

長期投与の対象症例を選択する上での参考となる。				
1. ペグインターフェロン/リバビリン併用療法をおこなうも非 SVR と判定された症例(140, 141) 2. 肝硬変 (F4) や線維化の進展した慢性肝炎症例 (F3) (140, 141) 3. 60 歳以上の症例(143) 4. AFP 高値例(142, 143)				

CQ-8. 血小板低値の C 型慢性肝疾患に対して、IFN 以外の治療法として肝庇護療法および線維化抑制療法の有効性および対象は？

大阪市立大学大学院医学研究科 肝胆膵病態内科 河田則文
奈良県立医科大学 消化器内科 福井 博

ステートメント	グレード	エビデンスレベル		保険適用
		海外	日本	
CQ-8: 血小板低値の C 型慢性肝疾患に対して、IFN 以外の治療法として肝庇護療法はどの程度有効なのか？				
肝庇護療法および線維化抑制療法には、グリチルリチン製剤（強力ネオミノファーゲンシー：SNMC）、ウルソデオキシコール酸 (UDCA)、アンジオテンシン変換酵素阻害薬 (ACE-I) やアンジオテンシン受容体阻害薬 (ARB) が報告されている。しかし、血小板低値例など進行例に限っての有効性に関する明らかなエビデンスはない。肝庇護療法および線維化抑制療法の対象は IFN 治療にてウイルス排除し得なかった症例や、血小板低値あるいは副作用により抗ウイルス療法が遂行不能であった症例などが対象となる。	C1	II	II	有

解説：

1. SNMC

通常慢性 C 型肝炎における ALT 安定化に関しては Rossum らによる二重盲検 RCT の報告がある(レベル II) (144)。また本邦から、ALT の安定化に加えて、肝癌の発生抑制効果を示した報告がある (レベル IVb) (145, 146)。しかしこれらの報告は血小板低値例などの進行例の効果を検討した報告ではなく、血小板低値例に限定したエビデンスレベルの高い論文は見られない。

線維化進展抑制に関しても、慢性肝炎を対象とした SNMC 治療群 178 例、対照群 100 例で 13 年経過観察したところ肝硬変進展率に有意差があったという総説の記述があるが詳細は記載されていない。また血小板低値例などの進行例に限定して効果を検討した報告はエビデンスレベルの高い論文は見られない。

2. UDCA

通常の慢性 C 型肝炎における ALT 安定化に関しては Puoti や Takano による 450mg および 600mg 以上の投与量による ALT 安定化報告がある(レベル II) (147, 148)。しかし、血小板低値例などの進行例に限定して効果を検討した報告はエビデンスレベルの高い論文は見られない。

線維化進展抑制に関しても、HCV 陽性 45 例を含む 56 例の慢性肝疾患患者で UDCA を 1 年間投与した RCT の結果、有意差がなかったことが報告されている (レベル II) (149)。また、血小板低値例などの進行慢性肝炎例に限定して効果を検討した報告はエビデンスレベルの高い論文は見られない。

3. ACE-I/ARB

通常の慢性 C 型肝炎における ALT 安定化に関しては Enjouji による少数例での ALT 安定化報告がある(レベル IVb) (150)。しかし、血小板低値例などの進行例に限定して効果を検討した報告はエビデンスレベルの高い論文は見られない。

慢性肝炎を対象とした ARB 投与による肝線維化進展抑制効果について短期間の少数例における有効性が報告されている(レベル IVb) (151, 152)。しかし、血小板低値例などの進行例においては、HALT-C で対象となっている症例に対する ACE-I/ARB による肝線維化進展抑制効果は認められていない (レベル II) (115)。他、血小板低値例などの進行例に限定して効果を検討したエビデンスレベルの高い論文は見られない。

なお、上記以外に分岐鎖アミノ酸 (BCAA)、栄養療法 (適正エネルギー)、就寝時補食 (LES)には病期進展に対する抑制効果が報告されているが、いずれも肝硬変(非代償期)患者を対象とした検討である。

参考文献 : (115, 144-152)。

<検索詳細>

#1 ((肝炎-ウイルス性-ヒト/th or ウイルス性慢性肝炎/al)) and (DT=1983:2007 LA=日本語,英語 PT=原著論文,会議録除く CK=ヒト) 13,078 · #2 血小板低値/AL or (血小板/ta and 低値/ta) 993 · #3 (肝線維症/TH or 肝線維化/AL) or (線維症/TH or 線維化/AL) or (肝硬変/th or 肝硬変/al) 58,869 · #4 ("Glycyrrhizic acid"/TH or "Glycyrrhizic acid"/AL or グリチルリチン/al) or ("Stronger neo-minophagen c"/th or "Stronger neo-minophagen c"/AL or 強力ミノファーゲン/AL) 2,342 · #5 #1 and #2 and #3 and #4 1

#1 Search Chronic Hepatitis Limits: Humans, English, Japanese, Publication Date from 1983 to 2010 20:15:57 29114 · #2 Search platelet low 20:16:26 20991 · #3 Search "stronger neo-minophagen C" or SNMC or minophagen or "glycyrrhizic Acid"[MAJR] 20:24:36 510 · #4 Search #1 and #2 and #3 20:25:44 1

#1 Search Chronic Hepatitis Limits: Humans, English, Japanese, Publication Date from 1983 to 2010 20:15:57 29114 · #2 Search platelet low 20:16:26 20991 · #3 Search angiotensin 20:31:16

97114·#4 Search (ACE inhibitor or ACE inhibitors) OR (angioensin-converting enzyme inhibitors or angiotensin-converting enzyme inhibitor) 20:32:06 51444 · #5 Search angiotensinII type 1 receptor blockers or arb or arbs 20:32:58 3132 · #6 Search Meta-Analysis[PT] or clinical trial[pt] or practice guideline[pt] or randomized controlled trial[PT] 20:33:59 685068 · #7 Search #1 and #2 and (#3 or #4 or #5) and #6 20:35:43 0 · #8 Search liver cirrhosis Limits: Humans, English, Japanese, Publication Date from 1983 to 2010 20:20:52 33558 · 9 Search #8 and #2 and (#3 or #4 or #5) and #6 20:35:43 0

#1 ((肝炎-ウイルス性-ヒト/th or ウイルス性慢性肝炎/al)) and (DT=1983:2010 LA=日本語,英語 PT=原著論文,会議録除く,症例報告除く CK=ヒト) 10,912 · #2 血小板低値/AL or (血小板/ta and 低値/ta) 993 · #3 angiotensins/th or (Angiotensins/TH or アンジオテンシン/AL) 16,889 · #4 ACE 阻害/AL or アンジオテンシン変換酵素阻害/AL or "angiotensin-concertiong enzyme inhibitors"/th or · "angiotensin-concertiong enzyme inhibitors"/AL 5,128 · #5 ("Angiotensin II Type 1 Receptor Blockers"/TH or ARB/AL) or アンジオテンシン II 受容体拮抗/AL or "angiotensin II receptor antagonists"/th or ("Angiotensin II Type 1 Receptor Blockers"/TH or "angiotensin II receptor antagonists"/AL) 67,115 · #6 #1 and #2 and (#3 or #4 or #5) 0 · #7 ((肝炎-ウイルス性-ヒト/th or ウイルス性慢性肝炎/al)) and (DT=1983:2007 and LA=日本語,英語 and PT=原著論文, 会議録除く,症例報告除く and CK=ヒト) 10,912 · #8 #2 and #7 and (#3 or #4 or #5) 0

