Innovative Drugs for bowel and liver diseases

Modern formulations and specially designed delivery systems ensure targeted release of the active drug.

Scientific Dialogue in the interest of therapeutic progress

Continuing medical education seminars

Comprehensive literature service for healthcare professionals and patients with more than 200 publications

Falk Symposia and Workshops nearly 250 attended by more than 100,000 participants from over 100 countries since 1967

Continuing medical education seminars over 14,000 attended by more than one million physicians and patients in Germany alone

http://www.falkfoundation.org

http://www.drfalkpharma.com

Leinenweberstr. 5 79108 Freiburg Germany
Tel +49 (0)761/1514-0 Fax +49 (0)761/1514-321 Mail zentrale@drfalkpharma.de

www.falksymposium174.com

Abstracts/Poster Abstracts

Poster Abstracts

Falk Symposium 174

Abstracts/Poster Abstracts

Falk Symposium 174

Gut and Liver

August 27 – 28, 2010
Shangri-La’s Kerry Centre Hotel
Beijing, P.R. China

Falk Symposium 174

Gut and Liver

August 27 – 28, 2010
Shangri-La’s Kerry Centre Hotel
Beijing, P.R. China

Falk Symposium 174

Gut and Liver

August 27 – 28, 2010
Shangri-La’s Kerry Centre Hotel
Beijing, P.R. China
Abstracts of Invited Lectures
Poster Abstracts

Falk Symposium 174

GUT AND LIVER

Beijing (P. R. China)
August 27 – 28, 2010

Scientific Organization:
C.-W. Chen, Shanghai (P. R. China)
J. Cheng, Beijing (P. R. China)
P. Ginès, Barcelona (Spain)
Q. Ouyang, Chengdu (P. R. China)
J. Schölmerich, Regensburg (Germany)
CONTENTS

Inflammatory bowel diseases

Session I

Pathophysiology

Chair:
P. Gibson, Melbourne
B. Xia, Wuhan

IBD genetics around the world
J. Cho, New Haven 21 – 22

The barrier as etiologic and pathophysiologic principle
M.F. Neurath, Erlangen 23

Environmental factors: Different in China versus the western world?
Y.-L. Liu, Beijing 24 – 25

Session II

Diagnostics

Chair:
S. Feuerbach, Regensburg
K.-C. Wu, Xi’an

Modern endoscopy and radiology in the diagnosis of inflammatory bowel disease
Z.-H. Ran, Shanghai 29 – 30

Serological markers in IBD
F. Rieder, G. Rogler, Zurich 31 – 32

Stool markers/microbiology
R.B. Sartor, Chapel Hill 33
State-of-the-Art Lecture I

Chair:
J.-J. Zheng, Suzhou

New insights into IBD epidemiology – Are there any lessons for treatment?
C.N. Bernstein, Winnipeg 34 – 38

Session III

Therapeutics I: Ulcerative colitis

Chair:
J.-M. Qian, Beijing
J.D. Sollano, Manila

Oral/rectal or combination 5-ASA?
P. Marteau, Paris 41 – 42

The choice of the immunosuppressant
G.J. Mantzaris, Athens 43

When is surgery indicated in UC?
Q. Ouyang, Y. Pan, Chengdu 44 – 45

Session IV

Therapeutics II: Crohn’s disease

Chair:
P.-J. Hu, Guangzhou
S.R. Targan, Los Angeles

Basic treatment and prediction of a severe course in Crohn’s disease
M. Simadibrata, Jakarta 49 – 50

Immunosuppressive therapy
T. Hibi, Tokyo 51 – 52

Surgical options
W.A. Bemelman, Amsterdam 53 – 54
State-of-the-Art Lecture II

Chair:
Y.-Z. Yuan, Shanghai

What should we expect from future therapies for Crohn’s disease?
S.B. Hanauer, Chicago 55

Liver diseases

Session V

Chronic liver inflammation

Chair:
X.-H. Miao, Shanghai
G. Paumgartner, Munich

New antiviral therapies in the management of hepatitis C virus infection
S. Zeuzem, Frankfurt 59 – 60

Management of hepatitis C, West and East
L. Wei, Beijing 61

Pathogenesis and management of non-alcoholic steatohepatitis
G.C. Farrell, Canberra 62 – 64

Session VI

Chronic liver failure – Clinical aspects

Chair:
P. Ginès, Barcelona
G.-Q. Wang, Beijing

Acute-on-chronic liver failure – Pathogenesis and diagnosis
R. Moreau, Clichy 67

Emerging role of adrenal insufficiency in chronic liver failure
M.-H. Tsai, Taipei 68 – 69
Pathogenesis and clinical significance of cirrhotic cardiomyopathy
S.S. Lee, Calgary 70

State-of-the-Art Lecture III

Chair:
E.J. Gane, Auckland

Management of chronic hepatitis B infection
C.-L. Lai, Hong Kong 71

Session VII

Chronic liver failure management

Chair:
J.-L. Hou, Guangzhou
F. Wong, Toronto

Renal complications
V. Arroyo-Perez, Barcelona 75

Management of bacterial infections
K.-H. Han, Seoul 76

Hepatic encephalopathy
D. Häussinger, Düsseldorf 77 – 78

Session VIII

Liver cancer

Chair:
J. Cheng, Beijing
A.M. Di Bisceglie, St. Louis

The antiviral therapy for decompensated hepatitis B-related cirrhosis
Q.-C. Fu, Shanghai 81

Diagnosis and stratification of hepatocellular carcinoma
M. Colombo, Milan 82
The diagnosis and management of small HCC
F. Shen, Shanghai 83 – 84

State-of-the-Art Lecture IV

Chair:
J. Fan, Shanghai

Management of hepatocellular carcinoma
G. Gores, Rochester 85

List of Chairpersons, Speakers and Scientific Organizers 87 – 91
1. Characteristics of ulcerative colitis in country with low prevalence of inflammatory bowel disease

2. Impaired endothelial function in patients with inflammatory bowel disease
H. Akpinar, H. Kayahan, I. Sari, N. Cullu, M. Akarsu, S. Demir, F. Yüksel, Y. Göktay, B. Ünsal (Izmir, TR)

3. Prevalence of microscopic colitis in patients with chronic non-bloody diarrhea and normal colonoscopy in Tugurejo Hospital Semarang, Indonesia
J.A. Auwyang, M. Simadibrata, A. Tarius (Semarang, Jakarta, RI)

4. Prevalence of mutations in thiopurine S-methyltransferase gene among Slovak IBD patients
M. Bátovska, B. Desatová, T. Hlavaty, M. Huorka, Z. Zelinková, P. Celec, D. Baláková, L. Kádesi, M. Gregus, M. Zakuciová, M. Hlista, M. Horáková (Bratislava, Nitra, Kosice, Trencin, Martin, SK; Rotterdam, NL)

5. Mutations in thiopurine S-methyltransferase gene increases risk of azathioprine-induced leukopenia in Slovak IBD patients
M. Bátovska, B. Desatová, T. Hlavaty, M. Huorka, Z. Zelinková, P. Celec, D. Baláková, L. Kádesi, M. Gregus, M. Zakuciová, M. Hlista, M. Horáková (Bratislava, Nitra, Kosice, Trencin, Martin, SK; Rotterdam, NL)

6. Immunomodulatory effect and mechanism of tuftsin in inflammatory bowel disease
C. Chen (Shanghai, RC)

7. Colorectal and rectocolic reflexes in canines: Involvement of tone, compliance and anal sphincter relaxation
J.-H. Chen, J.D.Z. Chen (Wuhan, RC; Galveston, USA)

8. Gastric electrical stimulation reduces visceral sensitivity to gastric distention in healthy canines
J.-H. Chen, J.D.Z. Chen (Wuhan, RC; Galveston, USA)

9. Traditional Chinese physician pattern of syndrome and correlation shown by the colonoscope of part of ulcerative colitis in Urumqi
J. Chen, H. Wang (Urumqi, RC)

10. Structural shifts of gut flora in rat acute alcoholic liver injury and Jianpihuoxue decoction's effect displayed by ERIC-PCR fingerprint
Y. Cheng, H. Wang, Y. Hu, G. Chen, J. Ping, J. Pen, Q. Fen (Shanghai, RC)
11. Capsule enteroscopy diagnostic yield for chronic abdominal pain
   J. Derova, A. Derovs, S. Sitkin, J. Pokrotnieks (Riga, LV; St. Petersburg, R)

12. Quality of bowel cleansing level before video capsule endoscopy, using most popular bowel cleansing scheme
   A. Derovs, J. Derova, S. Sitkin, J. Pokrotnieks (Riga, LV; St. Petersburg, R)

13. High depression and anxiety scores in a systematic review of psychological questionnaires in irritable bowel syndrome

14. NKX2-3 rs10883365 is associated with disease susceptibility to both Crohn's disease and ulcerative colitis while IRGM rs13361189 variant allele increased the risk for Crohn's disease in Eastern European patients

15. Increased intestinal permeability to iohexol as a marker of disease activity in patients with inflammatory bowel disease
   V. Gerova, D. Svinarov, S. Stoynov (Sofia, BG)

16. Proliferating cell nuclear antigen (PCNA) is associated with dysplasia in ulcerative colitis
   K. Guzinska-Ustymowicz, A. Pryczynicz, M. Ustymowicz, M. Sokolowski, A. Kemona (Bialystok, PL)

17. The natural history of adult Crohn's disease in China
   J. Hu, Q. Mei, J. Xu (Hefei, RC)

18. Study on the correlation of colonic pathologic changes due to ulcerative colitis and tongue proper, tongue four and pulse condition
   J. Han (Zhengzhou, RC)

19. The estimation of late rectal mucosal damage after conformal radiotherapy for prostate carcinoma
   P. Kedzierawski, T. Wollny, A. Salata (Kielce, PL)

20. The clinical and molecular features of ulcerative colitis related colon cancer
   J. Li, W. Zheng, J.-M. Qian (Beijing, RC)

21. Prevention of colonic fibrosis by taurine in rats with colitis induced by 2,4,6-trinitrobenzene sulphonic acid
   L. Lin, J. Cheng, Y. Ning, W. Zhang, H. Zhang (Nanjing, RC)

22. The clinical value of miniature ultrasonic probes on diagnosis and treatment of digestive tract diseases
   P. Liu (Jiangsu, RC)
23. The study of intestinal mucosal permeability of ulcerative colitis patients  
   X. Liu, Q. Mei, J. Xu, J. Jin, Q. Xia, D. Xu, J. Hu (Hefei, RC)

24. Effects of military training on food intake-related changes of automatic nervous system in new college students  
   X. Liu, Z. Li, Q. Zhang, C. Zhang, J.-H. Chen (Wuhan, RC)

25. Foxp3+ IL-17+ T cells in inflammatory intestinal mucosa show inflammatory features  
   Z. Liu, J. Su, X. Wang, P.-C. Yang (Shanghai, RC; Hamilton, CDN)

26. Downregulation of survivin by RNAi inhibits the growth of human gastric carcinoma cells SGC7901  
   Q.-M. Lu, G.-Y. Miao (Lanzhou, RC)

27. Practices of using methotrexate as monotherapy and in combination with azathioprine in patients with ulcerative colitis  
   P. Makarchuk (Moscow, R)

28. Improved quality-of-life in Crohn's disease after the intake of a probiotic  
   P. Nikolov, D. Panova (Sofia, BG)

29. Alterations of CRP in patients with inflammatory bowel disease after the intake of a probiotic  
   P. Nikolov (Sofia, BG)

30. Diagnostic criteria of IBD  
   Q. Ouyang, L.-Y. Xue (Chengdu, RC)

31. The role of complementary alternative medicine in inflammatory bowel disease – Focus on Traditional Chinese Medicine in UC  
   Y. Pan, Q. Ouyang, X. Chen, C. Ye (Chengdu, RC)

32. Capsule enteroscopy small bowel transit time doesn't correlate with vital signs  
   J. Pokrotnieks, J. Derova, S. Sitkin, A. Derovs (Riga, LV; St. Petersburg, R)

33. Comparative studies on the PCNA expression in inflammatory bowel diseases and colorectal cancer  
   A. Pryczynicz, K. Guzinska-Ustymowicz, M. Ustymowicz, M. Sokolowski, A. Kemona (Bialystok, PL)

34. Results of surgery in carcinoma rectum with sphincter preservation  
   M. Sahni, S. Jain, K.S. Sodhi (Hoshiarpur, IND)

35. Delayed gastric emptying in Indonesian population with reflux esophagitis  
   D. Samosir, L.A. Lesmana, M. Abdullah (Jakarta, RI)
36. Crohn's disease in the Endoscopic Unit, Division of Gastroenterology, Department of Internal Medicine, Cipto Mangunkusumo General Hospital, Jakarta in the year 2007–2008

37. Evaluation of Ki-67 and PCNA expression in Crohn's disease
M. Sokolowski, K. Guzinska-Ustymowicz, A. Pryczynicz, M. Ustymowicz, A. Kemona (Bialystok, PL)

38. Clinical study on effect of compound glutamin entersolube capsule combined clysis therapy on ulcerative colitis
H. Tan, M.-Y. Sun, J. Yang (Tianjin, RC)

39. Epidemiological prospective study in inflammatory bowel disease in Aljarafe region (Seville)

40. Clinical and epidemiological characteristics of Crohn's disease, depending on age at onset

41. Duodenal histologic alterations in lactose intolerance

42. Serum lipopolysaccharide-binding protein and soluble CD14 are markers of disease activity in patients with Crohn's disease
T.G. Toth, P. Fuszek, L.S. Kiss, K. Palatka, I. Altorjay, P. Antal-Szalmas, E. Palyu, M. Udvardy, T. Molnar, K. Farkas, J. Papp, M. Papp, P.L. Lakatos (Budapest, Debrecen, Szeged, H)

43. Ki-67 overexpression in Crohn's disease, colitis ulcerosa and colorectal adenocarcinoma
M. Ustymowicz, A. Pryczynicz, K. Guzinska-Ustymowicz, A. Kemona (Bialystok, PL)

44. Therapeutic effect of CXCR4 antagonist AMD3100 on experimental colitis induced by DSS in mice
F. Wang, X. Xia (Nanjing, RC)

45. The role of enteral nutrition in adult Crohn's disease patients
L. Wang, J. Guo, G. Zhang (Wuxi, RC)

46. The curative effect of moderate and severe ulcerative colitis treated by mesalazine combined with Tripterygium hypoglaucum Hutchins
L. Wang, Y.-S. Xiang, R. Jiang, C.-Q. Liu (Jingmen, RC)
<table>
<thead>
<tr>
<th>No.</th>
<th>Title</th>
<th>Authors</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>47</td>
<td>The frequency and function of Th-17 cells producing IL-17A in inflammatory bowel disease</td>
<td>Y. Wang, X. Liu, Z. Zhao, J. Chen, C. Yu</td>
<td>Nanjing, RC</td>
</tr>
<tr>
<td>48</td>
<td>The prevalence status of inflammatory bowel disease in China</td>
<td>Y. Wang, Q. Ouyang, R. Hu</td>
<td>Chengdu, RC</td>
</tr>
<tr>
<td>49</td>
<td>Human intestinal lamina propria CD4+CD25++ T regulatory cells (Treg) can be expanded in vitro with retention of potent suppressor function</td>
<td>Z. Wen, Q. Ouyang, G. West, C. Fiocchi</td>
<td>Chengdu, RC; Cleveland, USA</td>
</tr>
<tr>
<td>50</td>
<td>Hypoxia in perspective from inflammatory bowel disease to colorectal cancer – Study of hypoxia-inducible protein. EPO serum levels as prognostic marker of survival of colorectal cancer patients</td>
<td>A. Wincewicz, A. Pietrzykowski, L. Kanczuga-Koda, M. Baltaziak, M. Sulkowska, M. Koda, W. Famulski, S. Sulkowski</td>
<td>Bialystok, PL</td>
</tr>
<tr>
<td>51</td>
<td>A case-control study on dietary and living style factors for the development of inflammatory bowel disease in Hunan province</td>
<td>X. Wu, Y. Mo, X. Liu</td>
<td>Changsha, RC</td>
</tr>
<tr>
<td>52</td>
<td>Expression of proteinase-activated receptor-2 in intestinal mucosa of patients with ulcerative colitis</td>
<td>Z.-X. Wu</td>
<td>Hefei, RC</td>
</tr>
<tr>
<td>53</td>
<td>Effect of total glucosides of paeony on oxazolone-induced colitis in mice</td>
<td>J. Xiang, R. Hu, Q. Ouyang</td>
<td>Nanchong, Chengdu, RC</td>
</tr>
<tr>
<td>54</td>
<td>Role of endoscopy and histopathology in distinguishing between Crohn's disease and intestinal tuberculosis in Kunming, China</td>
<td>Y. Xiao, Y. Miao, Y. Du, P. Pu</td>
<td>Kunming, RC</td>
</tr>
<tr>
<td>55</td>
<td>Follow-up of surgical treatment for ulcerative colitis</td>
<td>S. Yang, R. Li, W. Fu</td>
<td>Beijing, RC</td>
</tr>
<tr>
<td>56</td>
<td>The relationship between tumor necrosis factor-α and ulcerative colitis</td>
<td>Y. Yang</td>
<td>Harbin, RC</td>
</tr>
<tr>
<td>57</td>
<td>Diagnosis of obscure gastrointestinal hemorrhages with capsule endoscopy in the different ages</td>
<td>B.-L. Zhang, C.-X. Chen, Y.-M. Li</td>
<td>Hangzhou, RC</td>
</tr>
<tr>
<td>58</td>
<td>The effect of military training impact on freshmen's electrogastrogram (EGG)</td>
<td>Q. Zhang, Z. Li, C. Zhang, X. Liu, J.-H. Chen</td>
<td>Wuhan, RC</td>
</tr>
<tr>
<td>59</td>
<td>Expression and clinical significance of GAFP and COX-2 in the colonic mucosa of patients with ulcerative colitis and irritable bowel syndrome</td>
<td>Y.-Q. Zhong, R. Yan</td>
<td>Guangzhou, RC</td>
</tr>
</tbody>
</table>
60. HIV protease inhibitors induce gut microbial translocation and systemic inflammation by disrupting intestinal epithelial barrier integrity through activating the ER stress response
H. Zhou, Y. Huang, X. Li, E. Studer, W.M. Pandak, P.B. Hylemon (Richmond, USA; Wenzhou, RC)

