Biselli M, Gramenzi A, Cursaro C, Morelli MC, Sama C, Lorenzini S, Spinucci G, Porzio F, Feline F, Di Giammarino L, Bernardi M: Efficacy of lamivudine therapy for advanced liver disease in patients with precore mutant hepatitis B virus infection awaiting liver transplantation. *Transplantation* 2002;74:1119-24.
4. Oh JM, Kyun J, Cho SW: Long-term lamivudine therapy for chronic hepatitis B in patients with and without cirrhosis. *Pharmacotherapy* 2002;22:1226-34.
5. Yao FY, Bass NM: Lamivudine treatment in patients with severely decompensated cirrhosis due to replicating hepatitis B infection. *J Hepatol* 2000;33:301-7.
6. Lai CL, Chien RN, Leung NW, Chang TT, Guan R, Tai DI, Ng KY, Wu PC, Dent JC, Barber J, Stephenson SL, Gray DF: A one-year trial of lamivudine for chronic hepatitis B. Asia Hepatitis Lamivudine Study Group. *N Engl J Med* 1998;339:61-8.

20. B 型肝炎にたいしてラミブジンを投与することでウイルスの陰性化あるいはセロコンバージョンが得られるか

1. Shindo M, Hamada K, Nishioji K, Muramatsu A, Oda Y, Okuno T: The predictive value of liver fibrosis in determining the effectiveness of interferon and lamivudine therapies for chronic hepatitis B. *J Gastroenterol* 2004;39:260-7.
2. Lavanchy D: Hepatitis B virus epidemiology, disease burden, treatment, and current and emerging prevention and control measures. *J Viral Hepat* 2004;11:97-107.
3. Chien RN, Liaw YF: Short-term lamivudine therapy in patients with chronic hepatitis B. *Intervirology* 2003;46:362-6.
4. Fontana RJ: Management of decompensated HBV cirrhosis: lamivudine and beyond. *Am J Gastroenterol* 2004;99:64-7.
5. Manolakopoulos S, Karatapanis S, Elefsiniotis J, Mathou N, Vlachogiannakos J, Iliadou E, Kougioumtzan A, Economou M, Triantos C, Tzourmakliotis D, Avgerinos A: Clinical course of lamivudine monotherapy in patients with decompensated cirrhosis due to HBeAg negative chronic HBV infection. *Am J Gastroenterol* 2004;99:57-63.
6. Hann HW, Fontana RJ, Wright T, Everson G, Baker A, Schiff ER, Riely C, Anschuetz G, Gardner SD, Brown N, Griffiths D: A United States compassionate use study of lamivudine treatment in nontransplantation candidates with decompensated hepatitis B virus-related cirrhosis. *Liver Transpl* 2003;9:49-56.
7. Dienstag JL, Goldin RD, Heathcote EJ, Hann HW, Woessner M, Stephenson SL, Gardner S, Gray DF, Schiff ER: Histological outcome during long-term lamivudine therapy. *Gastroenterology* 2003;124:105-17.
8. Oh JM, Kyun J, Cho SW: Long-term lamivudine therapy for chronic hepatitis B in patients with and without cirrhosis. *Pharmacotherapy* 2002;22:1226-34.
9. Sponseller CA, Bacon BR, Di Bisceglie AM: Clinical improvement in patients with decompensated