#1 ((肝炎-ウイルス性-ヒト/th or ウイルス性慢性肝炎/al)) and (DT=1983:2010 LA=日本語,英語 PT=原著論文,会議録除く CK=ヒト) 13,078 · #2 血小板低値/AL or (血小板/ta and 低値/ta) 993 · #3 (肝線維症/TH or 肝線維化/AL) or (線維症/TH or 線維化/AL) or (肝硬変/th or 肝硬変/al) 58,869 · #4 ("Glycyrrhizic acid"/TH or "Glycyrrhizic acid"/AL or グリチルリチン/al) or ("Stronger neo-minophagen c"/th or "Stronger neo-minophagen c"/AL or 強力ミノファーゲン/AL) 2,342 · #5 #1 and #2 and #3 and #4 1

#1 Search Chronic Hepatitis Limits: Humans, English, Japanese, Publication Date from 1983 to 2010 20:15:57 29114 · #2 Search ursodeoxycholic acid 20:16:13 3961 · #3 Search platelet low 20:16:26 20991 · #4 Search Meta-Analysis or Clinical trials or epidemiologic studies or "Meta-Analysis"[PT] or "clinical trial"[pt] or "practice guideline"[pt] or "randomized controlled trial"[PT] or "controlled clinical trial"[pt] or "multicenter study"[pt] 20:16:49 2049402 · #5 Search #1 and #2 and #3 and #4 20:17:34 0 · #6 Search liver cirrhosis Limits: Humans, English, Japanese, Publication Date from 1983 to 2010 20:20:52 33558 · #7 Search #6 and #2 and #3 and #4 20:21:47

CQ-9-1. 血小板数低値の C 型慢性肝疾患に対して、IFN 以外の治療法として瀉血療法の有効性は？

CQ-9-2. 瀉血療法の対象は？

川崎医科大学 肝胆膵内科学 日野啓輔

ステートメント	グレード	エビデンスレベル		保険適用
		海外	日本	
CQ-9-1：血小板数低値の C 型慢性肝疾患に対して、IFN 以外の治療法として瀉血療法の有効性は？				
ペグインターフェロン/リバビリン不応例あるいは非適応例の C 型慢性肝炎に対して、瀉血療法は血清トランスアミナーゼを低下させることのできる安全な治療法である。	B	II	II	有
<p>ペグインターフェロン/リバビリン不応例あるいは非適応例の C 型慢性肝炎に対して、瀉血療法は血清トランスアミナーゼを低下させることのできる安全な治療法である。</p> <p>解説：C 型慢性肝炎に対する瀉血療法の有効性は日本から初めて報告された(153)。また、厚生労働省研究班の C 型慢性肝疾患に対するガイドラインにおいて、肝発癌抑制を目的とした補助療法のひとつとして瀉血療法が挙げられている(154)。C 型慢性肝炎に対する 3 ヶ月間の瀉血療法により血清 ALT 値が有意に低下することが、多施設共同 RCT により明らかにされている(155)。米国からは瀉血単独と瀉血後 IFN 治療を行う RCT の報告があり、瀉血単独群での血清トランスアミナーゼの低下と有意差はないものの軽度の組織学的改善が報告されている(156)。さらに C 型慢性肝炎に対する長期（4 年～5 年以上）の瀉血療法により組織学的改善や肝発癌抑制効果が報告されているが(157-159)、これらは RCT によるものではなく、エビデンスレベルとしては III～IVa である。</p> <p>C 型慢性肝炎において血小板低値の場合は根治療法としてのインターフェロン治療を行えない場合も多いので、そのような場合には肝発癌抑制を目的として瀉血療法も選択されるが、肝硬変に対する瀉血についてはアルブミンの低下等の問題もあり、その安全性は確立されていない。</p> <p>参考文献：(153-159)</p>				
ステートメント	グレード	エビデンスレベル		保険適用
		海外	日本	
CQ-9-2：血小板低値の C 型慢性肝炎に対して、IFN 以外の治療法としての瀉血療法の対象は？				
抗ウイルス療法（ペグインターフェロン/リバビリンなど）不応例あるいは非適応例で、血清 ALT 値が正常上限を超える C 型慢性肝炎	B	II	II	有

解説：明確な適応基準は存在しないが、厚生労働省研究班のガイドラインにおいて抗ウイルス療法（ペグインターフェロン/リバビリンなど）不応例あるいは非適応例の C 型慢性肝炎に対する肝発癌抑制目的の治療法の一つとして推奨されている(154)。開始時 Hb 値については男性 13 g/dL、女性 11 g/dL 以上とする報告(155, 159)が認められる。C 型慢性肝炎の場合は線維化が中等度以上の進展例（F2 又は F3）を対象としている報告(158)が見られる。

参考文献： (154, 155, 158, 159)

PubMed において “phlebotomy” と “hepatitis C” の 2 つのキーワードで検索した結果 136 の文献がヒットしました。このなかでステートメント作成に適した内容で、RCT study、C 型慢性肝炎に対する瀉血第一報、瀉血の長期効果、および適応等を中心にステートメントに挙げた 7 つの文献を選択しました。

参考文献

1. Heathcote EJ, Shiffman ML, Cooksley WG, Dusheiko GM, Lee SS, Balart L, Reindollar R, et al. Peginterferon alfa-2a in patients with chronic hepatitis C and cirrhosis. *N Engl J Med* 2000;343:1673-1680.
2. Manns MP, McHutchison JG, Gordon SC, Rustgi VK, Shiffman M, Reindollar R, Goodman ZD, et al. Peginterferon alfa-2b plus ribavirin compared with interferon alfa-2b plus ribavirin for initial treatment of chronic hepatitis C: a randomised trial. *Lancet* 2001;358:958-965.
3. Fried MW, Shiffman ML, Reddy KR, Smith C, Marinos G, Goncales FL, Jr., Haussinger D, et al. Peginterferon alfa-2a plus ribavirin for chronic hepatitis C virus infection. *N Engl J Med* 2002;347:975-982.
4. Abergel A, Hezode C, Leroy V, Barange K, Bronowicki JP, Tran A, Alric L, et al. Peginterferon alpha-2b plus ribavirin for treatment of chronic hepatitis C with severe fibrosis: a multicentre randomized controlled trial comparing two doses of peginterferon alpha-2b. *J Viral Hepat* 2006;13:811-820.
5. Morisco F, Stroffolini T, Medda E, Amoruso DC, Almasio PL, Villa E, Zuin M, et al. Retrospective, observational, multicentre study on an Italian population affected by chronic hepatitis C who failed to clear HCV-RNA after the combined therapy (PEG-IFN and ribavirin): NADIR study. *J Viral Hepat* 2010;17:427-434.
6. Marrache F, Consigny Y, Ripault MP, Cazals-Hatem D, Martinot M, Boyer N, Degott C, et al. Safety and efficacy of peginterferon plus ribavirin in patients with chronic hepatitis C and bridging fibrosis or cirrhosis. *J Viral Hepat* 2005;12:421-428.
7. Di Marco V, Almasio PL, Ferraro D, Calvaruso V, Alaimo G, Peralta S, Di Stefano R, et al. Peg-interferon alone or combined with ribavirin in HCV cirrhosis with portal hypertension: a randomized controlled trial. *J Hepatol* 2007;47:484-491.
8. Oze T, Hiramatsu N, Yakushijin T, Mochizuki K, Oshita M, Hagiwara H, Mita E, et al. Indications and limitations for aged patients with chronic hepatitis C in pegylated interferon alfa-2b plus ribavirin combination therapy. *J Hepatol* 2011;54:604-611.
9. Okanoue T, Itoh Y, Hashimoto H, Yasui K, Minami M, Takehara T, Tanaka E, et al. Predictive values of amino acid sequences of the core and NS5A regions in antiviral therapy for hepatitis C: a Japanese multi-center study. *J Gastroenterol* 2009;44:952-963.
10. Arase Y, Suzuki F, Suzuki Y, Akuta N, Kawamura Y, Kobayashi M, Hosaka T, et al. Side effects of combination therapy of peginterferon and ribavirin for chronic hepatitis-C. *Intern Med* 2007;46:1827-1832.
11. Fernandez-Rodriguez CM, Alonso S, Martinez SM, Fornes X, Sanchez-Tapias JM, Rincon D, Rodriguez-Caravaca G, et al. Peginterferon plus ribavirin and sustained virological response in HCV-related cirrhosis: outcomes and factors predicting response. *Am J Gastroenterol* 2010;105:2164-2172; quiz 2173.
12. McHutchison JG, Manns M, Patel K, Poynard T, Lindsay KL, Trepo C, Dienstag J, et al. Adherence to combination therapy enhances sustained response in genotype-1-infected patients