61. The quantitative analysis of the contrast-enhanced ultrasonography in colorectal carcinomas
H. Zhuang, Z.-G. Yang (Chengdu, RC)

Liver

62. The amount of alcohol consumption negatively impacts short-term mortality in patients with alcoholic hepatitis: Clinical implications

63. Hepatitis B virus genotypes and subtypes among chronic hepatitis B, liver cirrhosis and hepatocellular carcinoma patients in Pekanbaru, Indonesia
A. Arfianti, A. Zainal, R. Endriani, F. Andrini (Pekanbaru, RI)

64. Value of large volume paracentesis in management of ascitic patients with acute variceal bleeding
A. Bahnacy, M. Alserafy (Menoufiya, Cairo, ET)

65. State hepatobiliary system in children with obesity and metabolic syndrome
T.A. Bokova (Moscow, R)

66. Effects of ursodeoxycholic acid in treatment of children with metabolic syndrome
T.A. Bokova (Moscow, R)

67. The value of MESO (MELD/Na index) scoring system in predicting prognosis of patients with cirrhosis
L. Chen, N. Hu, Y. Wang (Hefei, RC)

68. The clinical analysis of 82 patients with drug-induced liver injury
C.-L. Cong, B.-Z. Su (Hohhot, RC)

69. Clinical features and effects of ursodeoxycholic acid on Chinese patients with primary biliary cirrhosis
W.-J. Duan, X.-J. Ou, F.-K. Zhang, H. You, H. Ma, J.-D. Jia (Beijing, RC)

70. Frequent hypermethylation of the 14-3-3 sigma gene in human hepatitis B virus-related hepatocellular carcinoma
Y.-F. Gao, Q. Su, J.-B. Li, X. Li (Hefei, RC)
71. Small intestinal dysmotility and bacterial overgrowth in patients with liver cirrhosis
   V. Gerova, S. Stoynov (Sofia, BG)

72. Attenuation of hepatic triglyceride accumulation and insulin resistance in ob/ob mice by macrophage (Kupffer cell)-specific overexpression of cholesteryl ester hydrolase
   S. Ghosh, J. Bie, B. Zhao (Richmond, USA)

73. Beta lipoprotein faster migration is sensitive parameter for acute and chronic active hepatitis
   K. Hameed Hassan (Basra, IRQ)

74. The role of TGF-βs expressed by biliary epithelial cells in the pathogenesis of cholestatic liver disease
   Y. He, B.-L. Chen, R.-P. Yang, Z.-R. Zeng, M. Ren (Guangzhou, RC)

75. Analysis of risk factors of patients with chronic liver failure complicated invasive fungal infections
   A.-R. Hu, J. Tan (Ningbo, RC)

76. Short-term efficacy and safety of standard interferon with a low accelerating dosage regimen in HCV-related decompensated cirrhotics
   F. Ji, H. Deng, Z. Cai, H. Xue, C. Tian (Xi’an, RC)

77. Waist-to-hip ratio is a superior predictor for nonalcoholic fatty liver disease

78. Abdominal ultrasound accurately detects complications in patients with hepaticojejunoanastomosis
   I. Kajzlrikova, P. Vitek, J. Chalupa (Frydek-Mistek, CZ)

79. The correlation between liver stiffness and serum markers of fibrosis in patients with chronic hepatitis B
   V. Kawengian, B.J. Waleleng, N. Tendean Wenas, L. Rotty, M. Abdullah, A.A. Rani (Manado, Jakarta, RI)

80. Stimulation of human hepatic stellate cells by cytochrome P4502E1-mediated oxidative stress
   J. Li, T.-H. Liu, H. You, Y.-Q. Xu (Beijing, RC)

81. The role and clinical significance of hepatic stellate cells in hepatocellular carcinoma
   L. Li, L. Yang, J. Ye, B. Wang, W. Zhou, X. Hou (Wuhan, RC)

82. Adjuvant gene therapy followed by orthotopic liver transplantation (OLT) for hepatocellular carcinoma (HCC) beyond the Milan criteria – A prospective study
   L. Li (Beijing, RC)
83. Analysis of 42 potential antiviral resistance mutation sites of HBV reverse transcriptase in chronic HBV infection patients with nucleos(t)ide treatment
X.-G. Li, J. Xu, T. Li, J.-X. Yang, B.-M. Liu, L. Li (Beijing, RC)

84. Expression of leptin and its correlation with component of extracellular matrix in hepatic fibrosis
C. Lu, J. Xu (Nantong, RC)

85. Liver injury in experimental sepsis: The late phase effects of hyperbaric and normobaric oxygen therapies

86. The role of heme oxygenase-1 on nutritional steatohepatitis in mice
Y.-M. Nan, R.-Q. Wang, W.-J. Wu, B.-L. Liang, S.-X. Zhao, N. Fu, J. Yu (Shijiazhuang, RC)

87. Viral hepatitis in patients with chronic renal insufficiency on hemodialysis
O.B. Nepesova, A.G. Japarova, H.E. Blum (Ashgabat, XTU; Freiburg, D)

88. Adipose tissue-derived MSCs are an eligible option to human hepatocytes

89. Predictors of development hepatocellular carcinoma in chronic hepatitis C
S. Pavic, G. Lucic (Uzice, SRB)

90. Quality of life in patients with chronic hepatitis C after antiviral therapy
S. Pavic, N. Svirtlih, D. Delic, J. Simonovic (Uzice, Belgrade, SRB)

91. Treatment of severe hepatitis with transplantation of autologous bone-marrow stem cells in human
Y. Peng, D. Hu, S. Wang (Beijing, RC)

92. MMP-9 and TNF-α as factors implicated in pathogenesis of autoimmune hepatitis type 1
C.A. Silosi, I. Silosi, V. Biciusca (Craiova, RO)

93. Clinical utility of autoantibodies in liver disease patients
I. Silosi, C.A. Silosi, V. Biciusca, F. Petrescu (Craiova, RO)

94. Influential factors of prognosis in lamivudine treatment for patients with acute-on-chronic hepatitis B liver failure
L.-J. Sun, J.-W. Yu, Y.-H. Zhao, P. Kang, S.-C. Li (Harbin, RC)

95. Active state of T lymphocytes and expression of CD45RA, CD45RO and CXCR3 of liver infiltrating lymphocytes and peripheral blood mononuclear cells in primary biliary cirrhosis
96. Expression of pituitary homeobox 1 gene in human hepatocellular carcinoma and its clinic pathological significance
B. Wang, J. Ye, L. Li, W. Zhou, L. Yang, X. Hou (Wuhan, RC)

97. The clinical features of parenteral nutrition-associated cholestasis (PNAC) in preterm infants
C. Wang, L. Shi, Z. Chen (Xi’an, RC)

98. Prognostic factors and outcome of 438 Chinese patients with hepatocellular carcinoma underwent partial hepatectomy in a single centre
J. Wang, L.-B. Xu, C. Liu, H.-W. Pang, Y.-J. Chen, J.-S. Chen, Q.-J. Ou (Guangzhou, RC)

99. Management experiences for portal vein thrombosis in liver transplantation
Z.-X. Wang, H. Yin, G.-S. Ding, Z.-R. Fu (Shanghai, RC)

100. Altered gene profile of placenta from women with intrahepatic cholestasis of pregnancy
J. Wei, H. Wang, X. Yang, M. Dong, Z. Wang (Hangzhou, RC)

101. Case report of 5 patients with hepatic veno-occlusive disease induced by herbs and literature review

102. Fuzheng Huayu formula inhibits activation of primary hepatic stellate cells through inhibiting apoptosis of primary hepatocytes
X. Yan, Q. Wang, Y. Ran, C. Liu (Shanghai, RC)

103. Biliary decompression strategies in relation to acute suppurative cholangitis with intestinal dysfunction

104. Logistic regression analysis of risk factors on hepatitis B-related liver cirrhosis complicated by hepatorenal syndrome
J.-S. Yang, C.-S. Wang, S.-B. Yang, J.-H. Yang, Y.-L. Yu (Wuhu, RC)

105. Clinical analysis of 94 cases with Budd-Chiari syndrome
L. Yang, S. Tang, J. Ye, X. Hou (Wuhan, RC)

106. Analysis of clinical features and prognostic factors in inpatients with nonalcoholic fatty liver disease
Y.-T. Yao, W.-H. Sha, Q.-Y. Wang, R.-Y. Cen, Y. Zheng (Guangzhou, RC)

107. Anti-inflammatory effects of Traditional Chinese Medicine on nonalcoholic steatohepatitis
L. Ying, B.-D. Lu, L.-Q. Guo, C.-M. Jiang (Dalina, RC)
108. Analysis of the efficacy of treatment with peginterferon α2a and ribavirin in patients coinfected with hepatitis B virus and hepatitis C virus
J.-W. Yu, L.-J. Sun, Y.-H. Zhao, P. Kang, S.-C. Li (Harbin, RC)

109. Effects of grape extract on endoplasmic reticulum stress-induced apoptosis
J. Yu, V. Khaoustov, Y.-M. Xu, B. Yoffe (Nanning, RC; Houston, USA)

110. Clinicopathological characteristics of 20 cases of hepatocellular carcinoma with bile duct tumour thrombi

111. An experimental study on the relationship between 5-hydroxytryptamine (5-HT) and human hepatocellular carcinoma

112. Antibiotics in primary prophylaxis of spontaneous bacterial peritonitis in cirrhotic patients with ascites: A meta-analysis
Y.-D. Zhong, Y.-F. Yang, W.-M. Lu, P. Huang, N. Zhang (Nanjing, RC)
Inflammatory bowel diseases

Session I

Pathophysiology
IBD genetics around the world

J. Cho, MD
Yale University School of Medicine, Department of Internal Medicine, New Haven, CT 06520, USA

An important clue in dissecting the overall genetic architecture of inflammatory bowel disease (IBD) may be provided by comparing the association patterns in different population cohorts around the world. In complex genetic disorders, such as IBD, multiple genetic loci, combined with developmental and stochastic factors contribute to increased disease susceptibility. Possibilities for cross-population association patterns are that a) the same causal alleles contribute in different populations, b) the same loci are involved, but with different risk and susceptibility alleles, and c) different loci are involved. IBD results from altered host-microbial interactions, and human genetic variation has been significantly shaped by selection factors in response to evolutionarily significant pathogens. Therefore, comparative IBD genetics studies between populations may provide important clues to both IBD pathogenesis and host-microbial interactions.

In Crohn’s disease (CD), markedly different association patterns between populations have been observed for the three most significant associations, at NOD2, IL23R (interleukin 23 receptor) and ATG16L1 (autophagy). In general, less common polymorphisms have developed more recently in time, and therefore, may not be found in different populations. The three major CD-associated NOD2 polymorphisms are relatively uncommon in European control cohorts, are not found in Asian populations, and are present in African-American populations at decreased frequency compared to European populations. Specifically, the African-American NOD2 carriage rates are consistent with the expected frequency given the fraction of European admixture. Similarly, the uncommon protective allele within IL23R, Arg381Gln is not present within Asian populations. Both positive and negative association studies to CD have been reported for the other, more common association signals present within the IL23R gene region. Finally, early studies with the common ATG16L1 risk alleles have not demonstrated association in Asian CD populations. Taken together, these early findings comparing CD genetics around the world would indicate that significant new information will be attained by comparative genetics studies in non-European ancestry cohorts.

In ulcerative colitis (UC), in both European and Asian populations, the most significant association signals reside within the major histocompatibility complex (MHC) on chromosome 6p21. However, the MHC region is the most genetically diverse region in the genome, reflecting enormous genetic selection, and very different allelic and haplotype patterns are observed between populations. One of the most significant association signals in a region on chromosome 1q23 containing the FCGR2A (immunoglobulin Fc receptor) gene shows association in both a Japanese UC genome-wide association study (GWAS) as a well as in a European UC meta-analysis.
Interestingly, a GWAS involving leprosy patients ascertained from South China demonstrated associations to multiple CD loci. Specifically, associations were observed in the NOD2, TNFSF15 (tumor necrosis factor superfamily) and LRRK2 (leucine rich repeat kinase) gene regions. Of note, TNFSF15 is associated in both Japanese and European ancestry CD. Interestingly, the leprosy GWAS also demonstrated association to RIPK2 (receptor interacting serine-threonine kinase), a signaling partner of NOD2. The overlap between between leprosy and CD loci brings into greater focus the finding that certain bacteria, including mycobacterial species, express glycolyl-MDP (muramyl dipeptide) which more potently activates the NOD2 pathway. Because the CD-associated NOD2 alleles sense MDP less effectively, these findings support the hypothesis that impaired defense against certain bacteria contributes to CD pathogenesis.

Despite the enormous progress through GWAS in identifying over 70 loci contributing to IBD, much work remains. These loci account for less than 25% of the predicted heritability in IBD. More precisely defining the causal alleles at these loci may account for some of this missing heritability. Because of the greater genetic diversity and shorter regions of linkage disequilibrium (correlation patterns within a contiguous genomic regions) found in African populations, these cohorts may assist in refining association patterns within complex association regions. It is anticipated that rare variants currently not well-assayed through GWAS approaches may also contribute significantly to this missing heritability. These rare variants may have greater functional effects and provide significant, additional insight into mechanisms of IBD.
The barrier as etiologic and pathophysiologic principle

Markus F. Neurath
Medizinische Klinik I, Universität Erlangen-Nürnberg, Erlangen, Germany

Various studies underline the pathophysiological relevance of barrier dysfunction for the development of chronic intestinal inflammation. For instance, studies in mutant mice such as the NEMO-villin Cre line have unequivocally shown that alterations of the intestinal barrier and intestinal epithelial cells are sufficient to cause infiltration and expansion of antigen presenting cells and T cells as well as chronic intestinal inflammation. Furthermore, studies in patients with IBD reveal that changes in barrier function, antimicrobial defensins and tight junction proteins occur in patients with inflammatory bowel diseases. Moreover, SNPs in certain barrier related genes appear to predispose for the development of intestinal inflammation.

Taken together, these findings underline the role of the barrier as key pathophysiological principle in IBD. Strategies to restore barrier function in IBD patients may help to develop new therapeutic strategies for IBD patients.
Environmental factors: Different in China versus the western world?

Yu-Lan Liu, MD, PhD
Department of Gastroenterology, Peking University People’s Hospital, Beijing, China

The pathogenesis of inflammatory bowel disease (IBD) is only partially understood; various environmental and host factors are involved. The critical role for environmental factors is strongly supported by recent worldwide trends in IBD epidemiology. A rising trend in the incidence of inflammatory bowel disease (IBD) in China has been recognized for the past two decades. It is very unlikely that these rapid changes of IBD in China can be attributed to variations in the genetic factors. On the contrary, environmental factors are likely to play an important role. Studying these environmental factors may allow the opportunity to better understand the etiopathogenesis of IBD.