- liver disease caused by hepatitis B after treatment with lamivudine. *Liver Transpl* 2000;6:715-20.
10. Kapoor D, Guptan RC, Wakil SM, Kazim SN, Kaul R, Agarwal SR, Raisuddin S, Hasnain SE, Sarin SK: Beneficial effects of lamivudine in hepatitis B virus-related decompensated cirrhosis. *J Hepatol* 2000;33:308-12.
 11. Yao FY, Bass NM: Lamivudine treatment in patients with severely decompensated cirrhosis due to replicating hepatitis B infection. *J Hepatol* 2000;33:301-7.
 12. Villeneuve JP, Condreay LD, Willems B, Pomier-Layrargues G, Fenyves D, Bilodeau M, Leduc R, Peltekian K, Wong F, Margulies M, Heathcote EJ: Lamivudine treatment for decompensated cirrhosis resulting from chronic hepatitis B. *Hepatology* 2000;31:207-10.
 13. Omata M: Treatment of chronic hepatitis B infection. *N Engl J Med* 1998;339:114-5.
 14. Lai CL, Chien RN, Leung NW, Chang TT, Guan R, Tai DI, Ng KY, Wu PC, Dent JC, Barber J, Stephenson SL, Gray DF: A one-year trial of lamivudine for chronic hepatitis B. Asia Hepatitis Lamivudine Study Group. *N Engl J Med* 1998;339:61-8. ID:9654535

2 1 . B 型肝硬変に対するラミブジン治療は肝硬変の進展を抑制するか

1. Fontana RJ: Management of decompensated HBV cirrhosis: lamivudine and beyond. *Am J Gastroenterol* 2004;99:64-7.
2. Manolakopoulos S, Karatapanis S, Elefsiniotis J, Mathou N, Vlachogiannakos J, Iliadou E, Kougioumtzan A, Economou M, Triantos C, Tzourmakliotis D, Avgerinos A: Clinical course of lamivudine monotherapy in patients with decompensated cirrhosis due to HBeAg negative chronic HBV infection. *Am J Gastroenterol* 2004;99:57-63.
3. Andreone P, Biselli M, Gramenzi A, Cursaro C, Morelli MC, Sama C, Lorenzini S, Spinucci G, Porzio F, Felling F, Di Giammarino L, Bernardi M: Efficacy of lamivudine therapy for advanced liver disease in patients with precore mutant hepatitis B virus infection awaiting liver transplantation. *Transplantation* 2002;74:1119-24.
4. Yao FY, Terrault NA, Freise C, Maslow L, Bass NM: Lamivudine treatment is beneficial in patients with severely decompensated cirrhosis and actively replicating hepatitis B infection awaiting liver transplantation: a comparative study using a matched, untreated cohort. *Hepatology* 2001;34:411-6.
5. Villeneuve JP, Condreay LD, Willems B, Pomier-Layrargues G, Fenyves D, Bilodeau M, Leduc R, Peltekian K, Wong F, Margulies M, Heathcote EJ: Lamivudine treatment for decompensated cirrhosis resulting from chronic hepatitis B. *Hepatology* 2000;31:207-10.

2 2 . ラミブジン内服により B 型非代償性肝硬変の予後は改善するか

1. Shindo M, Hamada K, Nishioji K, Muramatsu A, Oda Y, Okuno T: The predictive value of liver fibrosis in determining the effectiveness of interferon and lamivudine therapies for chronic hepatitis B. *J Gastroenterol* 2004;39:260-7.
2. Fontana RJ: Management of decompensated HBV cirrhosis: lamivudine and beyond. *Am J Gastroenterol* 2004;99:64-7.
3. Manolakopoulos S, Karatapanis S, Elefsiniotis J, Mathou N, Vlachogiannakos J, Iliadou E, Kougioumtzan A, Economou M, Triantos C, Tzourmakliotis D, Avgerinos A: Clinical course of lamivudine monotherapy in patients with decompensated cirrhosis due to HBeAg negative chronic HBV infection. *Am J Gastroenterol* 2004;99:57-63.
4. Hann HW, Fontana RJ, Wright T, Everson G, Baker A, Schiff ER, Riely C, Anschuetz G, Gardner SD, Brown N, Griffiths D: A United States compassionate use study of lamivudine treatment in nontransplantation candidates with decompensated hepatitis B virus-related cirrhosis. *Liver Transpl* 2003;9:49-56.
5. Yao FY, Terrault NA, Freise C, Maslow L, Bass NM: Lamivudine treatment is beneficial in patients with severely decompensated cirrhosis and actively replicating hepatitis B infection awaiting liver transplantation: a comparative study using a matched, untreated cohort. *Hepatology* 2001;34:411-6.
6. Da Silva LC, Pinho JR, Sitnik R, Da Fonseca LE, Carrilho FJ: Efficacy and tolerability of long-term