with chronic hepatitis C. *Gastroenterology* 2002;123:1061-1069.

13. 菊地陽. 【臨床に役立つ貧血治療の実際】 その他 血液腫瘍性疾患以外の全身疾患に伴う貧血. *小児科診療* 2009;72:361-367.

14. Shah SH, Hayes PC, Allan PL, Nicoll J, Finlayson ND. Measurement of spleen size and its relation to hypersplenism and portal hemodynamics in portal hypertension due to hepatic cirrhosis. *Am J Gastroenterol* 1996;91:2580-2583.

15. Fellay J, Thompson AJ, Ge D, Gumbs CE, Urban TJ, Shianna KV, Little LD, et al. ITPA gene variants protect against anaemia in patients treated for chronic hepatitis C. *Nature* 2010;464:405-408.

16. Tanaka Y, Kurosaki M, Nishida N, Sugiyama M, Matsuura K, Sakamoto N, Enomoto N, et al. Genome-wide association study identified ITPA/DDR1 variants reflecting thrombocytopenia in pegylated interferon and ribavirin therapy for chronic hepatitis C. *Hum Mol Genet* 2011;20:3507-3516.

17. 井出達也. インターフェロン治療におけるうつ病発症と血小板数について. 厚生労働科学研究費補助金「血小板低値例へのインターフェロン治療法の確立を目指した基礎および臨床的研究」平成 22 年度総括・分担研究報告書. . 厚生労働科学研究費補助金 2011:33-35.

18. 内村直尚. インターフェロンに誘発されるうつ状態とその対処法の確立. 厚生労働科学研究費補助金「血小板低値例へのインターフェロン治療法の確立を目指した基礎および臨床的研究」平成 22 年度総括・分担研究報告書. . 厚生労働科学研究費補助金 2011:31-32.

19. Kurosaki M, Tanaka Y, Nishida N, Sakamoto N, Enomoto N, Honda M, Sugiyama M, et al. Pre-treatment prediction of response to pegylated-interferon plus ribavirin for chronic hepatitis C using genetic polymorphism in IL28B and viral factors. *J Hepatol* 2011;54:439-448.

20. Mauss S, Hueppe D, John C, Goelz J, Heyne R, Moeller B, Link R, et al. Estimating the likelihood of sustained virological response in chronic hepatitis C therapy. *J Viral Hepat* 2011;18:e81-90.

21. Inoue Y, Hiramatsu N, Oze T, Yakushijin T, Mochizuki K, Hagiwara H, Oshita M, et al. Factors affecting efficacy in patients with genotype 2 chronic hepatitis C treated by pegylated interferon alpha-2b and ribavirin: reducing drug doses has no impact on rapid and sustained virological responses. *J Viral Hepat* 2010;17:336-344.

22. Shiffman ML, Ghany MG, Morgan TR, Wright EC, Everson GT, Lindsay KL, Lok AS, et al. Impact of reducing peginterferon alfa-2a and ribavirin dose during retreatment in patients with chronic hepatitis C. *Gastroenterology* 2007;132:103-112.

23. Mangia A, Minerva N, Bacca D, Cozzolongo R, Agostinacchio E, Sogari F, Scotto G, et al. Determinants of relapse after a short (12 weeks) course of antiviral therapy and re-treatment efficacy of a prolonged course in patients with chronic hepatitis C virus genotype 2 or 3 infection. *Hepatology* 2009;49:358-363.

24. Akuta N, Suzuki F, Tsubota A, Suzuki Y, Someya T, Kobayashi M, Saitoh S, et al. Efficacy of interferon monotherapy to 394 consecutive naive cases infected with hepatitis C virus genotype 2a in Japan: therapy efficacy as consequence of tripartite interaction of viral, host and interferon

treatment-related factors. *J Hepatol* 2002;37:831-836.

25. Iwasaki Y, Shiratori Y, Hige S, Nishiguchi S, Takagi H, Onji M, Yoshida H, et al. A randomized trial of 24 versus 48 weeks of peginterferon alpha-2a in patients infected with chronic hepatitis C virus genotype 2 or low viral load genotype 1: a multicenter national study in Japan. *Hepatol Int* 2009.

26. Louie KS, Micallef JM, Pimenta JM, Forssen UM. Prevalence of thrombocytopenia among patients with chronic hepatitis C: a systematic review. *J Viral Hepat* 2011;18:1-7.

27. George JN, Woolf SH, Raskob GE, Wasser JS, Aledort LM, Ballem PJ, Blanchette VS, et al. Idiopathic thrombocytopenic purpura: a practice guideline developed by explicit methods for the American Society of Hematology. *Blood* 1996;88:3-40.

28. Rodeghiero F, Stasi R, Gernsheimer T, Michel M, Provan D, Arnold DM, Bussel JB, et al. Standardization of terminology, definitions and outcome criteria in immune thrombocytopenic purpura of adults and children: report from an international working group. *Blood* 2009;113:2386-2393.

29. Dufour JF, Pradat P, Ruivard M, Hot A, Dumontet C, Broussole C, Trepo C, et al. Severe autoimmune cytopenias in treatment-naive hepatitis C virus infection: clinical description of 16 cases. *Eur J Gastroenterol Hepatol* 2009;21:245-253.

30. Liebman HA, Stasi R. Secondary immune thrombocytopenic purpura. *Curr Opin Hematol* 2007;14:557-573.

31. 日本超音波検査学会監修. 腹部超音波テキスト 2002:133-151.

32. 西田 潤子 万恭. 脾臓. 消化器超音波医学 2000:135.

33. 朽尾人司, 岡部純弘, 工藤正俊. 【門脈圧亢進症の病態と治療】 超音波による門脈圧亢進症の診断. 消化器画像 2001;3:712-721.

34. 松谷正一. 【び慢性肝疾患の超音波診断】 門脈圧亢進症と側副血行路. 超音波医学 2009;36:319-327.

35. Friedrich-Rust M, Ong MF, Martens S, Sarrazin C, Bojunga J, Zeuzem S, Herrmann E. Performance of transient elastography for the staging of liver fibrosis: a meta-analysis. *Gastroenterology* 2008;134:960-974.