Some same risk factors for IBD reported in white populations were also associated with Chinese IBD patients. Specifically, smoking was a protective factor for UC, while a risk factor for CD. Family history of IBD was a risk for UC, but with an incidence of 4.4–6.7%, lower than the western world (reported as 10–20%). Appendectomy and breast feeding in infancy were associated with a low risk for Chinese UC. Some also reported long-term oral contraception increases the risk of UC.

Westernized lifestyle has been blamed for the increase of IBD in Asia, which was also the case in China. With economic improvement, it seems as if China is undergoing what happened in western countries several decades ago. Chinese IBD has been shown to be associated with young adult professional males with a high level of education. And city-countryside-related differences of UC were observed in the Chinese population. Lifestyle factors such as psychological stress and fatigue, may contribute to the expression of UC. Crowded living condition may increase CD. Besides, in a smaller study, the absence of refrigerator seems to be a protective factor for CD.

Chinese have a unique dietary habit compared with the west, which also gives some interesting hints for the pathogenesis of IBD. Spicy food was a protective factor for UC according to a report from Hubei Province, China, where spicy food is quite popular. Tea was another protective factor for Chinese UC. High concentration of fiber and vitamin C in tea are believed to be responsible. In some smaller studies, more eggs, milk and fried food, less fish, fruit or beans were associated with CD. Some report the consumption of vegetables and fruit was low in Chinese IBD patients. High intake of sugar has been reported to be associated with increase IBD in other Asian countries, such as Japan. But in China, the relation between sugar and IBD was not established in some small surveys.

Same as western countries, dysregulation of gut flora exists in Chinese IBD, including altered composition and reduced species of intestinal microbiota, especially in active UC. Probiotics is an effective complemental therapy.
The relation between infection and IBD is not quite clear. Same as the western world, infective intestinal diseases increase the risk of UC in China. CD was reported to have a quite close correlation with *Mycobacterium avium paratuberculosis* (MAP) and interestingly there is a striking resemblance between intestinal tuberculosis (ITB) and CD. China has a high incidence of tuberculosis compared to the west. Sometimes it is very difficult to distinguish ITB from CD. One Chinese study showed increase of CD from 1996 to 2006, while decrease of ITB at the same time in the same hospital. But in another study, both CD and ITB increase at the same period, which may be partly due to difficulty in distinguishing MAP infection with ITB. Further study needs to be investigated in the relation among CD, MAP and ITB in China.

In one Chinese study, the seasonality in UC was reported. The symptom flares of UC occurred more frequently in the spring and summer, while the births of UC patients occurred more often in the autumn and winter. These data are not consistent with those obtained from Western populations, and the underlying factors for the difference should be intensively studied.

There are 56 ethnics in China, with different dietary habit, life style and economic situation, which make it difficult to investigate IBD in consistency. The wide territory and large population make the problem more complex. But at the same time, these conditions also give chances for the observation of different environmental pathogenesis among different Chinese people. Besides the largest ethnic-Han, other minorities have also reported IBD, such as Uigur and Tibetan in China. But there is no confirmed study among different ethnics in IBD up till now.

In summary, rapid increase of IBD in China allows detailed study in the environmental factors of IBD, which showed some certain differences between Chinese and Western population. These data may help to investigate the pathogenesis of IBD. Further population-based, better-designed epidemiological study is necessary in the future in Chinese people.
Session II

Diagnostics
Modern endoscopy and radiology in the diagnosis of inflammatory bowel disease

Zhi-Hua Ran
Department of Gastroenterology, Renji Hospital, Shanghai Jiao Tong University, School of Medicine, Shanghai Institute of Digestive Disease, Shanghai 200001, China, E-Mail: z-ran@online.sh.cn

The term inflammatory bowel disease (IBD) denotes a genetically, immunologically and histopathologically heterogeneous group of inflammatory bowel disorders. At present, it is broadly classified as ulcerative colitis (UC) or Crohn’s disease (CD). However, the term IBD-unclassified (IBDU) applies to the subset of 10–15% of patients with IBD in whom this subcategorization is not possible. Further, CD itself represents a heterogeneous entity comprising a variety of complex phenotypes. There is no gold standard single test that provides the diagnosis of IBD. So, assigning a diagnosis of IBD is often not straightforward and involves integration of historical factors, physical examination findings, and evidence of inflammation on endoscopic, histologic, and radiologic evaluations. The uncertainty in diagnosing IBD and the need to get the diagnosis right has fueled improvements in endoscopic and radiologic tools to assess bowel inflammation. Patients with established IBD typically undergo many investigations over a lifetime. Novel imaging studies are emerging which offer advantages in the diagnosis, follow up, and management of CD and UC. Approximately 40% of CD patients have disease involving both the small bowel and colon. Another one third has disease confined to the small bowel, primarily the ileum. Wireless capsule endoscopy (WCE), was first introduced in 2001 and has emerged as a highly sensitive modality for the detection of small intestinal pathology including Crohn’s disease. WCE enables a painless and radiation free examination of much of the small bowel in an unsedated patient. The performance of capsule endoscopy has been evaluated in multiple studies. WCE is emerging as a modality, superior to other conventional modalities. WCE can diagnose small bowel disease in some instances when CD has been considered and conventional tests are negative. However, specificity and positive predictive values for WCE have not been established. Because of the costs relative to conventional imaging and the inability to take tissue samples, WCE is unlikely to become the primary modality to initiate a diagnosis of CD in routine cases.

While WCE represents a monumental advance in the diagnosis of small bowel lesions, biopsies and endoscopic intervention are not possible. Double-balloon enteroscopy (DBE) was first described in 2001 as a technique that allows deep intubation of the small intestine with an endoscope. A single-balloon device has also been developed with a similar intention. The balloon technique allows the endoscopist to pull and pleat the bowel over the scope using an overtube. The enteroscope can be inserted via the oral or anal route and, using the combination of these approaches, complete examination of the entire small bowel can be achieved in many patients. Balloon enteroscopy is most useful for obtaining mucosal biopsies of lesions detected with WCE, but its exact role in the diagnosis and management of IBD remains to be established.

Patients with a long-standing history of UC or CD with a history of inflammation in the colon have a risk for the development of colon cancer. High-resolution videoendoscopy and magnification endoscopy, the application of dyes applied via a spraying
catheter are of additional diagnostic value with a factor 3–4 higher detection rate of intraepithelial neoplasia (IEN). It is under current evaluation if the use of computerized virtual chromoendoscopy techniques (NBI, FICE, High Line/HD+) has the same diagnostic output compared to classical spraying techniques. The detection rate of IEN can be further improved by using newly developed in-vivo histology techniques. A combination of chromoendoscopy with confocal endomicroscopy (CEM) can detect 5-fold higher rates of IEN compared with random biopsy protocols.

CT scan has been an important tool in the diagnosis and follow-up of IBD. CT can depict segmental thickening, extraluminal lesions, and complications such as sinus tracts, fistulas, and abscesses. While CT and MRI both provide cross sectional imaging of extraintestinal organs, a significant disadvantage of CT is its radiation, which is greater than that of small bowel X-ray. A relatively new diagnostic tool is CT enteroclysis which combines conventional small bowel enteroclysis with helical CT. Compared with MRI, CT has greater availability, is less expensive, and is less time consuming. By comparison, CT enterography (CTE) uses the combination of neutral (low-density) oral contrast and intravenous (IV) contrast to provide optimal distinction between the enhancing small intestinal wall and the adjacent low-attenuation intestinal lumen. This technique facilitates evaluation of the bowel wall and mucosa. Bowel distention is typically achieved with a low-concentration barium solution mixed with sorbitol and water.

Magnetic resonance imaging (MRI) is having an increasing diagnostic impact on patients suffering from IBD. Its attributes include high soft tissue contrast, multiplanar capabilities, and the use of non-ionising radiation. It can provide information about extraintestinal intra-abdominal structures and is functional as well as anatomical. MRI has been shown to be superior to CT scan and fistulography in assessing perineal complications of CD as well as fistula and sinus tracts. MR enterography is a safe and accurate method of evaluating the small bowel and extraluminal structures in patients with Crohn’s disease. The advantages of this technique over CT include a lack of ionizing radiation, greater safety in renal insufficiency and in pregnancy, and superior evaluation of the pelvic soft tissues and perianal fistula. The main advantage of MRI over other modalities is its ability to differentiate active inflammation from fibrosis in a thickened bowel segment. MRI is safe in pregnancy and in renal failure. Whether MRI should supplant routine barium imaging is still debatable, especially as the best way of conducting the study (with or without enteroclysis) remains to be proven.

Positron emission tomography (PET) scanning is a nuclear medicine technique that uses [18F] fluoro-2-deoxy-D-glucose to identify areas of increased metabolic activity, and it has been used to evaluate multiple infectious, inflammatory, and malignant diseases. Although data are quite limited, PET appears to have excellent sensitivity and may even be able to detect subclinical inflammation in patients with UC. However, questions remain about its specificity, and the practical application of PET in IBD management has not been established.

In conclusion, modern endoscopy and radiology for evaluating patients with IBD are developed with the goals of improving early and accurate diagnosis, clarifying disease type and distribution in order to select optimal therapy, identifying patients at high risk.
Serological markers in IBD

Florian Rieder, Gerhard Rogler

Klinik für Gastroenterologie und Hepatologie, Department für Innere Medizin, Universitätsspital Zürich, Zürich, Switzerland

The diagnosis of inflammatory bowel disease (IBD) and the differentiation between ulcerative colitis (UC) and Crohn’s disease (CD) usually is established by the combination of clinical, laboratory, radiological, endoscopic and histopathologic criteria. Nevertheless, in about 10–15% of patients with colitis patients a definitive discrimination between UC and CD is not possible, a condition known as indeterminate colitis (IC). Furthermore, increasing treatment options (such as biologics) have generated the wish to have predictive markers for complicated disease course. The determination of such markers at onset of disease or during the disease course could then trigger adaption of treatment strategies, i.e. more aggressive treatment if a more aggressive disease course (penetrating, strictureting) could be predicted.

Serological markers linked to CD (such as anti-Saccaromyces cervisiae [ASCA], anti-Pseudomonas-associated sequence I2 [anti-I2], outer membrane porin C [OmpC] of Escherichia coli antibodies and antibodies against the bacterial flaggelin cBir1) as well as UC (such as perinuclear anti-neutrophil cytoplasmic antibodies, p-ANCA) have been extensively investigated for diagnosis and disease stratification [1, 2, 3]. Further recently described circulating anti-microbial antibodies are the so called anti-glycan-antibodies (such as anti-mannobioside carbohydrate antibodies [AMCA], anti-laminaribioside carbohydrate antibodies [ALCA], anti-chitobioside carbohydrate antibodies [ACCA], anti-laminarin carbohydrate antibody [Anti-L] and anti-chitin carbohydrate antibody [Anti-C]). We and others have shown that they have high discriminatory capacity for CD versus UC and association with and prediction of complicated CD behavior [4, 5, 6, 7, 8, 9, 10]. Analysing those new antibodies directed against microbial glycans we found marked changes in the overall immune response and levels of individual markers in a subgroup of CD subjects over time. In contrast, the marker status (positive versus negative) remained widely stable. None of the tested clinical phenotypes in our analysis was associated with stronger maximal changes in markers levels. Only internal fistulizing disease courses had the tendency to more frequent changes in marker status. In a longitudinal analysis neither changes in disease activity, CD behavior or surgery, nor the intake of immunosuppressive medication led to changes in the overall immune response. Similar to our findings it has been described that once diagnosis of CD is established disease duration does not influence serological responses with respect to investigating ASCA, OmpC, Anti-I2 and CBir1 [11, 12]. In contrast to this others found significant higher antibody responses against ASCA, AMCA, ACCA and OmpC associated with an increasing disease duration [4, 6]. Changes in disease activity do not seem to influence marker levels [6, 7].

Therefore; at present, serological markers are of some value for the discrimination of CD and UC. The presence of several markers has some positive predictive value for complicated disease course; however, the clinical impact is still limited.
References:


Stool markers/microbiology

R. Balfour Sartor, MD
Distinguished Professor of Medicine, Microbiology and Immunology, University of North Carolina at Chapel Hill, NC, USA

Stool markers of disease activity of ulcerative colitis and Crohn’s disease, which primarily include the neutrophil products calprotectin and lactoferrin, have both diagnostic and prognostic function. These are fairly sensitive indicators of inflammation but lack specificity for any single disease process. These neutrophil products are nonspecifically secreted into the intestinal lumen as neutrophils migrate through the inflamed epithelium in response to intestinal infection, acute injury such as ischemia, or chronic inflammation such as Crohn’s disease and ulcerative colitis. Fecal calprotectin and lactoferrin can predictably distinguish IBD from noninflammatory conditions such as irritable bowel syndrome, but cannot distinguish IBD from infections. These fecal markers can be used as noninvasive indicators of IBD disease activity, since they correlate with endoscopic findings, and as a predictor of relapse, for example, after tapering corticosteroids. If further validated, they may allow clinicians to reliably document active disease without a colonoscopy.

The analysis of fecal bacteria has been transformed by rapid sequencing technology. 16s ribosomal DNA sequencing uses polymerase chain reaction amplification with primers that recognize conserved regions of ribosomal DNA that flank unique segments that can be used to identify individual bacteria. Intestinal bacteria that outnumber our human cells ten fold include > 1000 species but only 10–12 large phyla that are dominated by 2 groups, Firmicutes and bactericides. Fecal bacterial profiles of patients with active Crohn’s disease, ulcerative colitis and pouchitis are abnormal with decreased diversity, while numbers of mucosally associated bacteria are increased. Scientists are working diligently to define unique compositional alterations (dysbiosis) in these disorders. It is quite likely that subsets of IBD patients can be identified by their fecal bacterial patterns that can help guide antibiotic, probiotic and dietary treatments, predict disease relapses and to guide individual treatment. Developing evidence suggests that serologic profiles of antibacterial species may have prognostic benefit. Soon, it is likely that efficient and cheap fecal diagnostic tests at the time of diagnosis and during treatment can help predict the natural history of an individual patient’s disease course and optimize treatment.
New insights into IBD epidemiology – Are there any lessons for treatment?

Charles N. Bernstein, MD
Professor of Medicine, Head, Section of Gastroenterology, Director, University of Manitoba IBD Clinical and Research Centre, Winnipeg, MB, Canada
Bingham Chair in Gastroenterology

The epidemiology of IBD has evolved. Western nations had a head start with Crohn’s disease and ulcerative colitis emerging through the mid to latter half of the twentieth century. Canada and New Zealand have had the highest incidence rates of Crohn’s disease while Denmark has continued to have the highest incidence rate of ulcerative colitis. However, over the past two decades these diseases have emerged in developing nations as well as in the developed nations of Asia such as Japan and South Korea. When IBD emerges as in the West 60 years ago, and in developing nations more recently, ulcerative colitis is the predominant form. But over the past several years in the West, Crohn’s disease has become the predominant form. Furthermore, while the sex ratio has remained equal in ulcerative colitis, the female predominance in Crohn’s disease has given way to equality between the sexes or even a male predominance. While these trends are interesting and potentially provide etiologic clues, no definitive etiologic clue has emerged. So are there environmental clues that might be harnessed for therapy?

Smoking has consistently been shown to be associated with Crohn’s disease. This and the fact that smokers consistently have been shown to have a worse course of disease, it could be argued that a compound that neutralizes smoking components might have therapeutic value. That having been said the countries with the highest smoking rates in the world have among the lowest rates of Crohn’s disease and countries with relatively high incidence rates such as Canada and Sweden have relatively low smoking rates among adult males. Quitting smoking though seems to have potential benefit, since quitters likely have a better course after medically or surgically induced remissions than continued smokers. Smoking cessation strategies need to be more fully explored with Crohn’s disease subjects and more successful smoking cessation strategies need to be discovered. In ulcerative colitis smokers seem to have a better course and quitters seem to be more likely to exacerbate. With this in mind nicotine enemas and patches have been tested therapeutically in ulcerative colitis without any enhanced benefit over placebo (enemas) or standard therapy (patches).