- therapy using high lamivudine doses for the treatment of chronic hepatitis B. *J Gastroenterol* 2001;36:476-85.
7. Sponseller CA, Bacon BR, Di Bisceglie AM: Clinical improvement in patients with decompensated liver disease caused by hepatitis B after treatment with lamivudine. *Liver Transpl* 2000;6:715-20.
 8. Fontana RJ, Lok AS: Lamivudine treatment in patients with decompensated hepatitis B cirrhosis: for whom and when? *J Hepatol* 2000;33:329-32.
 9. Kapoor D, Guptan RC, Wakil SM, Kazim SN, Kaul R, Agarwal SR, Raisuddin S, Hasnain SE, Sarin SK: Beneficial effects of lamivudine in hepatitis B virus-related decompensated cirrhosis. *J Hepatol* 2000;33:308-12.
 10. Yao FY, Bass NM: Lamivudine treatment in patients with severely decompensated cirrhosis due to replicating hepatitis B infection. *J Hepatol* 2000;33:301-7.
 11. Kitay-Cohen Y, Ben-Ari Z, Tur-Kaspa R, Fainguelernt H, Lishner M: Extension of transplantation free time by lamivudine in patients with hepatitis B-induced decompensated cirrhosis. *Transplantation* 2000;69:2382-3. ID:10868644
 12. Villeneuve JP, Condreay LD, Willems B, Pomier-Layrargues G, Fenyves D, Bilodeau M, Leduc R, Peltekian K, Wong F, Margulies M, Heathcote EJ: Lamivudine treatment for decompensated cirrhosis resulting from chronic hepatitis B. *Hepatology* 2000;31:207-10.
 13. Ben-Ari Z, Zemel R, Kazetsker A, Fraser G, Tur-Kaspa R: Efficacy of lamivudine in patients with hepatitis B virus precore mutant infection before and after liver transplantation. *Am J Gastroenterol* 1999;94:663-7.

2 3 . ラミブジンによる治療は B 型肝炎硬変の肝発癌を抑制するか

2 4 . B 型肝炎硬変に対して IFN 療法を行うことでウイルスの陰性化、あるいはセロコンバージョンは得られるか

1. Shindo M, Hamada K, Nishioji K, Muramatsu A, Oda Y, Okuno T: The predictive value of liver fibrosis in determining the effectiveness of interferon and lamivudine therapies for chronic hepatitis B. *J Gastroenterol* 2004;39:260-7.
2. Hadziyannis SJ, Papatheodoridis GV, Vassilopoulos D: Treatment of HBeAg-negative chronic hepatitis B. *Semin Liver Dis* 2003;23:81-8.
3. Schieman U, Walli R, Schmidt F, Bogner J, Gross M: Thyroid hypoechogenicity in patients with chronic hepatitis receiving interferon-alpha therapy: evaluation by standardized grey scale ultrasonography. *Eur J Med Res* 2002;7:271-7.
4. Alberti A, Brunetto MR, Colombo M, Craxi A: Recent progress and new trends in the treatment of hepatitis B. *J Med Virol* 2002;67:458-62.
5. Tangkijvanich P, Thong-ngam D, Mahachai V, Kladchareon N, Suwangool P, Kullavanijaya P: Long-term effect of interferon therapy on incidence of cirrhosis and hepatocellular carcinoma in Thai patients with chronic hepatitis B. *Southeast Asian J Trop Med Public Health* 2001;32:452-8.
6. Brunetto MR, Oliveri F, Coco B, Leandro G, Colombatto P, Gorin JM, Bonino F: Outcome of anti-HBe positive chronic hepatitis B in alpha-interferon treated and untreated patients: a long term cohort study. *J Hepatol* 2002;36:263-70.
7. Yuen MF, Hui CK, Cheng CC, Wu CH, Lai YP, Lai CL: Long-term follow-up of interferon alfa treatment in Chinese patients with chronic hepatitis B infection: The effect on hepatitis B e antigen seroconversion and the development of cirrhosis-related complications. *Hepatology* 2001;34:139-45.
8. Camma C, Giunta M, Andreone P, Craxi A: Interferon and prevention of hepatocellular carcinoma in viral cirrhosis: an evidence-based approach. *J Hepatol* 2001;34:593-602.
9. Baffis V, Shrier I, Sherker AH, Szilagyi A: Use of interferon for prevention of hepatocellular carcinoma in cirrhotic patients with hepatitis B or hepatitis C virus infection. *Ann Intern Med* 1999;131:696-701.
10. Effect of interferon-alpha on progression of cirrhosis to hepatocellular carcinoma: a retrospective