36. Talwalkar JA, Yin M, Fidler JL, Sanderson SO, Kamath PS, Ehman RL. Magnetic resonance imaging of hepatic fibrosis: emerging clinical applications. *Hepatology* 2008;47:332-342.

37. Hoefs JC, Wang FW, Lilien DL, Walker B, Kanel G. A novel, simple method of functional spleen volume calculation by liver-spleen scan. *J Nucl Med* 1999;40:1745-1755.

38. 勝谷慎也, 杉原清香, 木村昭郎. 特発性血小板減少性紫斑病(ITP)に対する H.pylori 除菌治療の有用性の検討. 消化器の臨床 2010;13:477-481.

39. Jackson SC, Beck P, Buret AG, O'Connor PM, Meddings J, Pineo G, Poon MC. Long term platelet responses to *Helicobacter pylori* eradication in Canadian patients with immune thrombocytopenic purpura. *Int J Hematol* 2008;88:212-218.

40. 善田貴裕, 増永高晴, 篠崎公秀, 岡田俊英, 近藤恭夫, 中尾眞二. C 型肝硬変に併発し, *Helicobacter pylori* 除菌療法が有用と考えられた特発性血小板減少性紫斑病の 1 例. 肝臓

2005;46:431-436.

41. Sakuraya M, Murakami H, Uchiyumi H, Hatsumi N, Akiba T, Yokohama A, Matsushima T, et al. Steroid-refractory chronic idiopathic thrombocytopenic purpura associated with hepatitis C virus infection. *Eur J Haematol* 2002;68:49-53.
42. Fujimura K, Kuwana M, Kurata Y, Imamura M, Harada H, Sakamaki H, Teramura M, et al. Is eradication therapy useful as the first line of treatment in *Helicobacter pylori*-positive idiopathic thrombocytopenic purpura? Analysis of 207 eradicated chronic ITP cases in Japan. *Int J Hematol* 2005;81:162-168.
43. Neunert C, Lim W, Crowther M, Cohen A, Solberg L, Jr., Crowther MA. The American Society of Hematology 2011 evidence-based practice guideline for immune thrombocytopenia. *Blood* 2011;117:4190-4207.
44. McHutchison JG, Dusheiko G, Shiffman ML, Rodriguez-Torres M, Sigal S, Bourliere M, Berg T, et al. Eltrombopag for thrombocytopenia in patients with cirrhosis associated with hepatitis C. *N Engl J Med* 2007;357:2227-2236.
45. Akahoshi T, Tomikawa M, Kawanaka H, Furusyo N, Kinjo N, Tsutsumi N, Nagao Y, et al. Laparoscopic splenectomy with IFN therapy in one hundred HCV-cirrhotic patients with hypersplenism and thrombocytopenia. *J Gastroenterol Hepatol* 2011.
46. Shigekawa Y, Uchiyama K, Takifuji K, Ueno M, Hama T, Hayami S, Tamai H, et al. A laparoscopic splenectomy allows the induction of antiviral therapy for patients with cirrhosis associated with hepatitis C virus. *Am Surg* 2011;77:174-179.
47. Ikezawa K, Naito M, Yumiba T, Iwahashi K, Onishi Y, Kita H, Nishio A, et al. Splenectomy and antiviral treatment for thrombocytopenic patients with chronic hepatitis C virus infection. *J Viral Hepat* 2010;17:488-492.
48. Akahoshi T, Tomikawa M, Korenaga D, Ikejiri K, Saku M, Takenaka K. Laparoscopic splenectomy with peginterferon and ribavirin therapy for patients with hepatitis C virus cirrhosis and hypersplenism. *Surg Endosc* 2010;24:680-685.
49. Tahara H, Takagi H, Sato K, Shimada Y, Tojima H, Hirokawa T, Ohyama T, et al. A retrospective cohort study of partial splenic embolization for antiviral therapy in chronic hepatitis C with thrombocytopenia. *J Gastroenterol* 2011;46:1010-1019.
50. Moreno A, Barcena R, Blazquez J, Quereda C, Gil-Grande L, Sanchez J, Moreno L, et al. Partial splenic embolization for the treatment of hypersplenism in cirrhotic HIV/HCV patients prior to pegylated interferon and ribavirin. *Antivir Ther* 2004;9:1027-1030.
51. Barcena R, Moreno A, Foruny JR, Blazquez J, Graus J, Riesco JM, Blesa C, et al. Partial splenic embolization and peg-IFN plus RBV in liver transplanted patients with hepatitis C recurrence: safety, efficacy and long-term outcome. *Clin Transplant* 2010;24:366-374.
52. Foruny JR, Blazquez J, Moreno A, Barcena R, Gil-Grande L, Quereda C, Perez-Elias MJ, et al. Safe use of pegylated interferon/ribavirin in hepatitis C virus cirrhotic patients with hypersplenism after partial splenic embolization. *Eur J Gastroenterol Hepatol* 2005;17:1157-1164.
53. Hadziyannis SJ, Sette H, Jr., Morgan TR, Balan V, Diago M, Marcellin P, Ramadori G, et al.

Peginterferon-alpha2a and ribavirin combination therapy in chronic hepatitis C: a randomized study of treatment duration and ribavirin dose. *Ann Intern Med* 2004;140:346-355.

54. Roomer R, Hansen BE, Janssen HL, de Knecht RJ. Thrombocytopenia and the risk of bleeding during treatment with peginterferon alfa and ribavirin for chronic hepatitis C. *J Hepatol* 2010;53:455-459.

55. Cheng WS, Roberts SK, McCaughan G, Sievert W, Weltman M, Crawford D, Rawlinson W, et al. Low virological response and high relapse rates in hepatitis C genotype 1 patients with advanced fibrosis despite adequate therapeutic dosing. *J Hepatol* 2010;53:616-623.

56. Hayashi PH, Mehta C, Joachim Reimers H, Solomon HS, Bacon BR. Splenectomy for thrombocytopenia in patients with hepatitis C cirrhosis. *J Clin Gastroenterol* 2006;40:740-744.

57. Morihara D, Kobayashi M, Ikeda K, Kawamura Y, Saneto H, Yatuji H, Hosaka T, et al. Effectiveness of combination therapy of splenectomy and long-term interferon in patients with hepatitis C virus-related cirrhosis and thrombocytopenia. *Hepatol Res* 2009;39:439-447.

58. Park A, Marcaccio M, Sternbach M, Witzke D, Fitzgerald P. Laparoscopic vs open splenectomy. *Arch Surg* 1999;134:1263-1269.

59. Park A, Targarona EM, Trias M. Laparoscopic surgery of the spleen: state of the art. *Langenbecks Arch Surg* 2001;386:230-239.

60. Cogliandolo A, Berland-Dai B, Pidoto RR, Marc OS. Results of laparoscopic and open splenectomy for nontraumatic diseases. *Surg Laparosc Endosc Percutan Tech* 2001;11:256-261.

61. Winslow ER, Brunt LM. Perioperative outcomes of laparoscopic versus open splenectomy: a meta-analysis with an emphasis on complications. *Surgery* 2003;134:647-653; discussion 654-645.

62. Kercher KW, Matthews BD, Walsh RM, Sing RF, Backus CL, Heniford BT. Laparoscopic splenectomy for massive splenomegaly. *Am J Surg* 2002;183:192-196.