Recently, there has been emerging interest in the association of adherent invasive E coli (AIEC) and Crohn’s disease. At least 7 groups in North America and Europe have reported on this association. If this organism should prove to be etiologic it raises the issue as to why quinolone antibiotics, generally bactericidal for AIEC and widely used in Crohn’s disease are not particularly effective for luminal disease. Is insufficient antibiotic reaching the site of disease? Does antibiotic resistance develop too quickly? Or is the absence of response, an indication that AIEC are not causing
inflammation? It is unclear how AIEC emerge within the bowel of patients with Crohn’s disease. In fact it is unclear how the balance of flora within the gut of subjects with Crohn’s disease becomes altered such that Firmicutes are reduced, while Bacteroidetes and Proteobacteria are increased. Could administration of probiotics improve this balance? To date the data on probiotics in IBD have failed to show a benefit in Crohn’s disease. E coli Nissle is no more effective than low dose 5-ASA in ulcerative colitis. VSL#3 may have some benefit in pouchitis, an IBD-associated condition that does seem to consistently respond to antibiotics as well. Interesting data from a French group have shown a higher postoperative recurrence rate in Crohn’s disease in patients who harbor less Fecalobacterium prausnitzii (a member of the Firmicutes phylum). Further, less F. prausnitzii has been reported in the stool of patients with active colitis of either IBD or infection. This type of focused approach to finding a potential probiotic to administer based in evidence of its absence or reduction during pathologic states makes more sense than guessing as to which probiotics might be beneficial.

While patients are often craving dietary advice in terms of managing their IBD there is little evidence that there are specific diets or foodstuffs that predispose to developing the disease. One study from Japan previously showed an association between Crohn’s disease and consumption of total animal protein and intake of total animal fat, particularly ω-6 polyunsaturated fatty acids (and a high ratio of intake of ω-6 to ω-3 fatty acids). A second study suggested that a higher consumption of sweets was positively associated with ulcerative colitis risk and the consumption of sugars and sweeteners, fats and oils, fish and shellfish were positively associated with Crohn’s disease risk. In Crohn’s disease even the intake of ω-3 fatty acids positively correlated with disease as did the intake of ω-6 fatty acids.

In a pediatric survey study from Quebec higher amounts of dietary vegetables, fruits, fish, and fiber was protective against Crohn’s disease. Consumption of long-chain ω-3 fatty acids was negatively associated with CD and a higher ratio of ω-6/ω-3 fatty acids was significantly associated with higher risks for CD. In this study, sucrose consumption was not associated with an increased risk for Crohn’s disease.

Can we learn anything from these data about dietary advice and management once disease is diagnosed? Two important studies have shown that fish oil does not have a protective effect against disease recurrence once Crohn’s disease has been diagnosed. However, much like smoking avoidance among persons considered at high risk for disease (strong family history) it may also be prudent to encourage an increased diet of vegetables, fruit and fish. The data on ω-6 and ω-3 fatty acids seem conflicting and I would not recommend getting more specific in recommendations regarding these fatty acids and diet.

While there has been debate as to whether NSAIDs, antibiotics, infections or stress may trigger IBD, a recent review supports that the most robust data support a role for stress and more specifically the perception of stress as opposed to simply an accounting of stressful events. It has been shown that patents with IBD are more likely to have an antecedent diagnosis of depression than community based controls and that those with depression present at a younger age than those without. A series of elegant studies in an animal model of depression and colitis has shown that depression can exacerbate colitis and antidepressants can ameliorate the colitis.
Hence, it is rational for IBD management to incorporate stress management and even to consider antidepressant therapy. While I would not recommend antidepressant therapy at this stage solely to treat active disease in the absence of clinical trials proving their efficacy, these agents should be considered in patients who are depressed and who have chronic abdominal pain. Clinicians must ensure that they inquire of their patients as to their stress levels and for the presence of depression and other mood disorders. Identifying these issues in IBD patients so as they can be treated before the disease is flared may be of value.

Selected references:


www.nationmaster.com/graph/hea_tob_adu_mal_smo-health-tobacco-adult-male-smokers


Singh S, Graff LA, Bernstein CN. Do NSAIDs, antibiotics, infections or stress trigger flares in IBD? Am J Gastroenterol. 2009;104:1298–313.


Session III

Therapeutics I: Ulcerative colitis
Oral/rectal or combination 5-ASA?

Professor Philippe Marteau, MD, PhD
Medico-surgical Department of Digestive Diseases, AP-HP, Hôpital Lariboisière, Paris, France
E-Mail: philippe.marteau@lrb.aphp.fr

Aminosalicylates (ASA) are major drugs in the treatment of ulcerative colitis (UC). Their anti-inflammatory efficacy has been well established during flares of the disease and in the prevention of relapse. Various formulations have been developed to convey this active molecule to the colon orally or rectally (as enemas, foams or suppositories). I will present the studies which compared their efficacy as rectal, oral or combinations in these situations and which compared them to other drugs especially local steroids.

Distal UC:
In mild to moderate acute episodes, it is recommended (depending on countries) either to use rectal 5-ASA, 1 g/d as monotherapy for at least 4 weeks (and a combination of local ASA and oral 5-ASA (4 g/d) in case of failure) or to use from the beginning a combination therapy of rectal + oral 5-ASA which showed a higher efficacy in randomised controlled trials.
For the prevention of relapse, the minimal effective dose is recommended either rectally (3 g/week) or orally or in combination when needed.

Extensive colitis (i.e. beyond the splenic flexure):
For mild to moderate acute episodes, some guidelines recommend oral 5-ASA as a first line treatment (4 g/d for at least 4 weeks). However, the ECCO consensus proposed to use from the beginning a combination therapy which proved to be significantly and importantly more effective in a randomized, double-blind study to induce a rapid improvement or remission, and to improve the quality of life and cost.

Bibliography:


The choice of the immunosuppressant

Gerassimos J. Mantzaris, MD, PhD
Consultant Gastroenterologist, Head; A’ Department of Gastroenterology, Evangelismos Hospital, Athens, Greece

Immunosuppressants are indicated for IBD patients who are dependent or refractory to or intolerant of steroids and/or 5-ASA and for prevention of post operative recurrence of Crohn’s disease (CD). The choice of immunosuppressant should be made after critical evaluation of various patient and disease parameters aiming at treating a life-long disease, not a flare. Tolerance is also important. Decision should be balanced against surgical options which may offer an effective long-term alternative.

Steroids with thiopurines (or methotrexate) are the preferred options for active proximal or extensive small bowel, mild/moderate steroid-dependent and, infrequently relapsing CD. For relapsers and patients with highly or chronically active steroid-refractory CD irrespective of location biologics with or without thiopurines should be preferred. Bridging to thiopurine maintenance may be effective in thiopurine-naïve patients. Immunosuppressants are more effective if administered early in the course of disease; thus, factors predicting a disabling course of CD at disease onset may aid in selecting patients for early treatment. For localized ileocolonic CD minimal laparoscopic surgery offers an effective alternative. Complex perianal fistulizing CD may be treated with thiopurines or biologics after surgical drainage and seton placement. For safety reasons, immunosuppressant maintenance monotherapy is preferred.

Ciclosporin is indicated for patients with severe UC who fail i.v. steroids and surgery threatens. Infliximab is indicated for patients who have responded partially to steroids and are thiopurine failures. Successive ciclosporin-infliximab treatment is potentially lethal. For chronically active steroid-refractory/dependent UC, thiopurines, if tolerated, or infliximab should be offered. The role of methotrexate is disputed. Adalimumab should only be used as compassionate therapy in infliximab failures.

The role of non anti-TNFα biologics, calcineurin inhibitors other than ciclosporin and mofetil mycophenolate is currently restricted for IBD patients who are refractory to all treatments and are poor surgical candidates.
When is surgery indicated in UC?

Qin Ouyang, Yan Pan
Department of Gastroenterology, West China Hospital, Sichuan University, Chengdu, China 610041

Even with tremendous advances of medications for UC during past decades, medical therapy is still directed at controlling symptoms or inflammatory process and is not curative (1). However, surgery does cure the disease by removing the colon, rectum and eliminating the target organ (1). With innovated techniques and emerging concept, surgery continues to play an important role in UC therapy. The cumulative surgical rates for severe colitis maintain 25–30% in western countries (2).

The indications of surgery traditionally are categorized into absolute and selective one (3, 4). For former, three indications, massive uncontrolled hemorrhage, frank perforation and malignancy, which are potentially fatal without controversial for the decisions from country to country (5, 6). But for latter, the indications are not quite clear-cut defined including failure of medical therapy, refractory to steroid or immunosuppressant and complications, some extra-intestinal manifestations etc., which are generally not fatal with different definition and decisions from different countries and culture background. This group of patients represents common indication for surgery with persistence of refractory symptoms, physical debility, psychosocial dysfunction or intolerable side effects for medical therapy (5, 6).

The timing of surgery for severe colitis is the most difficult decision that gastroenterologists have to make. In acute cases, the decision for operation is still based on the old Truelove and Witts criteria (Oxford index) (7). New therapeutic approaches, in particular biological therapies, are promising, but whether they could reduce the operation rate remains to be defined. Therefore, in patients not responding to these agents within 7–10 days, the operation should be considered (8). Prolonged observation may exhaust their physiologic reserve and increase the risk for septic and other complications (9). In fact, unacceptably high mortality rates have recently been reported in non-specialized centers, due to delayed decision making in the peri-operative management (10).

Recently, we search for Chinese literatures about surgery for UC from CBM and VIP database during 1985–2009. There are totally only 70 papers published including systemic review, nursing care clinical analysis etc. Only 19 papers about indication and timing of surgical management on UC with less than 20% of operation rate for severe colitis and rather high mortality in some groups.

In West China Hospital from 1996–2009, there were totally 412 hospitalized UC cases with 29 of 163 (17.9%) severe colitis operated on. The most of them were acutely ill and incomplete response to maximal medical therapy. The in-patient duration of pre-operation were 22.6 ± 13.9 days and intravenous steroid duration were 17 ± 9.0 days with rather poor health condition, low Hb, low albumin, high post operative complications (55.2%) and reoperation rates (44.4%). Fortunately, in following-up study, IPAA patients had better QoL.
The limited data showed that surgery for UC is an important therapeutic alternative but not last decision for failure of the medical therapy. The delay or conservative in surgical treatment should be avoided for better functional outcome and QoL for UC patients.

References:


Session IV

Therapeutics II: Crohn’s disease
Basic treatment and prediction of a severe course in Crohn’s disease

Marcellus Simadibrata, MD, PhD, FACG, FINASIM
Division Gastroenterology Department of Internal Medicine Faculty of Medicine
University of Indonesia, Jakarta, Indonesia

Inflammatory bowel disease (IBD) is increasing in Asian countries. Treatment of IBD is difficult in Asian countries due to low socio-economy status, no or lack of medical facilities, more prevalent infections which has to be excluded before treating IBD such as: tuberculosis, hepatitis virus etc. The severity of Crohn’s disease can be categorized as mild, moderate and severe. The severe Crohn’s disease has poor prognosis, characterized by severe lower gastrointestinal bleeding, intestinal stricture or stenosis, intestinal fistula, severe condition, fever, severe ileocolitis appearances in colonoscopy examination and chronic activity index (CDAI) more than 450. The mild Crohn’s disease has good prognosis, characterized by mild lower condition, no fever, mild ileocolitis appearances in colonoscopy examination and CDAI 150–220. The moderate Crohn’s disease has severity between the mild and severe Crohn’s disease and CDAI 220–450.

The basic treatment for Crohn’s disease (CD) includes nutritional, pharmacological, surgical and CD complication treatment. In severe CD usually we give low residue diet. In mild CD we give balanced nutrition, high protein depend to the daily demand, food that does not irritates and food that does not causing lactose intolerance, avoid cow’s milk, and food contains lactase (lactaid). Iron, calcium, magnesium, zinc, vitamin B12, vitamin D, vitamin K, vitamin E, vitamin C supplementation must be given according to the deficiency. Pharmacological treatment is divided into general supportive therapy (antidiarrheal, antispasmodic, analgesic), antiinflammatory drugs (aminosalicylates, corticosteroids), immunosuppressive drugs, biological agents, antibiotic, probiotic, Complementary alternative medicine (CAM)/herbal drugs and other medications. Aminosalicylates include sulphasalazine (SASP), 5-aminosalicylates (5-ASA = mesalazine = mesalamine), olsalazine and balsalazide. Corticosteroids include prednisone/prednisolone, methylprednisolone and budesonide. Immunosuppressive drugs that can be given are 6-MP, azathioprine and methotrexate. Biological agents include infliximab, adalimumab (fully human), certolizumab pegol and natalizumab. Antibiotics that can be given to CD patients are metronidazole, ciprofloxacin, rifaximin, anti mycobacterial agents. Probiotics can be given to CD but it is still controversy. Herbals that can be given to CD include Boswellia serrata gum resin and extracts, Curcuma longa. Non herbal medicine which has already been given for CD includes seal oil, acupuncture and moxibustion. Other medications that can be given to CD are anti-diarrheal drugs, laxatives, acetaminophen, teduglutide, helminthic therapy, cannabis-based drug and stem cell therapy.

The prediction of severe course or prognosis of CD may use the disease activity (severity) index and the endoscopic disease activity score.
The endoscopic response to treatment in Crohn’s disease (CD) is defined as a significant change of endoscopic disease activity score, such as the CDEIS or the SES-CD. The disease activity (severity) index can be evaluated with some scoring parameters such as the Crohn’s Disease Endoscopic Index of Severity (CDEIS), the Simple Endoscopic Score for Crohn’s Disease (SES-CD), the Rutgeerts score and the Crohn’s Disease Activity Index (CDAI).

Key words: Crohn’s disease (CD), severity, basic treatment, prediction
Immunosuppressive therapy

T. Hibi
Keio University School of Medicine, Tokyo, Japan

Crohn’s disease is chronic disabling inflammatory bowel disease. The patients with Crohn’s disease are commonly in young generation. The number of patients has been increasing in Japan as well as other Asian countries.

Although the causes of Crohn’s disease are unknown, recent studies have demonstrated that dysregulation of innate and adaptive immune system is a central role for initiation and perpetuation of this disease. Therefore, modulation of immune system is a quite reasonable concept in therapeutic strategy of Crohn’s disease. Immunosuppressive therapy targets several proinflammatory cytokines and chemokines produced by abnormally activated host immune cells such as, macrophage, dendritic cell and T cell.

The ideal therapeutic strategies for patients with Crohn’s disease are rapid induction of remission and long-term maintenance of remission without steroid exposure and minimal urgeries. Corticosteroids have been used in the treatment of active Crohn’s disease. However, they are not effective for maintenance of remission and their long-term use causes serious adverse effects.

Immunomodulator (IM), especially thiopurine such as azathioprine (AZA) and 6-mercaptopurine (6-MP) have been used for induction and maintenance therapy for corticosteroids dependent patients. They may show steroid-sparing effect. The fully effect of thiopurine is not reached until 2–3 months after initiation. Metabolism of thiopurine is regulated by metabolic enzymes (e.g. TPMT, ITPase) and the activity of these enzymes is varied in individuals. Adverse events associated with AZA and 6-MP include nausea, allergic reaction, flu-like illness, malaise, fevers, rash, abdominal pain, pancreatitis, hepatotoxicity, myelosuppression, and an increased risk of lymphoma.

Methotrexate is also effective in inducing and maintaining remission in patients with Crohn’s disease. IMs contribute to maintaining remission and prevention of post operative recurrence, while it is still uncertain whether or not use of IMs has improved natural history of Crohn’s disease (e.g. reducing the risk of operation in whole life).

The introduction of biologics such as infliximab has dramatically changed the treatment strategy of Crohn’s disease. Tumor necrosis factor-α (TNF-α) is a major proinflammatory cytokine and plays an important role in the pathogenesis of chronic inflammatory disorders such as IBD, multiple sclerosis, rheumatoid arthritis, and psoriasis. Inhibition of TNF-α shows the remarkable efficacy in these diseases. Currently, three kinds of anti-TNF antibodies are used to treat Crohn’s disease. Infliximab is a chimeric monoclonal IgG1 against TNFα. Adalimumab is a fully human recombinant IgG1 monoclonal antibody against TNF-α. Certolizumab pegol is a pegylated humanized Fab that binds TNF-α. Scheduled maintenance use of these anti-TNF drugs shows the efficacy in inducing and maintaining remission. Therefore, inhibition of TNF-α is expected as a novel therapeutic strategy that can improve “natural history” of Crohn’s disease (e.g. improving of QOL, reducing operation risk in a whole life, preventing the complication of fistula and stricture). The development of anti-TNF drugs and their strong efficacy cause us several considerations. 1) Step-up
vs. Top-down, 2) use with IM or without IM, 3) adverse effects in long-term use, 4) high medical cost by long-term use.