- cohort study. International Interferon-alpha Hepatocellular Carcinoma Study Group. *Lancet* 1998;351:1535-9.
11. Fattovich G, Giustina G, Sanchez-Tapias J, Quero C, Mas A, Olivetto PG, Solinas A, Almasio P, Hadziyannis S, Degos F, de Moura MC, Krogsgaard K, Pantalena M, Realdi G, Corrocher R, Schalm SW: Delayed clearance of serum HBsAg in compensated cirrhosis B: relation to interferon alpha therapy and disease prognosis. European Concerted Action on Viral Hepatitis (EUROHEP) *Am J Gastroenterol* 1998;93:896-900.
 12. Han SB, Martin P: Successful antiviral therapy and prognosis in cirrhosis due to hepatitis B. *Am J Gastroenterol* 1998;93:859-60.
 13. Lobello S, Lorenzoni U, Vian A, Floreani A, Brunetto MR, Chiaramonte M: Interferon treatment in hepatitis B surface antigen-positive hepatitis B e antibody-positive chronic hepatitis B: role of hepatitis B core antibody IgM titre in patient selection and treatment monitoring. *J Viral Hepat* 1998;5:61-6.
 14. Ikeda K, Saitoh S, Suzuki Y, Kobayashi M, Tsubota A, Fukuda M, Koida I, Arase Y, Chayama K, Murashima N, Kumada H: Interferon decreases hepatocellular carcinogenesis in patients with cirrhosis caused by the hepatitis B virus: a pilot study. *Cancer* 1998;82:827-35.
 15. Fattovich G, Giustina G, Realdi G, Corrocher R, Schalm SW: Long-term outcome of hepatitis B e antigen-positive patients with compensated cirrhosis treated with interferon alfa. European Concerted Action on Viral Hepatitis (EUROHEP). *Hepatology* 1997;26:1338-42.
 16. Marcellin P, Giuily N, Lorient MA, Durand F, Samuel D, Bettan L, Degott C, Bernuau J, Benhamou JP, Erlinger S: Prolonged interferon-alpha therapy of hepatitis B virus-related decompensated cirrhosis. *J Viral Hepat* 1997;4 Suppl 1:21-6.
 17. Sarin SK, Guptan RC, Thakur V, Malhotra S, Malhotra V, Banerjee K, Khandekar P: Efficacy of low-dose alpha interferon therapy in HBV-related chronic liver disease in Asian Indians: a randomized controlled trial. *J Hepatol* 1996;24:391-6.
 18. Teuber G, Dienes HP, Meyer Zum Buschenfelde KH, Gerken G: Long-term follow-up of patients with chronic hepatitis B after interferon treatment. *Z Gastroenterol* 1996;34:230-6.
 19. Perrillo R, Tamburro C, Regenstein F, Balart L, Bodenheimer H, Silva M, Schiff E, Bodicky C, Miller B, Denham C, et al.: Low-dose, titratable interferon alfa in decompensated liver disease caused by chronic infection with hepatitis B virus. *Gastroenterology* 1995;109:908-16.
 20. Wong JB, Koff RS, Tine F, Pauker SG: Cost-effectiveness of interferon-alpha 2b treatment for hepatitis B e antigen-positive chronic hepatitis B. *Ann Intern Med* 1995;122:664-75.
 21. Eisenburg J: [Indications for interferon therapy in hepatology] *Fortschr Med* 1993;111:157-9.
 22. Hoofnagle JH, Di Bisceglie AM, Waggoner JG, Park Y: Interferon alfa for patients with clinically apparent cirrhosis due to chronic hepatitis B. *Gastroenterology* 1993;104:1116-21.
 23. Nevens F, Goubau P, Van Eyken P, Desmyter J, Desmet V, Fevery J: Treatment of decompensated viral hepatitis B-induced cirrhosis with low doses of interferon alpha. *Liver* 1993;13:15-9.
 24. Dimopoulou M, Fafoutis K, Basiliou K, Ketikoglou J, Karvountzis G: Interferon alfa-2b for decompensated liver disease caused by either chronic hepatitis B or C: preliminary results of a pilot study. *Gut* 1993;34:S104-5.