63. Bell RL, Reinhardt KE, Cho E, Flowers JL. A ten-year, single institution experience with laparoscopic splenectomy. *JSLs* 2005;9:163-168.

64. Grahn SW, Alvarez J, 3rd, Kirkwood K. Trends in laparoscopic splenectomy for massive splenomegaly. *Arch Surg* 2006;141:755-761; discussion 761-752.

65. Mahon D, Rhodes M. Laparoscopic splenectomy: size matters. *Ann R Coll Surg Engl* 2003;85:248-251.

66. Patel AG, Parker JE, Wallwork B, Kau KB, Donaldson N, Rhodes MR, O'Rourke N, et al. Massive splenomegaly is associated with significant morbidity after laparoscopic splenectomy. *Ann Surg* 2003;238:235-240.

67. Casaccia M, Torelli P, Pasa A, Sormani MP, Rossi E. Putative predictive parameters for the outcome of laparoscopic splenectomy: a multicenter analysis performed on the Italian Registry of Laparoscopic Surgery of the Spleen. *Ann Surg* 2010;251:287-291.

68. Ohta M, Nishizaki T, Matsumoto T, Shimabukuro R, Sasaki A, Shibata K, Matsusaka T, et al. Analysis of risk factors for massive intraoperative bleeding during laparoscopic splenectomy. *J Hepatobiliary Pancreat Surg* 2005;12:433-437.

69. Targarona EM, Balague C, Cerdan G, Espert JJ, Lacy AM, Visa J, Trias M. Hand-assisted

laparoscopic splenectomy (HALS) in cases of splenomegaly: a comparison analysis with conventional laparoscopic splenectomy. *Surg Endosc* 2002;16:426-430.

70. Rosen M, Brody F, Walsh RM, Ponsky J. Hand-assisted laparoscopic splenectomy vs conventional laparoscopic splenectomy in cases of splenomegaly. *Arch Surg* 2002;137:1348-1352.

71. Kaban GK, Czerniach DR, Cohen R, Novitsky YW, Yood SM, Perugini RA, Kelly JJ, et al. Hand-assisted laparoscopic splenectomy in the setting of splenomegaly. *Surg Endosc* 2004;18:1340-1343.

72. Pietrabissa A, Morelli L, Peri A, Pugliese L, Zonta S, Dionigi P, Mosca F. Laparoscopic treatment of splenomegaly: a case for hand-assisted laparoscopic surgery. *Arch Surg* 2011;146:818-823.

73. Abbas A, K., Lichtman A, H., Pillai S. *Cellular And Molecular Immunology*. 6th Edition. SAUNDARS · ELSEVIER. 2007.

74. 眞一 吉, 雄介 柳, 泰信 吉. 戸田新細菌学改訂 33 版 南山堂. 2007.

75. Hadem J, Cornberg M, Hauptmann C, Suttman U, Manns MP, Wedemeyer H. Pneumococcal meningitis during antiviral treatment with interferon and ribavirin in a splenectomized patient with chronic hepatitis C - do not miss vaccination before starting therapy. *Z Gastroenterol* 2008;46:880-882.

76. Mourtzoukou EG, Pappas G, Peppas G, Falagas ME. Vaccination of asplenic or hyposplenic adults. *Br J Surg* 2008;95:273-280.

77. Landgren O, Bjorkholm M, Konradsen HB, Soderqvist M, Nilsson B, Gustavsson A, Axdorph U, et al. A prospective study on antibody response to repeated vaccinations with pneumococcal capsular polysaccharide in splenectomized individuals with special reference to Hodgkin's lymphoma. *J Intern Med* 2004;255:664-673.

78. Cherif H, Landgren O, Konradsen HB, Kalin M, Bjorkholm M. Poor antibody response to pneumococcal polysaccharide vaccination suggests increased susceptibility to pneumococcal infection in splenectomized patients with hematological diseases. *Vaccine* 2006;24:75-81.

79. Ejstrud P, Kristensen B, Hansen JB, Madsen KM, Schonheyder HC, Sorensen HT. Risk and patterns of bacteraemia after splenectomy: a population-based study. *Scand J Infect Dis* 2000;32:521-525.

80. Lehne G, Hannisdal E, Langholm R, Nome O. A 10-year experience with splenectomy in patients with malignant non-Hodgkin's lymphoma at the Norwegian Radium Hospital. *Cancer* 1994;74:933-939.

81. Deodhar M, Kakkar N. An audit of splenectomies in a teaching hospital in North India. Are postsplenectomy guidelines being complied with? *J Clin Pathol* 2004;57:407-410.

82. Rutherford EJ, Livengood J, Higginbotham M, Miles WS, Koestner J, Edwards KM, Sharp KW, et al. Efficacy and safety of pneumococcal revaccination after splenectomy for trauma. *J Trauma* 1995;39:448-452.

83. USA C. USA, CDC

http://www.surgicalcriticalcare.net/Guidelines/splenectomy_vaccines.pdf.

84. UK. UK <http://www.gpnotebook.co.uk/simplepage.cfm?ID=-1744437178>.
85. Australia. Australia <http://www.nevdgp.org.au/info/immunisation/part2.pdf>.
86. WHO. WHO <http://www.who.int/vaccines/en/pneumococcus.shtml>.
87. 社団法人日本感染症学会. 社団法人
http://www.kansensho.or.jp/topics/pdf/pneumococcus_vaccine.pdf.
88. Pietrabissa A, Moretto C, Antonelli G, Morelli L, Marciano E, Mosca F. Thrombosis in the portal venous system after elective laparoscopic splenectomy. *Surg Endosc* 2004;18:1140-1143.
89. Ikeda M, Sekimoto M, Takiguchi S, Kubota M, Ikenaga M, Yamamoto H, Fujiwara Y, et al. High incidence of thrombosis of the portal venous system after laparoscopic splenectomy: a prospective study with contrast-enhanced CT scan. *Ann Surg* 2005;241:208-216.
90. Miniati DN, Padidar AM, Kee ST, Krummel TM, Mallory B. Portal vein thrombosis after laparoscopic splenectomy: an ongoing clinical challenge. *JSLs* 2005;9:335-338.
91. Ikeda M, Sekimoto M, Takiguchi S, Yasui M, Danno K, Fujie Y, Kitani K, et al. Total splenic vein thrombosis after laparoscopic splenectomy: a possible candidate for treatment. *Am J Surg* 2007;193:21-25.
92. Krauth MT, Lechner K, Neugebauer EA, Pabinger I. The postoperative splenic/portal vein thrombosis after splenectomy and its prevention--an unresolved issue. *Haematologica* 2008;93:1227-1232.
93. Danno K, Ikeda M, Sekimoto M, Sugimoto T, Takemasa I, Yamamoto H, Doki Y, et al. Diameter of splenic vein is a risk factor for portal or splenic vein thrombosis after laparoscopic splenectomy. *Surgery* 2009;145:457-464; discussion 465-456.
94. Yoshida M, Watanabe Y, Horiuchi A, Yamamoto Y, Sugishita H, Kawachi K. Portal and splenic venous thrombosis after splenectomy in patients with hypersplenism. *Hepatogastroenterology* 2009;56:538-541.
95. Ushitora Y, Tashiro H, Takahashi S, Amano H, Oshita A, Kobayashi T, Chayama K, et al. Splenectomy in chronic hepatic disorders: portal vein thrombosis and improvement of liver function. *Dig Surg* 2011;28:9-14.
96. Kinjo N, Kawanaka H, Akahoshi T, Tomikawa M, Yamashita N, Konishi K, Tanoue K, et al. Risk factors for portal venous thrombosis after splenectomy in patients with cirrhosis and portal hypertension. *Br J Surg* 2010;97:910-916.
97. Kawanaka H, Akahoshi T, Kinjo N, Konishi K, Yoshida D, Anegawa G, Yamaguchi S, et al. Impact of antithrombin III concentrates on portal vein thrombosis after splenectomy in patients with liver cirrhosis and hypersplenism. *Ann Surg* 2010;251:76-83.
98. Wang H, Kopac D, Brisebois R, Sample C, Shapiro AM. Randomized controlled trial to investigate the impact of anticoagulation on the incidence of splenic or portal vein thrombosis after laparoscopic splenectomy. *Can J Surg* 2011;54:227-231.
99. Tran T, Demyttenaere SV, Polyhronopoulos G, Seguin C, Artho GP, Kaneva P, Fried GM, et al. Recommended timing for surveillance ultrasonography to diagnose portal splenic vein thrombosis after laparoscopic splenectomy. *Surg Endosc* 2010;24:1670-1678.