According to success of anti-TNF drugs, several biologics targeting cytokines, chemokines and adhesion molecules have been developed. Among them, natalizumab, recombinant humanized IgG4 monoclonal antibody against α4 integrin, is effective for active Crohn’s disease patients with increased CRP levels. However, should concern the risk of progressive multifocal leukoencephalopathy (PML) in use of natalizumab. Currently, natalizumab is approved for anti-TNF Ab resistant active Crohn’s disease in USA, but not Europe and Japan. Recently, clinical trials of other biologics, vedolizumab (anti-α4β7 integrin mAb), ABT-874 and CNTO-1275 (anti-IL-12/23 p40 mAb), are ongoing.
Surgical options

W.A. Bemelman
Department of Surgery, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands

The treatment of Crohn’s disease is principally medically and surgical treatment is reserved for complicated Crohn’s disease. Indications for surgery are limited to complications of Crohn’s disease like strictures, fistulation, uncontrolled bleeding and free perforation.

As a rule of thumb, surgical treatment of Crohn’s disease must be as limited and organ sparing as possible. Limited resection resecting only the affected part of the bowel, stricturoplasties and anal sphincter saving procedures are key.

Abdominal surgery is preferably done using minimal invasive methods. Laparoscopic surgery has proven to be superior to open surgery with respect to morbidity, hospital stay, incisional hernia’s, and body image and cosmesis particularly for ileocolic disease.

The most important indication for acute surgery is drainage of perianal abscesses. Other indications as intraabdominal abscesses, small bowel obstruction, free perforation or gastrointestinal bleeding are seldomly seen, and if occurring best treated medically or by the intervention radiologist.

The most important indications for elective surgery are stricturising disease, medical refractory disease and perianal fistula.

More than 80% of patients with Crohn's disease localized in the small bowel need surgical treatment during the course of their disease. Most of the patients develop obstruction, with or without abscess formation and fistulisation. Usually the first operation takes place in the third decade of life. The ten years surgical recurrence rate of disease is about 25%. The type of anastomosis does not seem to influence the surgical recurrence rate. Especially short, even multiple strictures are suitable for stricture plasty.

The indications for surgical treatment of Crohn’s colitis are medical refractory disease and specific complications like bleeding, extra intestinal manifestations, perianal disease and cancer. The surgical treatment of choice is dependant on several factors like: location of disease, the indication to operate, the age and condition of the patiënt and the dependence on steroids. Surgical options are subtotal colectomy and ileostomy indicated in the emergency setting or medical refractory disease of the colon in the presence of perianal fistula or proctitis, segmental colectomy in case of limited disease of the colon and subtotal colectomy and ileorectal anastomosis provided the rectum is spared. Proctectomy is indicated if the retained rectum is symptomatic causing discomfort due to discharge or perianal fistula.

Proctectomy and formation of an ileo anal pouch is an option if the proctocolon has to be removed because of failure of medical treatment. Prerequisites for restorative proctocolectomy in Crohns are the absence of disease activity in the small bowel and
the absence of perianal fistula. In that case a 10 years pouch survival can be expected of about 80%.

Fecal diversion is indicated in case of severe perianal sepsis with abscess. In cases with merely proctitis an end colostomy is indicated. In patients with proctocolitis, an end ileostomy may be necessary.

Source:

What should we expect from future therapies for Crohn’s disease?

Stephen B. Hanauer, MD
Professor of Medicine and Clinical Pharmacology, Section of Gastroenterology, Hepatology and Nutrition, University of Chicago Medical Center, Chicago, IL 60637, USA

Our current goals of medical therapy for Crohn’s disease are primarily “clinical” and include: induction and maintenance of (clinical) remissions, prevention of disease- and therapy-related side effects, maintenance of quality of life, and optimizing timing of surgery. Several factors have begun to emerge that will alter these therapeutic goals for future therapies. First, the natural history of Crohn’s disease has demonstrated a progression from, primarily, inflammatory changes to transmural complications of stricturing and fistulization. Second, there are evolving data that allow prognostication as to which patients are more likely to progress rapidly toward severe disease and complications. Thirdly, exploration of more objective, “inflammatory” end-points such as “mucosal healing” has demonstrated correlations with important clinical and pharmacoeconomic end-points such as the need for hospitalizations and surgeries.

Until the ultimate ability to cure or prevent Crohn’s disease the therapeutic expectations of future therapies will require evidence of “disease-modifying” end-points as have become routine in the setting of rheumatoid arthritis.

The evolution of medical therapies has already begun to demonstrate that “early-aggressive” treatment for patients with poor prognoses, in particular the need for corticosteroids, can lead to improved outcomes and long-term steroid sparing. Newer therapeutic targets are continually being identified such as TNF and alternative cytokines (IL-12/23, IL-6, etc.) and adhesion molecules (α4β7 integrins, MadCam-1, etc.) as well as antimicrobial and probiotic strains that will be held to more stringent criteria and will require testing in combination or in sequence to optimize long-term outcomes that reflect symptomatic control, anti-inflammatory effects and the prevention of structural damage leading to surgical resections.
Liver diseases

Session V

Chronic liver inflammation
New antiviral therapies in the management of hepatitis C virus infection

Stefan Zeuzem, MD
Professor of Medicine, Chief, Department of Medicine, Goethe University Hospital, 60590 Frankfurt a. M., Germany

Pegylated interferon alfa in combination with ribavirin administered for 48 and 24 weeks has been approved as standard antiviral treatment in patients with HCV genotype 1 (4–6) and 2/3 infection, respectively, in many countries. Different virus- and host-related baseline parameters are known to predict the probability of sustained virologic response including HCV genotype, HCV viral load, gamma glutamyltranspeptidase (GGT) levels, age and liver fibrosis. While HCV genotype 2, 3 infected patients are generally treated for 24 weeks, management of therapy is based on early discontinuation rules in HCV genotype 1 infected patients with a low or no chance of further sustained virologic response. Thereby, a decline of less than 2 log₁₀ steps at week 12 in comparison with baseline (early virologic response, EVR) and detectable HCV RNA at week 24 by a sensitive assay (detection limit ≤ 50 IU/ml) can be safely used as stopping rules with predictive values of 98–100% for virologic non-response. Future developments are aiming for individualization of treatment duration based on HCV RNA concentrations before initiation of therapy and decline early during therapy. Rapid virologic response (RVR) defined as undetectable HCV RNA at week 4 of therapy (≤ 50 IU/ml) together with low baseline viral load (≤ 600,000 IU/ml) were introduced as parameters for shortening of treatment duration in HCV genotype 1 infected patients without a loss of the probability of sustained virologic response. Vice versa in patients with a slow virologic response which become HCV RNA negative at the first time at week 24 of therapy prolongation of treatment duration to 72 weeks seems to be associated with increased sustained virologic response rates. Similar in HCV genotype 2, 3 infected patients reduction of treatment duration from 24 to 12–16 weeks was investigated in different clinical trials. However, in several studies shortening therapy to 12–16 weeks higher relapse rates were reported and future trials are needed to define subgroups of patients with specific baseline parameters (e.g. genotype, viral load, degree of fibrosis) and RVR at week 4 for a safe reduction of treatment duration.

Basic to the development of new specific anti-HCV drugs is the understanding of the viral life cycle, in particular the genomic organization and the polyprotein processing. Major progress in this field was achieved due to the development of sub-genomic and more recently full-genomic replicon systems. The HCV genome is a single-stranded RNA molecule that contains a single open reading frame encoding a polyprotein of about 3000 amino acids. The polyprotein is subsequently processed at the level of the endoplasmic reticulum (ER) by cellular and viral proteases to yield 4 structural and 6 non-structural proteins. The open reading frame is flanked by 5’ and 3’ untranslated regions. Each single HCV structure represents a potential antiviral target. Antisense oligonucleotides, ribozymes, siRNA, and small molecules have been targeted in particular against the 5’-noncoding region with substantial success in vitro but not yet in vivo. Inhibition of nucleocapsid formation to the icosahedral viral coat is an attractive target, however, no specific molecules have yet been developed. Envelope proteins HCV E1 and E2 are the basis for the development of prophylactic and/or therapeutic vaccines.
NS3 and NS4A are cleaved by the catalytic activity of the NS3 protease domain. In addition to the protease domain located in the 189 aminoterminal amino acids, NS3 also possesses a helicase domain located in the 442 carboxyterminal amino acids. The NS3 protease domain is responsible to complete the polyprotein processing down to NS4B, NS5A, and NS5B. Despite the fact that the catalytic site is a shallow and largely hydrophobic groove and therefore very difficult to target several compounds have been successfully designed (BILN 2061, VX-950, SCH503034, etc.). The NS5B RNA-dependent RNA polymerase is the key enzyme for synthesis of a complementary minus-strand RNA using the genome as template, and the subsequent synthesis of genomic plus-strand RNA from this minus-strand RNA template. The active site of the enzyme is a target for nucleoside/nucleotide analogue inhibitors. Nonnucleoside inhibitors, reported to bind at various sites, may act by blocking the enzyme in the initiation mode through inhibition of a conformational change needed to proceed with elongation.
Management of hepatitis C, West and East

Lai Wei
Peking University People’s Hospital, Peking University Hepatology Institute, Peking, P. R. China

With the Standard of Care, sustained virologic response achieved 50% for HCV genotype 1 patients and 70% for genotype 2/3 patients in North-America/Europe. However, there is also high prevalence of HCV genotype 1b and 2a in Asia, the SVR seems difference from North-America/Europe. SVR could be as high as around 70% for HCV genotype 1 infected patients and 90% for HCV genotype 2/3 infected patients in Asia. For the genotype 6, the most prevalence genotype in the area, the SVR is achieved around 80%. Recently identified SNP in IL28B suggested CC allele contribute to the difference of SVR between West and East, and also contribute to spontaneous HCV clearance after infection. High prevalence of CC allele is thought a key factor for superior response among Asian people. Lower body weight might also be related to the higher SVR in Asian patients. To individualize the dose and duration treatment regimens, RVR was used to shorten the duration and extended treatment was given to later response. But SVR is still lower in patients with 24 weeks treatment than 48 weeks treatment by pegylated-interferon in this area. Abbreviated 12–16 weeks duration has been suggested for HCV-2/3 infected patients with a RVR upon pegylated-interferon with weight-based doses ribavirin.
Pathogenesis and management of non-alcoholic steatohepatitis

Geoffrey C. Farrell
Professor of Hepatic Medicine, Australian National University Medical School, The Canberra Hospital, Canberra, ACT, Australia

Non-alcoholic steatohepatitis (NASH) is part of the broader spectrum of non-alcoholic fatty liver disease (NAFLD). It is present when a steatotic liver exhibits hepatocellular injury and inflammation, often with a characteristic pattern of centrilobular and pericellular fibrosis that can lead to cirrhosis and is also associated with hepatocellular carcinoma (HCC). NAFLD is intimately related to insulin resistance and cardiovascular risk factors. Thus, NASH is nearly always associated with central obesity (visceral adiposity) and insulin resistance, and metabolic syndrome is present in 85% of cases. Cirrhosis is most likely in older patients with type 2 diabetes (T2D) and at least 2 features of metabolic syndrome.

NAFLD starts with over-nutrition, imbalance between energy input and output; our understanding of the interactive roles of genetic predisposition and environmental factors (diet and physical activity) is under revision. Genetic polymorphisms are strongly associated with hepatic fat content and attendant liver injury. One such polymorphism, patatin-like phospholipase A3 (PNPLA3/adiponutrin), is also a determinant of fibrotic severity of NASH. Adiponutrin is an adipose protein which may influence activity of the insulin-suppressible pathway of adipose lipolysis, hormone-sensitive lipase. An apolipoprotein C3 gene polymorphism which likewise influences triglyceride (TG)/fatty acid turnover has also been associated with NAFLD, insulin resistance and prolonged hyperlipemia after TG administration. Post-prandial abnormalities of lipoprotein and/or glucose homeostasis are an emerging theme of NASH research; in lean men with NASH, prolonged hyperlipemia has been linked with adiponectin polymorphisms and lower serum adiponectin, decline of which is pivotal to pathogenesis of T2D, coronary events and NASH. Collectively, these findings are consistent with in vivo tracer studies in humans with NASH showing that peripheral tissues account for more than half of hepatic fatty acids; endogenous lipogenesis is somewhat increased but only accounts for ~25%. These observations allow us to propose that transition from simple steatosis (milder from of NAFLD) to NASH could be explained by unmitigated hepatic fatty acid partitioning with failure of local adaptive mechanisms (TG synthesis, storage and secretion) leading to lipotoxicity. We know that triacylglyceride (TG) stored in lipid bodies or cell membranes is non-toxic, but precursor diacylglycerides and free fatty acids are among contenders as lipotoxic (and insulin resistance inducing) molecules in NASH. Cholesterol has emerged as another possible mediator of liver injury, which would be consistent with NASH and atherosclerosis sharing common pathogenic mechanisms, as their intimate clinical relationships infers. There are also new data on dietary factors (a possible weak role of high fructose drinks in USA) and physical activity (NASH patients are very inactive) in NASH pathogenesis. It is therefore important to appreciate that NAFLD/NASH is now common not because of genetic variables, but because of population exposure to sedentary lifestyles and ready availability of cheap, processed foods that are often imbalanced in saturated fat and simple carbohydrate content.
The genetic variables simply explain which individuals among so many people living in this contemporary environment succumb to NASH and other metabolic complications of being overweight. Thus, less than one third of NAFLD patients have NASH, the severer form, on liver biopsy. Our current concept is that hepatic fibrosis is usually associated with NASH and is the key predictor of progression to cirrhosis or HCC. So a major challenge in NAFLD/NASH diagnosis is to identify those patients who have progressive forms of the disease. In addition to hyperglycemia/T2D, severe obesity, metabolic syndrome and age over 60 years, higher AST than ALT, low platelet count and hypoalbuminemia are associated with severely fibrotic or cirrhotic NASH. However, only liver biopsy can reliably distinguish NASH from benign forms of NAFLD. The lack of specific and effective therapy is a disincentive to persuade patients to undergo this invasive, unpleasant procedure. On the other hand, many will come to cholecystectomy for associated gallstone disease, bariatric surgery to control metabolic syndrome and diabetes, surgery for GERD or colorectal carcinoma – all increased with NAFLD: it is important that this opportunity for liver biopsy should not be missed! For the rest, non-invasive markers offer a promise to identify a smaller subgroup for whom biopsy can be considered if knowing that the patient has NASH and significant fibrosis is the indication for future specific therapies. Among physical/imaging methods, transient elastography has been shown to identify low and severe fibrosis reliably in Chinese patients; development of technically more satisfactory probes for larger patients may extend its application. Among serum biomarkers, the cytokeratin 18 cleavage peptide assay, which reflects hepatocellular caspase 3 activity (apoptosis) seems to separate NASH and not-NASH quite well, while fibrosis markers such as serum hyaluronan and composite scores like the European Liver Fibrosis Panel (ELF score) are accurate for severe or mild fibrosis but less so for in-between stages.

Pharmacological approaches to NASH treatment is most logically focussed on agents that correct insulin resistance, adipose lipolysis and hepatic lipid partitioning, perhaps with anti-inflammatory, cytoprotective and anti-fibrotic effects on the liver. Such agents are not yet in the clinic for NASH patients, partly because we are not clear about which are the most critical therapeutic targets, or which are the most potent and safest agents. Among “insulin sensitisers”, metformin has weak and transient effects, perhaps most effectively acting by causing anorexia which reduces food intake. PPAR-γ agonist “glitazones” have seemed promising, among which higher dose rosiglitazone (45 mg) appears most effective, but only in 40–50% of cases. There are concerns about major weight gain, cardiac complications and cost; relapse occurs with discontinuation. In the PIVEN study (NEJM May 2010), pioglitazone (30 mg/day, 96 wk) did not significantly improve liver histology (34% vs 19% of cases) but vitamin E 800 mg/day did so marginally (43% vs 19%). Among other antioxidants and “hepatoprotectants”, ursodeoxycholic acid was ineffective in one study but higher doses are under trial in France. Many other agents have been reported to show promise from open “pilot studies” or under-powered RCTs, such as the antioxidant/TNF-α release inhibitor pentoxifylline; histological endpoints and longer term data are required.