25. B型肝硬変に対するインターフェロン治療は肝硬変の進展を抑制するか

1. Farci P, Roskams T, Chessa L, Peddis G, Mazzoleni AP, Scioscia R, Serra G, Lai ME, Loy M, Caruso L, Desmet V, Purcell RH, Balestrieri A: Long-term benefit of interferon alpha therapy of chronic hepatitis D: regression of advanced hepatic fibrosis. *Gastroenterology* 2004;126:1740-9.
2. Shindo M, Hamada K, Nishioji K, Muramatsu A, Oda Y, Okuno T: The predictive value of liver fibrosis in determining the effectiveness of interferon and lamivudine therapies for chronic hepatitis B. *J Gastroenterol* 2004;39:260-7.
3. Alberti A, Brunetto MR, Colombo M, Craxi A: Recent progress and new trends in the treatment of hepatitis B. *J Med Virol* 2002;67:458-62.
4. Brunetto MR, Oliveri F, Coco B, Leandro G, Colombatto P, Gorin JM, Bonino F: Outcome of anti-HBe positive chronic hepatitis B in alpha-interferon treated and untreated patients: a long term cohort study. *J Hepatol* 2002;36:263-70.

5. Baffis V, Shrier I, Sherker AH, Szilagyi A: Use of interferon for prevention of hepatocellular carcinoma in cirrhotic patients with hepatitis B or hepatitis C virus infection. *Ann Intern Med* 1999;131:696-701.
6. Di Marco V, Lo Iacono O, Camma C, Vaccaro A, Giunta M, Martorana G, Fuschi P, Almasio PL, Craxi A: The long-term course of chronic hepatitis B. *Hepatology* 1999;30:257-64.
7. Fattovich G, Giustina G, Sanchez-Tapias J, Quero C, Mas A, Olivotto PG, Solinas A, Almasio P, Hadziyannis S, Degos F, de Moura MC, Krogsgaard K, Pantalena M, Realdi G, Corrocher R, Schalm SW: Delayed clearance of serum HBsAg in compensated cirrhosis B: relation to interferon alpha therapy and disease prognosis. European Concerted Action on Viral Hepatitis (EUROHEP) *Am J Gastroenterol* 1998;93:896-900.
8. Fattovich G, Giustina G, Realdi G, Corrocher R, Schalm SW: Long-term outcome of hepatitis B e antigen-positive patients with compensated cirrhosis treated with interferon alfa. European Concerted Action on Viral Hepatitis (EUROHEP). *Hepatology* 1997;26:1338-42.
9. Teuber G, Dienes HP, Meyer Zum Buschenfelde KH, Gerken G: Long-term follow-up of patients with chronic hepatitis B after interferon treatment. *Z Gastroenterol* 1996;34:230-6.
10. Dusheiko GM, Roberts JA: Treatment of chronic type B and C hepatitis with interferon alfa: an economic appraisal. *Hepatology* 1995;22:1863-73.
11. Perrillo R, Tamburro C, Regenstein F, Balart L, Bodenheimer H, Silva M, Schiff E, Bodicky C, Miller B, Denham C, et al.: Low-dose, titratable interferon alfa in decompensated liver disease caused by chronic infection with hepatitis B virus. *Gastroenterology* 1995;109:908-16.