100. Wang L, Liu GJ, Chen YX, Dong HP, Zhang YQ, Wang LX. Combined use of D-dimer and P-selectin for the diagnosis of splenic or portal vein thrombosis following splenectomy. *Thromb Res* 2010;125:e206-209.
101. Kato M, Shimohashi N, Ouchi J, Yoshida K, Tanabe Y, Takenaka K, Nakamuta M. Partial splenic embolization facilitates completion of interferon therapy in patients with chronic HCV infection and hypersplenism. *J Gastroenterol* 2005;40:1076-1077.
102. Miyake Y, Ando M, Kaji E, Toyokawa T, Nakatsu M, Hirohata M. Partial splenic embolization prior to combination therapy of interferon and ribavirin in chronic hepatitis C patients with thrombocytopenia. *Hepato Res* 2008;38:980-986.
103. T M. Usefulness of partial splenic embolization as auxiliary treatment for liver cirrhosis and hepatocellular carcinoma. *JJPH* 2009;15:337-343.
104. 高塚健太郎, 岩渕省吾, 吉松英輝. 新しい部分的脾動脈塞栓術(PSE)の手技と効果. *日本門脈圧亢進症学会雑誌* 2005;11:286-293.
105. 吉岡寛康, 黒田知純, 丸川太郎. 脾機能亢進症に対する脾動脈塞栓術 Steel coil と Gelfoam の比較. *臨床放射線* 1985;30:1549-1556.
106. Noguchi H, Hirai K, Aoki Y, Sakata K, Tanikawa K. Changes in platelet kinetics after a partial splenic arterial embolization in cirrhotic patients with hypersplenism. *Hepatology* 1995;22:1682-1688.
107. Sangro B, Bilbao I, Herrero I, Corella C, Longo J, Beloqui O, Ruiz J, et al. Partial splenic embolization for the treatment of hypersplenism in cirrhosis. *Hepatology* 1993;18:309-314.
108. 横井一, 山際健太郎, 東口高志, 他. 肝硬変症に合併した高度凝固線溶系機能異常に対する部分的脾動脈塞栓術(PSE)の効果と肝細胞癌切除への応用. *日本消化器外科学会雑誌* 1990;23:127-139.
109. Hayashi H, Beppu T, Masuda T, Mizumoto T, Takahashi M, Ishiko T, Takamori H, et al. Predictive factors for platelet increase after partial splenic embolization in liver cirrhosis patients. *J Gastroenterol Hepatol* 2007;22:1638-1642.
110. N'Kontchou G, Seror O, Bourcier V, Mohand D, Ajavon Y, Castera L, Grando-Lemaire V, et al. Partial splenic embolization in patients with cirrhosis: efficacy, tolerance and long-term outcome in 32 patients. *Eur J Gastroenterol Hepatol* 2005;17:179-184.
111. Owman T, Lunderquist A, Alwmark A, Borjesson B. Embolization of the spleen for treatment of splenomegaly and hypersplenism in patients with portal hypertension. *Invest Radiol* 1979;14:457-464.
112. Hayashi H, Beppu T, Okabe K, Masuda T, Okabe H, Baba H. Risk factors for complications after partial splenic embolization for liver cirrhosis. *Br J Surg* 2008;95:744-750.
113. Hayashi H, Beppu T, Okabe K, Masuda T, Okabe H, Ishiko T, Baba H. Therapeutic factors considered according to the preoperative splenic volume for a prolonged increase in platelet count after partial splenic embolization for liver cirrhosis. *J Gastroenterol* 2010;45:554-559.
114. Sakai T, Shiraki K, Inoue H, Sugimoto K, Ohmori S, Murata K, Takase K, et al. Complications of partial splenic embolization in cirrhotic patients. *Dig Dis Sci* 2002;47:388-391.
115. Ohmoto K, Yoshioka N, Tomiyama Y, Shibata N, Takesue M, Yoshida K, Kuboki M, et al.

- Improved prognosis of cirrhosis patients with esophageal varices and thrombocytopenia treated by endoscopic variceal ligation plus partial splenic embolization. *Dig Dis Sci* 2006;51:352-358.
116. Han MJ, Zhao HG, Ren K, Zhao DC, Xu K, Zhang XT. Partial splenic embolization for hypersplenism concomitant with or after arterial embolization of hepatocellular carcinoma in 30 patients. *Cardiovasc Intervent Radiol* 1997;20:125-127.
117. Koconis KG, Singh H, Soares G. Partial splenic embolization in the treatment of patients with portal hypertension: a review of the english language literature. *J Vasc Interv Radiol* 2007;18:463-481.
118. Amin MA, el-Gendy MM, Dawoud IE, Shoma A, Negm AM, Amer TA. Partial splenic embolization versus splenectomy for the management of hypersplenism in cirrhotic patients. *World J Surg* 2009;33:1702-1710.
119. Matsumoto T, Yamagami T, Terayama K, Kato T, Hirota T, Yoshimatsu R, Miura H, et al. Risk factors and clinical course of portal and/or splenic vein thrombosis after partial splenic embolization. *Acta Radiol* 2009;50:617-623.
120. 研道 清, 隆文 市. 肝移植診療ガイドブック (日本肝臓学会・日本肝移植研究会監修)アークメディア出版. 肝移植診療ガイドブック (日本肝臓学会・日本肝移植研究会監修) 2007:9.
121. 浅原利正, 梅下浩司, 門田守人, 日本肝移植研究会. 肝移植症例登録報告. 移植 2010;45:621-632.
122. Bzowej N, Nelson DR, Terrault NA, Everson GT, Teng LL, Prabhakar A, Charlton MR. PHOENIX: A randomized controlled trial of peginterferon alfa-2a plus ribavirin as a prophylactic treatment after liver transplantation for hepatitis C virus. *Liver Transpl* 2011;17:528-538.
123. Guillouche P, Feray C. Systematic review: anti-viral therapy of recurrent hepatitis C after liver transplantation. *Aliment Pharmacol Ther* 2011;33:163-174.
124. Triantos C, Samonakis D, Stigliano R, Thalheimer U, Patch D, Burroughs A. Liver transplantation and hepatitis C virus: systematic review of antiviral therapy. *Transplantation* 2005;79:261-268.
125. Berenguer M. Systematic review of the treatment of established recurrent hepatitis C with pegylated interferon in combination with ribavirin. *J Hepatol* 2008;49:274-287.
126. Angelico M, Petrolati A, Lionetti R, Lenci I, Burra P, Donato MF, Merli M, et al. A randomized study on Peg-interferon alfa-2a with or without ribavirin in liver transplant recipients with recurrent hepatitis C. *J Hepatol* 2007;46:1009-1017.
127. Shergill AK, Khalili M, Straley S, Bollinger K, Roberts JP, Ascher NA, Terrault NA. Applicability, tolerability and efficacy of preemptive antiviral therapy in hepatitis C-infected patients undergoing liver transplantation. *Am J Transplant* 2005;5:118-124.
128. Wang CS, Ko HH, Yoshida EM, Marra CA, Richardson K. Interferon-based combination anti-viral therapy for hepatitis C virus after liver transplantation: a review and quantitative analysis. *Am J Transplant* 2006;6:1586-1599.
129. Gane EJ, Lo SK, Riordan SM, Portmann BC, Lau JY, Naoumov NV, Williams R. A randomized study comparing ribavirin and interferon alfa monotherapy for hepatitis C recurrence