Today, management of NAFLD/NASH should focus on correcting over-nutrition. The best ways to do this will be discussed, but increasing physical activity (at least 150 min aerobic excercise/week), reducing food portion size (eating less) and improving dietary composition are each relevant. Younger patients are unlikely to have
cirrhosis; those who take up exercise and lose weight seem to reverse NAFLD, but motivation is the key to such lifestyle intervention. In older patients at later stages of liver disease, and particularly when obesity is refractory or morbid (BMI > 35 kg/m² for Chinese), such lifestyle interventions are usually ineffective, and bariatric surgery should be considered; it is very effective. Finally, NAFLD is extremely important as an overall health problem, and still neglected in primary care and gastroenterology. It is a predictor for future onset of metabolic syndrome, T2D and their cardiovascular complications, if these are not already evident, and the attendant overweight/insulin resistance increases risks of breast, colorectal and several other common cancers. Therefore, NAFLD should signal health interventions (lifestyle and weight reduction) designed to prevent these most common of medical conditions, as well as cirrhosis and HCC which are the complications of longstanding liver disease due to NASH.
Session VI

Chronic liver failure – Clinical aspects
Acute-on-chronic liver failure – Pathogenesis and diagnosis

Richard Moreau, MD
INSERM, U773, Centre de Recherche Biomédicale Bichat-Beaujon CRB3, Clichy/Paris; Université Denis Diderot, Paris 7, Site Bichat, Paris, and Service d'Hépatologie, Hôpital Beaujon, Clichy, France

Acute-on-chronic liver failure (ACLF) is characterized by the acute deterioration of liver function in a patient with compensated or decompensated, but hitherto stable cirrhosis. It is precipitated by an acute event and associated with failure of extra-hepatic organs. The pathophysiology of ACLF is still poorly understood. Bacterial infections and/or systemic release of bacterial components induce hyper-production of pro-inflammatory cytokines that play a central role in the development of multi-organ failure. At the level of the microvasculature of vital organs pro-inflammatory cytokines activate endothelial cells by up-regulating adhesion receptors and injure endothelial cells by inducing immune cells, and platelets to bind to endothelial cells. These effector cells release mediators such as proteases, oxidants, prostaglandins, and leukotrienes. These mediators injure endothelial cells, leading to increased permeability, vasodilation, and alteration of the pro-coagulant-anticoagulant balance. Cytokines also activate the coagulation cascade and trigger a damaging pro-coagulant response. Cytokines induce the inducible nitric oxide synthase, which produces nitric oxide, a potent vasodilator that worsens circulatory dysfunction. The diagnosis of ACLF is based on the recognition of the following module: i) the history of recent complication or an event that was the precipitating factor of ACLF; ii) the subsequent rapid worsening of liver function; and iii) the development of at least one extra-hepatic organ failure. Since the development of organ failures is associated with increased in-hospital mortality, any condition which could result in ACLF should be recognized at an early stage, in order to prevent the occurrence of organ failure.
Emerging role of adrenal insufficiency in chronic liver failure

Ming-Hung Tsai, MD
Chang Gung University, Taipei, Taiwan

Critical illness is accompanied by the activation of the hypothalamic-pituitary-adrenal (HPA) axis which is highlighted by increased serum corticotropin and cortisol levels. The activation of the HPA axis is a crucial component of the host’s adaptation to severe stress. Terms such as "relative adrenal insufficiency" (RAI) and, more precisely, "critical illness-related corticosteroid insufficiency" have been used to describe these conditions, in which the cortisol levels, even though high in terms of absolute value, are inadequate to control the inflammatory situation. Cortisol is essential for the normal function of the immune systems, maintenance of vascular tone and various cellular functions. Cortisol inhibits the mediators of inflammation such as neutrophil recruitment and cytokine release. In addition to these immunomodulatory effects, corticosteroids can restore vascular tone by their permissive effects in potentiating vascular responses to endogenous and exogenous vasoconstrictors. Indeed, the major effect of adrenal insufficiency in the critically ill patient is manifested through alterations in the systemic inflammatory response and cardiovascular function. Despite continuing debate over dosage, duration and need for adrenal function testing, administration of low doses of hydrocortisone in septic patients has been shown to restore the vascular hyporeactivity, reduce the incidence and the severity of organ failures, and probably improve the patients' prognosis. These hemodynamic effects of hydrocortisone may result from inhibition of cytokines and nitric oxide, which also mediates the vascular hyporeactivity in liver cirrhosis. The patients with adrenal insufficiency share many similar hemodynamic features with patients with liver cirrhosis, namely an increased cardiac output, a decreased peripheral vascular resistance, decreased mean arterial pressure and hyporesponsiveness to vasopressors. Recent data have shown that adrenal insufficiency is common in critically ill patients with liver disease and carry prognostic significance. In cirrhotic patients with septic shock, low dose of steroid has been shown to result in a quicker resolution of shock and survival benefit. However, RAI has been described in the absence of clinical sepsis raising the possibility that the RAI in liver disease may be a different entity to that observed in septic shock.

Whether RAI in liver disease represents an abnormality inherent to liver failure or occurs through the same mechanism(s) as in sepsis remains unknown. The high levels of inflammatory cytokines have been shown to directly inhibit cortisol synthesis and depress the magnitude of cortisol response to corticotropin. Cirrhotic patients are characterized by increased levels of endotoxin and inflammatory cytokines, which can contribute to hemodynamic impairment and potentially to adrenal dysfunction as well. On the other hand, the liver is the primary site of metabolism of adrenal steroid hormone and synthesis of cholesterol, which is the major precursor of steroid. The cirrhotic patients typically have a decreased cholesterol level. Whether hypocholesterolemia contributes to adrenal dysfunction in liver cirrhosis warrants further investigations. Furthermore, high level of bile acids has been shown to inhibit hepatic glucocorticoid clearance, and subsequently suppress HPA axis activity.
Despite the growing interest in liver failure-associated RAI, at this time point, no definitive recommendations can be given for the use of corticosteroid in liver failure. According to a recent consensus statements from American College of Critical Care Medicine, low dose of steroid can be used in those septic patients who are vasopressor-dependent. However, the efficacy of corticosteroids in other groups of cirrhotic patients is uncertain and requires further investigations.
Pathogenesis and clinical significance of cirrhotic cardio-myopathy

Samuel S. Lee, MD
University of Calgary Liver Unit, Calgary, AB, Canada

Cirrhosis is associated with cardiovascular abnormalities including hyperdynamic circulation which is characterized by increased cardiac output and decreased systemic vascular resistance and arterial pressure. Despite the increased resting cardiac output, ventricular contractile response to stimuli is attenuated. This blunted responsiveness along with other phenomena such as QT prolongation, chamber enlargement/hypertrophy and elevated levels of serum markers such as BNP and troponin I are features of cirrhotic cardiomyopathy. It is generally latent, but shows itself under stress such as exercise, drugs, hemorrhage and surgery. Major stresses on the cardiovascular system such as liver transplantation, infections and insertion of transjugular intrahepatic portosystemic stents (TIPS) can unmask the presence of cirrhotic cardiomyopathy, and sometimes convert latent to overt heart failure. Cirrhotic cardiomyopathy may also contribute to the pathogenesis of hepatorenal syndrome. Recent work shows that cardiac systolic and diastolic dysfunction may be a predictive marker of, or even contribute to increased mortality in patients with cirrhosis and ascites. Studies in experimental animal models of cirrhosis indicate multifactorial pathogenesis including abnormal membrane biophysical characteristics, impaired β-adrenergic signal transduction, increased activity of cardiodepressant systems mediated by cGMP such as nitric oxide and carbon monoxide, and abnormal myofibrillar structural proteins. Some of these mechanisms appear to be part of a generalized systemic/cardiovascular inflammatory phenotype, whilst others such as the membrane lipid changes and membrane fluidity abnormalities may be due to metabolic/biochemical changes specific to cirrhosis itself.
State-of-the-Art Lecture III

Management of chronic hepatitis B infection

Ching-Lung Lai
University Department of Medicine, Queen Mary Hospital, Hong Kong

The majority of the people with chronic hepatitis B infection in the world acquire the hepatitis B infection either at birth or within the first 1–2 years of life. There may be substantial injury to the liver before HBeAg seroconversion, with fibrosis developing before the age of 25. After HBeAg seroconversion, even with relatively low hepatitis B virus (HBV) DNA levels of < 2,000 IU/mL, disease can progress, with development of the complications of cirrhosis and hepatocellular carcinoma.

The ultimate aim of the treatment of chronic hepatitis B is the reduction of cirrhosis complications and hepatocellular carcinoma. Treatment may be initiated for patients with high HBV DNA levels (> 20,000 IU/mL or 100,000 copies/mL for HBeAg-positive patients, and > 2,000 IU/mL or 10,000 copies/mL for HBeAg-negative patients) when the ALT levels are elevated or when there are other evidence of active disease even when ALT levels are within normal limits. Modern treatment endpoints are HBeAg seroconversion (for HBeAg-positive subjects) and sustained reduction of HBV DNA to below PCR detectability.

Treatment options include immunomodulators such as pegylated interferon, or viral suppressors (nucleoside/nucleotide analogues). The nucleoside/nucleotide analogues have been proven to decrease the risk of cirrhosis development and hepatocellular carcinoma in cirrhotic and precirrhotic patients, but are associated with the development of resistance on prolonged therapy.

To minimize resistance, one should ensure patient compliance and choose an agent with high barrier to resistance. When resistance has developed, it is preferable to add on, rather than switch to, a second agent. The resistant mutants of nucleoside analogues (e.g., lamivudine, telbivudine, entecavir) are sensitive to nucleotide analogues (e.g., adefovir, tenofovir), and vice versa. Therefore the second agent should be chosen from a different group of analogues.
Session VII

Chronic liver failure management
Renal complications

Vicente Arroyo-Perez
Liver Unit. Hospital Clinic, University of Barcelona, Spain

A major event during the course of cirrhosis is the development of a progressive deterioration of circulatory function due to a decrease in splanchnic vascular resistance and impairment in cardiac function. The decrease in vascular resistance in the splanchnic microcirculation has been traditionally related to splanchnic arterial vasodilation due to massive local release of vasodilators secondary to portal hypertension. Recent data, however, suggest that an increase angiogenesis related to vascular endothelial growth factor and other pro-angiogenic substances can also play a role. The mechanism of the impaired cardiac function is probably multifactorial: reduced preload, cirrhotic cardiomiopathy and impaired chronotropic function.

The impairment in circulatory function determines a homeostatic activation of the renin-angiotensin-aldosterone system, sympathetic nervous system and antidiuretic hormone. The splanchic microcirculation is resistant to the vasoconstrictor effect of these systems. Therefore, the homeostasis of arterial pressure in cirrhosis occurs in the extra-splanchnic circulation, especially in the kidneys. The activation of the renin-angiotensin-aldosterone system and sympathetic nervous systems produces renal fluid retention which accumulates as ascites. The stimulation of antidiuretic hormone, which occurs later during the course of cirrhosis, leads to water retention and dilutional hyponatremia. Finally, at the latest phase of cirrhosis, when circulatory dysfunction is severe, renal vasoconstriction is intense and patients develop type-2 hepatorenal syndrome, a steady and moderate renal failure, and refractory ascites.

Type-1 hepatorenal syndrome is an acute and rapidly progressive renal failure that occurs usually in the setting of a precipitating event, commonly an infection. Patients with type-1 hepatorenal syndrome also present rapid deterioration of liver function (encephalopathy, jaundice) and relative adrenal insufficiency. The mechanism of this multiorgan failure is an acute deterioration in circulatory function due to both an accentuation of arterial vasodilation and of cardiac dysfunction. If not treated, patients with type-1 HRS dye within few days following the onset of the syndrome.

The treatment of choice of tense ascites in cirrhosis is paracentesis associated to i.v. albumin infusion. Moderate sodium restriction and diuretics (spironolactone alone or associated to furosemide) are subsequently given to prevent re-accumulation of ascites. Diuretics are the treatment of choice in patients with moderate ascites. Patients with type-2 HRS and refractory ascites (not responding to diuretics) could be treated by frequent paracentesis or by the insertion of a tranjugular intrahepatic portacaval shunt (TIPS). Finally, terlipressin plus albumin is the treatment of choice in type-1 hepatorenal syndrome. V2-vasopressin antagonists are currently explored for the treatment and dilutional hyponatremia.
Management of bacterial infections

Kwang-Hyub Han, MD
Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Korea

Bacterial infections are a common complication of patients with chronic liver failure such as cirrhosis. Rapid deterioration may follow after infection, which adversely affect survival. Cirrhotic patients are susceptible to bacterial infections because of increased bacterial translocation and reduced reticuloendothelial function.

Ascites, which is the most common complication of chronic liver failure, is also associated with increased risk of spontaneous bacterial peritonitis (SBP). The prevalence of SBP is about 10–30% in hospitalized cirrhotic patients with ascites.

For the diagnosis of SBP, clinical suspicion is important. The typical symptoms and signs are fever, abdominal pain, and leukocytosis. Presentation with unexplained sepsis, jaundice, hepatic encephalopathy, renal failure, or ileus may also indicate SBP. The diagnostic is made when there is ascitic fluid infection (a positive bacterial culture and/or an elevated absolute polymorphonuclear leukocyte (PMN) count ≥ 250 cells/mm³). The routine use of reagent strips at the bedside may help early detection of SBP. Empirical therapy with broad-spectrum antibiotics such as cefotaxime should be initiated when a PMN count > 250 cells/mm³ is detected in ascitic fluid. Cefotaxime or a similar third-generation may cover three most common isolated organisms such as Escherichia coli, Klebsiella pneumonia and pneumococci. Five days of treatment with cefotaxime is as effective as 10 day therapy. Resolution of infection in SBP is associated with an improvement in symptoms and signs. However, the proportion of antibiotic-resistant microorganisms is rising and it is becoming a clinical problem in managing SBP. In Korean study, cefotaxime-resistant Gram-negative bacilli had increased.

In the past, the in-hospital mortality rate was very high, but this rate has been lowered to less than 20% with the early diagnosis and effective antibiotic therapy. In patients who survive an episode of SBP, the cumulative recurrence rate at one year is approximately 70%. In patients who had one episode of SBP, oral norfloxacin (400 mg/day) reduces the probability of recurrence of SBP from 68% to 20%. However, patients receiving continuous norfloxacin had a higher risk of resistant flora. In our study, the in-hospital mortality rate was less than 15%. But the cumulative probability of survival at 12 months was also less than 15%. In the present study, we confirmed that SBP is correlated with poor survival rates similar to the previous reports and liver transplantation might be necessitated for cirrhotic.

**Conclusion:** Infection is directly responsible for 30–50% of deaths in cirrhosis. To reduce morbidity and mortality related bacterial infection, early diagnosis and effective infection control is the key issue in cirrhotic patients as well as effective management to prevent liver decompensation. In SBP, a high index of suspicion and early empirical treatment are important for the successful management. In addition, the prevention of SBP is effective and necessary for patients at high risk.
Hepatic encephalopathy

Prof. Dr. Dieter Häussinger
Department of Internal Medicine D, Heinrich Heine University, 40225 Düsseldorf, Germany, E-Mail: haeussin@uni-duesseldorf.de

Hepatic encephalopathy (HE) is a neuropsychiatric syndrome which can develop in the course of chronic and acute liver disease. It is characterized by cognitive and motoric deficits of varying severity. HE is functional in nature, potentially reversible and is thought to reflect the clinical manifestation of a low-grade cerebral edema, which exacerbates in response to ammonia and other precipitating factors, such as electrolyte disturbances, bleeding, infections, high protein diet, diuretics and sedatives. The action of these rather heterogeneous factors integrates at the level of astrocyte swelling, which is induced not only by ammonia, but also by benzodiazepines, hyponatremia and inflammatory cytokines. Astrocyte swelling induces oxidative/nitrosative stress, which leads to protein tyrosine nitration, RNA oxidation and zinc mobilization in the brain. These changes may affect signal transduction and enzyme activities in the brain, blood brain barrier permeability and can trigger neurosteroid synthesis with positive modulatory effects on GABA\(_A\) receptors by upregulating the expression of the peripheral benzodiazepine receptor. RNA oxidation may interfere with local postsynaptic protein synthesis, which is required for memory formation and may explain multiple effects on receptor expression. Most importantly, protein tyrosine nitration and RNA oxidation were also observed in post mortem human brain from patients with HE, but in brains from cirrhotics without HE. Thus, oxidative and nitrosative stress contribute to astrocyte and neuronal dysfunction, which results in disturbances of synaptic plasticity and pathologically altered oscillatory networks in the brain, which probably underly the motoric and cognitive deficits in patients with hepatic encephalopathy.