2 6 . IFN 治療は B 型肝硬変の肝発癌を抑制するか

1. Oon CJ, Chen WN: Lymphoblastoid alpha-interferon in the prevention of hepatocellular carcinoma (HCC) in high-risk HbsAg-positive resected cirrhotic HCC cases: a 14-year follow-up. *Cancer Invest* 2003;21:394-9.
2. Alberti A, Brunetto MR, Colombo M, Craxi A: Recent progress and new trends in the treatment of hepatitis B. *J Med Virol* 2002;67:458-62.
3. Tangkijvanich P, Thong-ngam D, Mahachai V, Kladchareon N, Suwangool P, Kullavanijaya P: Long-term effect of interferon therapy on incidence of cirrhosis and hepatocellular carcinoma in Thai patients with chronic hepatitis B. *Southeast Asian J Trop Med Public Health* 2001;32:452-8.
4. Ikeda K: [Prevention of hepatocellular carcinogenesis by interferon] *Nippon Rinsho* 2001;59 Suppl 6:755-63.
5. Yuen MF, Hui CK, Cheng CC, Wu CH, Lai YP, Lai CL: Long-term follow-up of interferon alfa treatment in Chinese patients with chronic hepatitis B infection: The effect on hepatitis B e antigen seroconversion and the development of cirrhosis-related complications. *Hepatology* 2001;34:139-45.
6. Camma C, Giunta M, Andreone P, Craxi A: Interferon and prevention of hepatocellular carcinoma in viral cirrhosis: an evidence-based approach. *J Hepatol* 2001;34:593-602.
7. Baffis V, Shrier I, Sherker AH, Szilagyi A: Use of interferon for prevention of hepatocellular carcinoma in cirrhotic patients with hepatitis B or hepatitis C virus infection. *Ann Intern Med* 1999;131:696-701.
8. Effect of interferon-alpha on progression of cirrhosis to hepatocellular carcinoma: a retrospective cohort study. International Interferon-alpha Hepatocellular Carcinoma Study Group. *Lancet* 1998;351:1535-9.
9. Fattovich G, Giustina G, Sanchez-Tapias J, Quero C, Mas A, Olivotto PG, Solinas A, Almasio P, Hadziyannis S, Degos F, de Moura MC, Krogsgaard K, Pantalena M, Realdi G, Corrocher R, Schalm SW: Delayed clearance of serum HBsAg in compensated cirrhosis B: relation to interferon alpha therapy and disease prognosis. European Concerted Action on Viral Hepatitis (EUROHEP) *Am J Gastroenterol* 1998;93:896-900.
10. Ikeda K, Saitoh S, Suzuki Y, Kobayashi M, Tsubota A, Fukuda M, Koida I, Arase Y, Chayama K, Murashima N, Kumada H: Interferon decreases hepatocellular carcinogenesis in patients with cirrhosis caused by the hepatitis B virus: a pilot study. *Cancer* 1998;82:827-35.
11. Bonino F, Oliveri F, Colombatto P, Brunetto MR: Impact of interferon-alpha therapy on the