- after liver transplantation. *Hepatology* 1998;27:1403-1407.
130. Lodato F, Berardi S, Gramenzi A, Mazzella G, Lenzi M, Morelli MC, Tame MR, et al. Clinical trial: peg-interferon alfa-2b and ribavirin for the treatment of genotype-1 hepatitis C recurrence after liver transplantation. *Aliment Pharmacol Ther* 2008;28:450-457.
131. Chalasani N, Manzarbeitia C, Ferenci P, Vogel W, Fontana RJ, Voigt M, Riely C, et al. Peginterferon alfa-2a for hepatitis C after liver transplantation: two randomized, controlled trials. *Hepatology* 2005;41:289-298.
132. Carrion JA, Navasa M, Garcia-Retortillo M, Garcia-Pagan JC, Crespo G, Bruguera M, Bosch J, et al. Efficacy of antiviral therapy on hepatitis C recurrence after liver transplantation: a randomized controlled study. *Gastroenterology* 2007;132:1746-1756.
133. Samuel D, Bizollon T, Feray C, Roche B, Ahmed SN, Lemonnier C, Cohard M, et al. Interferon-alpha 2b plus ribavirin in patients with chronic hepatitis C after liver transplantation: a randomized study. *Gastroenterology* 2003;124:642-650.
134. Firpi RJ, Abdelmalek MF, Soldevila-Pico C, Reed A, Hemming A, Howard R, Van Der Werf W, et al. Combination of interferon alfa-2b and ribavirin in liver transplant recipients with histological recurrent hepatitis C. *Liver Transpl* 2002;8:1000-1006.
135. Ahmad J, Dodson SF, Demetris AJ, Fung JJ, Shakil AO. Recurrent hepatitis C after liver transplantation: a nonrandomized trial of interferon alfa alone versus interferon alfa and ribavirin. *Liver Transpl* 2001;7:863-869.
136. Cotler SJ, Ganger DR, Kaur S, Rosenblate H, Jakate S, Sullivan DG, Ng KW, et al. Daily interferon therapy for hepatitis C virus infection in liver transplant recipients. *Transplantation* 2001;71:261-266.
137. Sheiner PA, Boros P, Klion FM, Thung SN, Schluger LK, Lau JY, Mor E, et al. The efficacy of prophylactic interferon alfa-2b in preventing recurrent hepatitis C after liver transplantation. *Hepatology* 1998;28:831-838.
138. Singh N, Gayowski T, Wannstedt CF, Shakil AO, Wagener MM, Fung JJ, Marino IR. Interferon-alpha for prophylaxis of recurrent viral hepatitis C in liver transplant recipients: a prospective, randomized, controlled trial. *Transplantation* 1998;65:82-86.
139. Kizilisik TA, al-Sebayel M, Hammad A, al-Traif I, Ramirez CG, Abdulla A. Hepatitis C recurrence in liver transplant recipients. *Transplant Proc* 1997;29:2875-2877.
140. Di Bisceglie AM, Shiffman ML, Everson GT, Lindsay KL, Everhart JE, Wright EC, Lee WM, et al. Prolonged therapy of advanced chronic hepatitis C with low-dose peginterferon. *N Engl J Med* 2008;359:2429-2441.
141. Lok AS, Everhart JE, Wright EC, Di Bisceglie AM, Kim HY, Sterling RK, Everson GT, et al. Maintenance peginterferon therapy and other factors associated with hepatocellular carcinoma in patients with advanced hepatitis C. *Gastroenterology* 2011;140:840-849; quiz e812.
142. Nomura H, Kashiwagi Y, Hirano R, Tanimoto H, Tsutsumi N, Higashi M, Ishibashi H. Efficacy of low dose long-term interferon monotherapy in aged patients with chronic hepatitis C genotype 1 and its relation to alpha-fetoprotein: A pilot study. *Hepatol Res* 2007;37:490-497.

143. Arase Y, Ikeda K, Suzuki F, Suzuki Y, Kobayashi M, Akuta N, Hosaka T, et al. Prolonged-interferon therapy reduces hepatocarcinogenesis in aged-patients with chronic hepatitis C. *J Med Virol* 2007;79:1095-1102.
144. van Rossum TG, Vulto AG, Hop WC, Brouwer JT, Niesters HG, Schalm SW. Intravenous glycyrrhizin for the treatment of chronic hepatitis C: a double-blind, randomized, placebo-controlled phase I/II trial. *J Gastroenterol Hepatol* 1999;14:1093-1099.
145. Tarao K, Ohkawa S, Shimizu A, Harada M, Nakamura Y, Ito Y, Tamai S, et al. Significance of hepatocellular proliferation in the development of hepatocellular carcinoma from anti-hepatitis C virus-positive cirrhotic patients. *Cancer* 1994;73:1149-1154.
146. Arase Y, Ikeda K, Murashima N, Chayama K, Tsubota A, Koida I, Suzuki Y, et al. The long term efficacy of glycyrrhizin in chronic hepatitis C patients. *Cancer* 1997;79:1494-1500.
147. Puoti C, Pannullo A, Annovazzi G, Filippi T, Magrini A. Ursodeoxycholic acid and chronic hepatitis C infection. *Lancet* 1993;341:1413-1414.
148. Takano S, Ito Y, Yokosuka O, Ohto M, Uchiumi K, Hirota K, Omata M. A multicenter randomized controlled dose study of ursodeoxycholic acid for chronic hepatitis C. *Hepatology* 1994;20:558-564.
149. Bellentani S, Podda M, Tiribelli C, Callea F, Marazzi M, Sodde M, Merlini R, et al. Ursodiol in the long-term treatment of chronic hepatitis: a double-blind multicenter clinical trial. *J Hepatol* 1993;19:459-464.
150. Enjoji M, Kotoh K, Kato M, Higuchi N, Kohjima M, Nakashima M, Nakamuta M. Therapeutic effect of ARBs on insulin resistance and liver injury in patients with NAFLD and chronic hepatitis C: a pilot study. *Int J Mol Med* 2008;22:521-527.
151. 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.
152. Sookoian S, Fernandez MA, Castano G. Effects of six months losartan administration on liver fibrosis in chronic hepatitis C patients: a pilot study. *World J Gastroenterol* 2005;11:7560-7563.
153. Hayashi H, Takikawa T, Nishimura N, Yano M, Isomura T, Sakamoto N. Improvement of serum aminotransferase levels after phlebotomy in patients with chronic active hepatitis C and excess hepatic iron. *Am J Gastroenterol* 1994;89:986-988.
154. Kumada H, Okanoue T, Onji M, Moriwaki H, Izumi N, Tanaka E, Chayama K, et al. Guidelines for the treatment of chronic hepatitis and cirrhosis due to hepatitis C virus infection for the fiscal year 2008 in Japan. *Hepatol Res* 2010;40:8-13.
155. Yano M, Hayashi H, Yoshioka K, Kohgo Y, Saito H, Niitsu Y, Kato J, et al. A significant reduction in serum alanine aminotransferase levels after 3-month iron reduction therapy for chronic hepatitis C: a multicenter, prospective, randomized, controlled trial in Japan. *J Gastroenterol* 2004;39:570-574.
156. Di Bisceglie AM, Bonkovsky HL, Chopra S, Flamm S, Reddy RK, Grace N, Killenberg P, et