Diagnosis of manifest HE is done on the basis of clinical symptoms according to the Westhaven criteria, whereas diagnosis of minimal HE requires psychometric or neurophysiological testings. Minimal HE impairs quality of life and is associated with poor prognosis, but is per definition without overt symptoms. Diagnostic approaches for grading low stages of HE severity are problematic, because clinical severity assessment is subjective and psychometric paper pencil tests suffer from serious drawbacks, such as training effects, education dependence, low sensitivity etc.). It was therefore recommended to separate only low grade (comprising previous minimal HE and HE grades I and II) from high grade encephalopathy (former grades III and IV) and to characterize low grade HE severity by an objective reproducible measure such as critical flicker frequency or evoked potentials.

Identification and treatment of precipitating factors are the mainstays of HE therapy. Correction of these precipitating factors can improve rapidly acute HE episodes and against this background of spontaneous improvement the efficacy of medical treatment is difficult to assess. Currently, intravenous ornithine aspartate, vegetable protein, oral branched chain amino acids, lactulose enemas and liver transplantation are considered to be effective. Whereas the efficacy of oral lactulose and non-resorbable antibiotics in the treatment of an acute HE attack is under debate, the beneficial effect of lactulose and rifaximin in the secondary HE prophylaxis has recently been established. Current therapy largely aims at lowering ammonia, and it
is hoped that the better understanding of the complex pathogenesis of HE will offer new therapeutic options.

References:


Session VIII

Liver cancer
The antiviral therapy for decompensated hepatitis B-related cirrhosis

Qingchun Fu
Shanghai Liver Diseases Research Center, Nanjing Military Command, Shanghai, China

Hepatitis B-related decompensated cirrhosis is associated with an extremely poor prognosis for survival. The development of specific antivirals improved the management of decompensated cirrhosis significantly over the past few years.

1. Hepatitis B virus replication is associated with a severe outcome in patients with decompensated cirrhosis. Anti-HBV therapy can suppress viral replication and hepatic inflammation leading to clinical stabilization and improvement.

2. Early initiation of effective antiviral therapy should be offered to these patients because of the delay in the restoration of liver functions.

3. Nucleos(t)ide analogues are effective, well tolerated and should be continued indefinitely. Lamivudine was widely used in China and early add-on therapy with adefovir allows us to rescue lamivudine resistance, but its use may be limited by nephrotoxicity.

4. Studies are ongoing with the newer generation of antivirals (telbivudine, tenofovir, entecavir, and emtricitabine) in monotherapy or in combination to determine the best strategy for achieving rapid and prolonged suppression of viral replication.

5. All decompensated patients should be referred promptly to a liver transplantation center for evaluation. Research is required to identify patients at risk for destabilization despite treatment to permit optimal utilization of the scarce organ resource.
Diagnosis and stratification of hepatocellular carcinoma

Massimo Colombo
A.M. & A. Migliavacca Center for Liver Disease, 1st Division of Gastroenterology, Fondazione IRCCS Ca’ Granda Maggiore Hospital, University of Milan, Italy

The definition of early hepatocellular carcinoma (HCC) incorporates a single < 5 cm nodule or up to 3 < 3 cm nodules (Milan criteria) in compensated cirrhosis, without tumor venous invasion. Recently, the very early tumor definition has been added incorporating a < 2 cm nodule with an “indistinct nodular pattern” and a hypoattenuated vascular pattern on contrast imaging, with a better prognosis compared to same size nodules with a “distinct nodular pattern” that are hypervascular on imaging and infiltrating at histology. In patients with an early detected HCC, diagnosis is achieved either by histology or by dynamic contrast imaging techniques (cirrhosis) like contrast-CT, gadolinium MRI and sonovue-US (CE-US). CE-US+MRI concurrently demonstrating contrast wash-in followed by contrast wash-out of the nodule, has 33% sensitivity and 100% specificity for 0.5–2.0 cm HCC, in cirrhosis. Nodules with discordant imaging results need either histological examination or enhanced follow-up (every 3 months) with imaging. In patients with ≥ 2 cm HCC one imaging with CT scan or MRI has absolute diagnostic accuracy: CE-US is discouraged owing to the high risk of false positive results due to intrahepatic cholangiocarcinoma. The BCLC staging system combining TNM, Child Pugh and Performance Status classification is endorsed by EASL and AASLD and allows to classify HCC patients into 4 classes each with the best therapeutic option available.

Correspondence to:
Massimo Colombo, MD
1st Division of Gastroenterology
Fondazione IRCCS Ca’ Granda Maggiore Hospital
University of Milan
Via F. Sforza 35
20122 Milan
Italy
Tel: 39-0255035432
Fax: 39-0250320410
E-Mail: massimo.colombo@unimi.it
The diagnosis and management of small HCC

Feng Shen
No. 1 Comprehensive Department, Shanghai Eastern Hospital, Shanghai, P. R. China

The early diagnosis and curative treatment of small hepatocellular carcinoma (SHCC, lesion ≤ 3 cm) is the key point to prolong the patient’s life. This abstract describes some critical data regarding the diagnosis and management of SHCC in our center.

**Diagnosis:** Although the introduction of new imaging techniques and serum tumor marker has improved the accuracy of characterizing HCC, the diagnosis of small nodules in liver is still a challenge for clinicians, especially under the background of cirrhosis. In this study, 107 patients (from 2003.1–2004.1) which undergoing surgical resection and be confirmed as SHCC by pathologic examination were analyzed. 83 patients have high risk for HCC or HCC family history and only 12.1% (n = 13) have symptom occurrence. 11 patients were found in the examination for other diseases or found occasionally. In order to evaluate the sensitivity accurately, the patients were divided into groups of AFP(+) (n = 70) and AFP(-) (n = 37) according to the level of AFP was higher than 200 ng/ml or not. In the group of AFP(+), combination of ultrasonography (US) and detection of hepatitis virus (HBV/HCV) has a 85% sensitivity. If computed tomography (CT) or magnetic resonance (MR) is used, the sensitivity can be raised to about 95% (67/70), the remainder were identified by lipiodol-CT (n = 2) and biopsy (n = 1). The data from group of AFP(-) is not satisfactory as that from group of AFP(+). US/HBV/HCV revealed only 21 patients (57%). In this condition, US plus CT/MRI raised the sensitivity to 80% (30/37). The rest patients were characterized by lipiodol-CT (n = 4) and biopsy (n = 3). These data show that difficulties still existing in diagnosis of SHCC with low level of AFP by invasive techniques.

**Therapeutic options:** 412 patients with SHCC accepted treatment in our center were analyzed (from 2003.1–2004.1). Nearly 30%(n = 107) patients with SHCC which have normal liver function and single nodule away from important structure in liver are chosen to resection. The 3-years overall and disease-free survival rate are 80% and 75% respectively. Percutaneous ethanol injection (PEI), radiofrequency ablation (RF) and microwave ablation (MW) are considered alternative options for decompensated cirrhotic patients or patients with nodules in difficult location (perivascular). Analyzed from the result of 118 patients, the overall survival rate of SHCC after PEI is about 100% at 1 year and 81% at 3 years. After treated with RF, 96% patients (110/115) obtained a total necrosis of SHCC. In order to reduce the recurrence, 13% (15/115) patients accepted two times RF and 3 patients accepted three times RF. The median survival time in patients treated with RF is 27.4 months and 1-year or 3-years non-disease survival rate is 88.2% or 67.1% respectively. 72 patients experienced MW. The survival rate is 98% at 1 year and 62% at 3 years. These results show us correct and effective treatment for SHCC should be adopted according to the liver function of patients and the location of lesions.

**Prognostic predication:** Although different groups are working to identify some pathological factors or genes and proteins that help predicing the prognosis of SHCC, the prognostic markers with clinical applicability for SHCC are so far lacking.
and specifically required. We firstly identified Aspartyl-(asparaginyl)-β-hydroxylase AAH as the most significantly overexpressed gene in HCC by cDNA microarray hybridization by a tissue microarray (TMA) with 233 paired HCC samples. In the further prospective observation, we found that AAH expression was an independent factor affecting the recurrence (HR, 3.161, 95% CI: 2.115–4.724, p < 0.001) and survival of the patients with curative resection (HR, 2.712, 95% CI: 1.734–4.241, p < 0.001) by multivariate analysis. In BCLC stage A patients with AAH over- or underexpression, the tumor recurrence and survival rates were also statistically different (45% and 85% vs. 16% and 33% in 1- and 3-year cumulative recurrence rates; 73% and 37% vs. 90% and 80% in 1- and 3-year survival rates; p < 0.001 for both). Furthermore, in stage A patients with tumor 5 cm in diameter, the time to recurrence (TTR) was 26.7 ± 1.6 versus 51.9 ± 2.8 months, and the one- and three-year survival rates were 97% and 52% versus 100% and 90% in AAH over- and underexpression patients (p < 0.001 for both). AAH likely provides a more precise prognostic predictor in early stage HCCs, especially in SHCC.

In conclusion, the critical point in diagnosis of SHCC is the screening of high risk population and applying the present serum marker and imaging techniques synthetically. In order to increase the efficacy of treatment, comprehensive not single means should be emphasized. Future scenarios will be the improvement of target detection and therapeutic strategies for SHCC.
Management of hepatocellular carcinoma

Gregory J. Gores, MD
President of the International Liver Cancer Association (ILCA), Chair of Gastroenterology and Hepatology, Professor of Medicine, Mayo Clinic, Rochester, MN, USA

The incidence of liver cancer is increasing in the United States of America and is a major cause of cancer-associated death worldwide. Although hepatitis B (HBV) vaccination and treatment will diminish the incidence of hepatocellular carcinoma (HCC), it will remain an important hepatobiliary disease. The worldwide epidemic of nonalcoholic liver disease (NAFLD) will result in a continual worldwide problem regarding HCC. The treatment of HCC must take into account the nature and severity of the underlying liver disease, the stage of the HCC and the performance status of the patient. The best classification for HCC takes into account these three clinical parameters, the Barcelona Clinic liver cancer classification. Patients without portal hypertension and unicentric disease benefit most from surgical resection. Patients fulfilling the Milan Criteria (one lesion ≤ 5 cm or three lesions ≤ 3 cm) with portal hypertension are optimal candidates for liver transplantation. Radiofrequency ablation is highly effective for patients not eligible for resection or liver transplantation. Patients not candidates for surgical extirpation have a survival advantage with transarterial locoregional therapy. This therapy is best performed with doxorubicin eluding beads. Although radio-embolization is used, its use is cumbersome logistically, is expensive and is unlikely to add any survival benefit over standard transarterial chemo-embolization therapy (TACE). Finally, for patients with disease not amendable for curative and/or local-regional therapies; targeted therapy with sorafenib extends survival.
List of Chairpersons, Speakers and Scientific Organizers

Prof. Dr. Vicente Arroyo-Perez  
Hospital Clínico y Provincial  
Universidad de Barcelona  
Unidad de Hepatologia  
Villarroel 170  
08036 Barcelona  
Spain

Dr. W. Bemelman  
Universiteit van Amsterdam  
Academisch Medisch Centrum  
Department of Surgery  
Meibergdreef 9  
1105 AZ Amsterdam  
The Netherlands

Dr. Charles N. Bernstein  
University of Manitoba  
Department of Gastroenterology  
804 F-175 McDermot Avenue  
Winnipeg, MB R3E 3P4  
Canada

Prof. Dr. Cheng-Wei Chen  
85th Hospital of PLA  
Liver Disease Research Center  
9585 Humin Road, Xuhui Distr.  
200235 Shanghai  
P. R. China

Prof. Dr. Jun Cheng  
Beijing Ditan Hospital  
Department of Infectious Disease  
13 Ditan Park, Anwai Street  
100011 Beijing  
P. R. China

Judy Cho, M.D.  
Yale University  
School of Medicine  
Department of Internal Medicine  
333 Cedar Street  
New Haven CT 06520  
USA

Prof. Dr. Massimo Colombo  
Ospedale Maggiore  
IRCCS Policlinico  
Dipartimento di Gastroenterologia ed Endocrinologia  
Via Francesco Sforza, 35  
20122 Milano  
Italy

Adrian M. Di Bisceglie, M.D.  
Professor of Medicine  
Saint Louis University  
School of Medicine  
Gastroenterology & Hepatology  
3635 Vista Ave. at Grand Blvd.  
St. Louis, MO 63110-0250  
USA

Dr. Dai-Ming Fan  
Xijing Hospital  
Institute of Digestive Diseases  
15 Western Changle Road  
710032 Xi'an, Shanxi Province  
P. R. China

Prof. Dr. Jia Fan  
Zhongshan Hospital  
Shanghai Fudan University  
Department of Hepatology  
Surgery  
180 Fenglin Road, Xuhui Distr.  
200032 Shanghai  
P. R. China

Prof. Dr. Geoffrey C. Farrell  
The Canberra Hospital  
Bldg. 10, Level 5  
P. O. Box 11 Woden  
Canberra, ACT 2606  
Australia

Prof. Dr. Stefan Feuerbach  
Röntgendiagnostik  
Klinikum der Universität Regensburg  
93042 Regensburg  
Germany
Prof. Dr. Samuel S. Lee
University of Calgary
Health Sciences Centre
Division of Gastroenterology
G130, Health Sciences Centre
3330 Hospital Drive N.W.
Calgary, AB T2N 4N1
Canada

Prof. Dr. Lan-Juan Li
The First Affiliated Hospital
Zhejiang Medical University
Department of Infectious Disease
261 Qingchun Road
310003 Hangzhou
P. R. China

Prof. Dr. Yu-Lan Liu
People's Hospital of
Beijing University
Department of Gastroenterology
11, Southern Street, Xizhimen
100044 Beijing
P. R. China

Dr. Gerassimos Mantzaris
Evangelismos Hospital
Dept. of Gastroenterology
45-47, Ipsilantou str.
106 75 Athens
Greece

Prof. Dr. Philippe Marteau
Lariboisiere Hôpital
Service d'Hépato-Gastroentérologie
2, rue Ambroise Paré
75010 Paris
France

Prof. Dr. Xiao-Hui Miao
Shanghai Changzheng Hospital
Department of Infectious Disease
415 Fengyang Road, Huangpu Dstr.
200003 Shanghai
P. R. China

Prof. Dr. Richard Moreau
Hôpital Beaujon
Service d'Hépatologie
100, Bd. Général Leclerc
92118 Clichy
France

Prof. Dr. Markus F. Neurath
Medizinische Klinik 1
Universitätsklinikum Erlangen
Ulmenweg 18
91054 Erlangen
Germany

Prof. Dr. Qin Ouyang
West China Hospital
Sichuan University
GI Department
37#, Guoxue Street
610041 Chengdu
P. R. China

Prof. Dr. Gustav Paumgartner
Medizinische Klinik II
Klinikum der Universität
München - Großhadern
Marchioninistr. 15
81377 München
Germany

Prof. Dr. Jia-Ming Qian
Beijing Union
Medical College Hospital
Department of Gastroenterology
1 Shuaifu Garden, Dongcheng
100730 Beijing
P. R. China

Prof. Dr. Zhi-Hua Ran
Renji Hospital
Shanghai Jiao Tong University
Department of Gastroenterology
1630 Dong Fang Rd, Pudong Distr.
200001 Shanghai
P. R. China
Prof. Dr. Dr. Gerhard Rogler  
Universitätsspital Zürich  
Klinik für Gastroenterologie & Hepatologie  
Rämistrasse 100  
8091 Zürich  
Switzerland

R. Balfour Sartor, M.D.  
Professor of Medicine  
University of North Carolina  
School of Medicine  
Gastroenterology & Hepatology  
111 Mason Farm Road  
Chapel Hill, NC 27599-7032  
USA

Prof. Dr. Jürgen Schölmerich  
Klinik für Innere Medizin I  
Klinikum der Universität Regensburg  
93042 Regensburg  
Germany

Prof. Dr. Feng Shen  
Shanghai Eastern Hospital  
No. 1 Comprehensive Department  
225 Changhai Road  
200438 Shanghai  
P. R. China

Dr. Marcellus Simadibrata  
University of Indonesia  
Faculty of Medicine  
Division of Gastroenterology  
Jl. Lombok 52  
10350 Jakarta  
Indonesia

Prof. Dr. Jose D. Sollano  
University of Santo Tomas  
Faculty of Medicine and Surgery  
Department of Gastroenterology  
Sampaloc  
1099 Manila  
Philippines