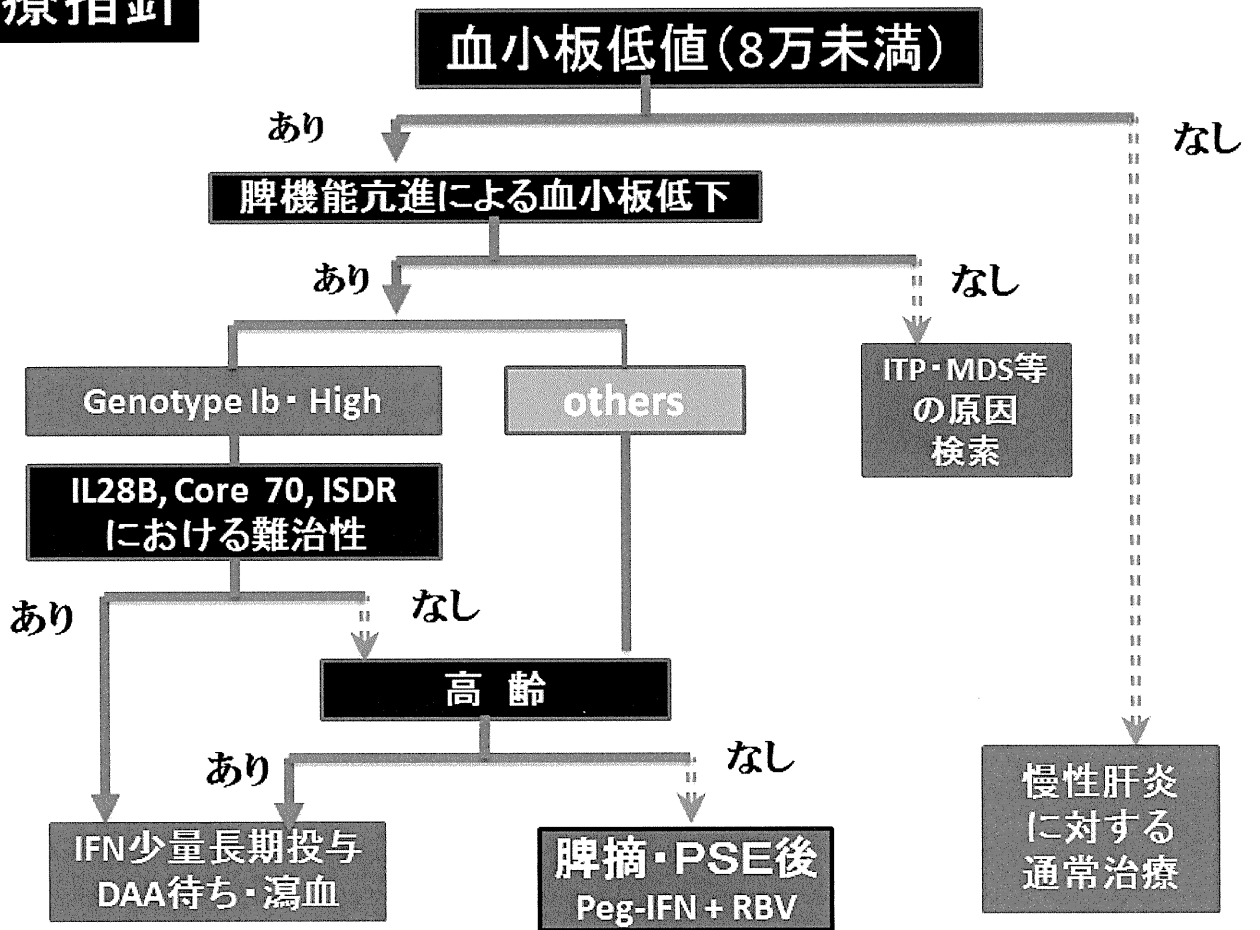
al. Iron reduction as an adjuvant to interferon therapy in patients with chronic hepatitis C who have previously not responded to interferon: a multicenter, prospective, randomized, controlled trial. *Hepatology* 2000;32:135-138.

157. Yano M, Hayashi H, Wakusawa S, Sanae F, Takikawa T, Shiono Y, Arao M, et al. Long term effects of phlebotomy on biochemical and histological parameters of chronic hepatitis C. *Am J Gastroenterol* 2002;97:133-137.

158. Kato J, Miyanishi K, Kobune M, Nakamura T, Takada K, Takimoto R, Kawano Y, et al. Long-term phlebotomy with low-iron diet therapy lowers risk of development of hepatocellular carcinoma from chronic hepatitis C. *J Gastroenterol* 2007;42:830-836.

159. Sartori M, Andorno S, Rossini A, Boldorini R, Bozzola C, Carmagnola S, Del Piano M, et al. Phlebotomy improves histology in chronic hepatitis C males with mild iron overload. *World J Gastroenterol* 2010;16:596-602.

治療指針



IV. 研究成果の刊行に関する一覧表

研究成果の刊行に関する一覧表

西口 修平 兵庫医科大学 内科学肝胆膵科 教授

書籍

著者氏名	論文タイトル名	書籍全体の編集者名	書籍名	出版社名	出版地	出版年	ページ
		西口修平	肝硬変のマネジメント (改定版)	医薬ジャーナル社	大阪	2011	

雑誌

発表者氏名	論文タイトル名	発表誌名	巻号	ページ	出版年
飯島尋子, 田中弘教, 吉田昌弘, 會澤信弘, 西上隆之, 廣田誠一, 西口修平.	慢性肝疾患の非侵襲的線維化診断法	総合臨床	60	43-48	2011
會澤信弘, 西口修平.	C型慢性肝炎に対するインターフェロン療法PEG-IFN・リバビリン併用療法を中心に血小板低値例に対するIFN療法脾摘術の功罪	日本臨床	69	201-205	2011
Shimomura S, Ikeda N, Saito M, Ishii A, Takashima T, Sakai Y, Yoshikawa S, Aizawa N, Tanaka H, Iwata Y, Enomoto H, Imanishi H, Yamamoto T, Jomura H, Nakamura H, Iijima H, Nishiguchi S.	Long-term interferon therapy after radiofrequency ablation is effective in treating patients with HCV-associated hepatocellular carcinoma.	Hepatol Int	5	559-566	2011
Shimomura S, Nishiguchi S.	Anticarcinogenic impact of interferon therapy on the progression of hepatocellular carcinoma in patients with chronic viral infection.	Hepatol Res.	26	1872-	2011