Stephen R. Targan, M.D.  
Professor of Medicine  
Cedars-Sinai Medical Center  
Davis Research Center  
#D-4063 (1865)  
8700 Beverly Blvd.  
Los Angeles, CA 90048  
USA

Dr. M.-H. Tsai  
Chang Gung University  
Division of Gastroenterology  
199, Tung Hwa North Road  
10591 Taipei  
Taiwan

Dr. Gui-Qiang Wang  
Beijing Medical University  
First Teaching Hospital  
Department of Hepatopathy  
8 Xishiku Street, Xicheng Distr.  
100034 Beijing  
P. R. China

Prof. Dr. Mamoru Watanabe  
Tokyo Medical & Dental Univ.  
School of Medicine  
Department of Gastroenterology  
1-5-45, Yushima, Bunkyo-ku  
Tokyo 113-8519  
Japan

Dr. Lai Wei  
People’s Hospital of Beijing University  
Department of Hepatopathy  
11, Southern Street, Xizhimen  
100044 Beijing  
P. R. China

Prof. Dr. Florence Wong  
University of Toronto  
Toronto General Hospital  
9EN/220  
200 Elizabeth Street  
Toronto, ON M5G 2C4  
Canada
Dr. Kai-Chun Wu  
Xijing Hospital  
Department of Gastroenterology  
15 Western Changle Road  
710032 Xi'an, Shanxi Province  
P. R. China

Prof. Dr. Bing Xia  
Zhongnan Hospital of Wuhan University  
Department of Gastroenterology  
169 Donghu Road, Wuchang  
430071 Wuhan  
P. R. China

Prof. Dr. Yao-Zong Yuan  
Ruijin Hospital  
Department of Digestive Diseases  
197 Second Ruijin Road, Luwan  
200025 Shanghai  
P. R. China

Prof. Dr. Stefan Zeuzem  
Innere Medizin I  
Klinikum der Johann Wolfgang Goethe-Universität Frankfurt  
Theodor-Stern-Kai 7  
60596 Frankfurt  
Germany

Prof. Dr. Jia-Ju Zheng  
Suzhou Municipal Hospital  
Department of Gastroenterology  
242 Guangji Road, Jinlv  
215008 Suzhou  
P. R. China
POSTER ABSTRACTS

Poster Numbers

Gut 1 – 61
Liver 62 – 112

Author Index to Poster Abstracts
Characteristics of ulcerative colitis in country with low prevalence of inflammatory bowel disease

Murdani Abdullah¹ Dolly D. Kansera² Jane Estherina², Nata P.H. Lugito², Rizki Yarantradhani², Fransiska Hardi², Nur Istia², Marcellus Simadibrata¹, Achmad Fauzi¹, Daldiyono Hardjodisastro¹, A. Aziz Rani¹

¹Division of Gastroenterology, Department of Internal Medicine, Faculty of Medicine, University of Indonesia, dr. Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia
²Department of Internal Medicine, Faculty of Medicine, University of Indonesia, dr. Cipto Mangunkusumo Hospital, Jakarta, Indonesia

Introduction: Several recent Asian studies confirm that the incidence and prevalence of both ulcerative colitis (UC) and Crohn’s disease (CD) are lower than in North America and Europe. However, the characteristics of UC in Indonesia were scarcely reported. Aim of this study was to provide the characteristics data of UC patients in Indonesia.

Method: All patients who underwent colonoscopy with any indication were recruited from endoscopy archives data in Division of Gastroenterology, Department of Internal Medicine, dr. Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia in year 2007–2008. The diagnosis was determined based on continuous repeated bloody diarrhea, diffuse inflammation from colonoscopy and confirmed by histopathology findings.

Results: There were 921 patients that underwent colonoscopy and 25 patients (2.7%) with clinical complaints, colonoscopy description and pathological findings suggestive of ulcerative colitis. The male and female ratio was 1:1.7. The mean age was 47.6 years with a peak in the age at presentation was noted during 40–50 years. Lower gastrointestinal bleeding (36%), diarrhea (32%), abdominal pain, fever, upper gastrointestinal bleeding and constipation (4%) were the main clinical complaints. In colonoscopic findings the involvement of rectum was 20%, isolated left colon was 64%, isolated right colon was 8%, pancolitis was 28%.

Conclusion: The finding of UC in our study was 2.7% with female predominance. There was only one peak of UC at the age of forties. Isolated left colon involvement was the dominant colonoscopy findings.

Key words: ulcerative colitis; incidence; clinical features; colonoscopy description
Impaired endothelial function in patients with inflammatory bowel disease

Akpınar H*, Kayahan H*, Sari İ**, Çullu N***, Akarsu M*, Demir S^, Yüksel F”
Göktay Y****, Ünsal B^

*Dokuz Eylül University Medical Faculty Division of Gastroenterology, İzmir Turkey
**Dokuz Eylül University Medical Faculty Division of Rheumatology, İzmir Turkey
***Dokuz Eylül University Medical Faculty Department of Radiology, İzmir Turkey
"Dokuz Eylül University Medical Faculty Division of Hematology, İzmir Turkey
^Atatürk State Hospital Division of Gastroenterology, İzmir Turkey

Objectives: Several studies have suggested that chronic inflammatory diseases might be associated with an acceleration of the atherosclerotic process. However, there is little information on the effect of inflammatory bowel disease (IBD) on the presence of increased intima media thickness (IMT) and impaired flow mediated dilatation (FMD) as markers for early atherosclerosis. The aim of study was to evaluate atherosclerosis and endothelial dysfunction in IBD patients by using IMT and FMD techniques, respectively and we also investigate possible involvement of sCD40L and IL-18 in this process. In this study we aimed to evaluate whether IBD is a risk factor for both impaired flow mediated dilatation (FMD) and increased common carotid artery IMT in clinically inactive IBD patients.

Methods: Brachial artery FMD and common carotid artery IMT were measured by high resolution ultrasound in 39 IBD patients (20 Crohn’s disease [CD], 19 ulcerative colitis [UC] patients) and in 31 healthy donors matched for age, sex and smoking status. Disease durations of IBD patients were recorded. CD activity index and modified Truelove-Witts criteria were used for disease activity. Blood glucose, lipids, high sensitive C-reactive protein (hsCRP), erythrocyte sedimentation rate (ESR), soluble CD40 ligand (sCD40L), interleukin (IL)-18, homocystein and plasminogen activator-inhibitor-1 (PAI-1) were assessed. Blood pressure, body mass index (BMI), waist/hip (W/H) proportions were noted in all participants.

Results: There was no difference mean IMT of common carotid artery between IBD and control groups (0.52 ± 0.07 mm vs 0.51 ± 0.05 mm, p = 0.822), while both endothelial dependent (11.90 ± 6.12 vs 18.60 ± 9.40%, p = 0.002) and independent (17.04 ± 6.79 vs 21.39 ± 9.79%, p = 0.048) dilatation responses on brachial arteries were impaired in IBD patients compared with control group. Inflammatory markers (ESR, hsCRP, sCD40L, IL-18) were significantly elevated (p < 0.05) while PAI-1 levels were decreased in IBD patients compared to controls (16.4 ± 13.2 ng/mL vs 26.3 ± 10.6 ng/mL, p = 0.002). Homocystein levels were similar in both groups (p > 0.05). BMI and mean artery pressure levels were significantly decreased in patients with IBD compared with controls (p < 0.05). W/H proportions were similar in both groups (p > 0.05). Endothelial dependent dilatation values were significantly negative correlated with sCD40L levels (r = -0.325, p = 0.01).
Conclusions: In our study, increased IMT of common carotid artery which is accepted as the late finding of early atherosclerosis was not found while impaired endothelial function which is frequently an initiator of the atherosclerotic process was demonstrated in IBD patients. Among inflammatory markers, only sCD40L levels were correlated with endothelial dependent dilatation values. This correlation suggested that sCD40L may be a common pathogenetic factor both of IBD and atherosclerosis.

Key words: inflammatory bowel disease; atherosclerosis; endothelial dysfunction; intima-media thickness; flow mediated dilatation
Prevalence of microscopic colitis in patients with chronic non-bloody diarrhea and normal colonoscopy in Tugurejo Hospital Semarang, Indonesia

Jacobus A. Auwyang¹, Marcellus Simadibrata², Adjeg Tarius³
¹Endoscopy Unit of Tugurejo Hospital Semarang/Fellow of Gastroenterology and Hepatology, Faculty of Medicine, University of Indonesia, dr. Ciptomangunkusumo Hospital, Jakarta, Indonesia
²Division of Gastroenterology, Departement of Internal Medicine, Faculty of Medicine, University of Indonesia, dr. Ciptomangunkusumo Hospital, Jakarta, Indonesia
³Histopathology Unit of Telogorejo Hospital, Semarang, Indonesia

Background: Microscopic colitis (MC), previously regarded rare, now has emerged as a common cause of chronic diarrhea. The condition is characterized clinically by chronic non-bloody diarrhea, a macroscopically normal or near-normal colonic mucosa, where microscopic examination of mucosal biopsies reveals diagnostic histopathological changes. Microscopic colitis mainly includes the two diseases collagenous colitis (CC) and lymphocytic colitis (LC).

Aim: To investigate the prevalence and demography of microscopic colitis in patients with chronic non-bloody diarrhea and normal colonoscopy in Tugurejo Hospital Semarang, Indonesia.

Methods: Between January 2005 to January 2009, 49 patients with chronic non-bloody diarrhea of unexplained etiology who had undergone full colonoscopy with no obvious abnormalities were included in the study. One biopsies were obtained from all colonic segments and terminal ileum for diagnosis of microscopic colitis. On histopathologic examination, criteria for lymphocytic colitis (intraepithelial lymphocyte ≥ 20 per 100 intercryptal epithelial cells, change in surface epithelium, mononuclear infiltration of the lamina propria) and collagenous colitis (subepithelial collagen band thickness ≥ 10 µm) were explored.

Results: Lymphocytic colitis was diagnosed in 5 (10.2%) patients (female/male 3/2, mean age: 45 year, range: 29–62) and collagenous colitis was diagnosed in only 3 (6.1%) patients (all male, mean age: 60 years, range: 54–65). 2 patients with collagenous colitis had diabetes mellitus.

Conclusion: Biopsy of Tugurejo Hospital patients with the diagnosis of chronic non-bloody diarrhea of unexplained etiology and normal colonoscopic findings will reveal microscopic colitis in approximately 16.3% of the patients. Lymphocytic colitis more frequent than collagenous colitis in these patients.

Key words: microscopic colitis, prevalence; Semarang, Indonesia
Prevalence of mutations in thiopurine S-methyltransferase gene among Slovak IBD patients

Marian Bátovský¹, Barbora Desatová¹, Tibor Hlavaty¹, Martin Huorka¹, Zuzana Zelinková², Peter Celec³, Denisa Baláková³, ’udevit Kádeš³, Miloš Greguš⁴, Mária Zakuciová⁵, Milan Hlista⁶, Marta Horáková⁷
¹Faculty Hospital Bratislava, Slovakia
²Erasmus Medical Centre, Rotterdam, The Netherlands
³Institute of Molecular Physiology and Genetics, Slovak Academy of Sciences, Bratislava, Slovakia
⁴Department of Gastroenterology, Hospital with Policlinic, Nitra, Slovakia
⁵1st Medical Clinic, Faculty Hospital, Košice, Slovakia
⁶Medical Department, Hospital with Policlinic, Trenčín, Slovakia
⁷2nd Medical Clinic, Faculty Hospital, Martin, Slovakia

Background: Thiopurines, such as azathioprine (AZA) and 6-mercaptopurine (6-MP) are effective in the induction and maintenance of remission of inflammatory bowel disease (IBD). Thiopurine S-methyltransferase (TPMT) plays an important role in the metabolism of thiopurines. Genetic polymorphisms of the gene encoding TPMT have been extensively studied in the past. It has been suggested that TPMT genetic polymorphisms lead to dose-related hematopoietic toxicity. Since there are major ethnic differences in the prevalence of particular TPMT variants, it is important for each country to study their own prevalence in order to estimate the role of TPMT variants-related thiopurines toxicity in the particular IBD population. The aim of this study was to determine the frequency of the four most common allelic variants of TPMT gene in the population of Slovak IBD patients.

Methods: TPMT*2, TPMT*3A, TPMT*3B, TPMT*3C polymorphisms were determined in IBD patients using the restriction fragment length polymorphism PCR (RFLP PCR). The allele frequencies of particular allelic variants were calculated and compared with other Caucasian populations reported so far.

Results: Three hundred and thirty IBD patients were included; 196/132/2 Crohn’s disease/ulcerative colitis/unclassified colitis, 180 (55%) males; mean age 37 years (range 17–75 years). Ninety-three percent of patients were homozygous for wild type TPMT variant. Heterozygous genotype of any of the studied polymorphisms was present in 6% of patients, only one patient was homozygous for TPMT*3A allele (0.3%). The most prevalent mutant allele was TPMT*3A (3.2%). The frequency of mutant alleles TPMT*3C and TPMT*2 was 0.2%. This distribution of the most common allelic variants of TPMT gene were in accordance with previously reported high prevalence of TPMT*3A variant and lower frequencies of TPMT*3C and TPMT*2 in Caucasian populations.

Conclusions: This study shows the prevalence of TPMT genetic polymorphisms in the Slovak IBD patients’ population. As in other Caucasian populations, the most common mutant allelic variant is TPMT*3A and the prevalence of homozygocity is relatively low.
Mutations in thiopurine S-methyltransferase gene increases risk of azathioprine-induced leukopenia in Slovak IBD patients

Marian Bátovský¹, Barbora Desatová¹, Tibor Hlavatý¹, Martin Huorka¹, Zuzana Zelinková², Peter Celec³, Denisa Baláková³, Ľudevíť Kádeši³, Miloš Greguš⁴, Mária Zakuciová⁵, Milan Hlísta⁶, Marta Horáková⁷
¹Faculty Hospital Bratislava, Slovakia
²Erasmus Medical Centre, Rotterdam, The Netherlands
³Institute of Molecular Physiology and Genetics, Slovak Academy of Sciences, Slovakia
⁴Department of Gastroenterology, Hospital with Policlinic, Nitra, Slovakia
⁵1st Medical Clinic, Faculty Hospital, Košice, Slovakia
⁶Medical Department, Hospital with Policlinic, Trenčín, Slovakia
⁷2nd Medical Clinic, Faculty Hospital, Martin, Slovakia

Background: Leukopenia in IBD patients treated with thiopurines (azathioprine and 6-mercaptopurine) has been associated with low thiopurine S-methyltransferase (TPMT) enzyme activity. Polymorphisms in the gene encoding for TPMT seem to lead to low TPMT activity. However, the data on the relationship of TPMT genotypes and thiopurines-induced myelosuppression are conflicting. The aim of this study was to analyze the relationship of mutant TPMT genotypes and azathioprine-induced leukopenia in IBD patients.

Methods and patients: All consecutive IBD patients treated with azathioprine in Slovakia between 2007 and 2009 were included. TPMT genetic polymorphisms (TPMT*2, TPMT*3A, TPMT*3B, TPMT*3C) were determined using the restriction fragment length polymorphism PCR. Leukopenia was defined as white blood cells count less than 3.0 x 10⁹/L occurring any time during the azathioprine treatment without any alternative explanation. The association with leukopenia was analyzed by Fisher’s exact test.

Results: Two-hundred and thirty eight IBD patients, 132 (56%) males; 149 (62.6%)/87 (36.6%)/2 (0.8%) Crohn’s disease/ulcerative colitis/unclassified colitis, average age 36.4 years, range 19–75 years). Two-hundred and twenty two patients (93%) were wild-type homozygous, 15 (6%) patients were heterozygous and only one patient was homozygous. Only TPMT*3A and TPMT*2 were present in the studied population (allele frequencies 3.4% and 0.2%, respectively). Twenty-eight patients developed leukopenia (11.8%). Leukopenia was observed in 63% (10/16) of patients with mutant variant of TPMT compared with only 8% (18/222) of patients with wild-type genotype (p < 0.0001). The risk of leukopenia was significantly increased in AZA treated IBD patients with mutant TPMT allele; odds ratio 13.75, confidence interval 5.292–35.726 (p < 0.0001).

Conclusion: Mutations in TPMT encoding gene are associated with the risk of azathioprine-induced leukopenia in Slovak IBD patients.
Immunomodulatory effect and mechanism of tuftsin in inflammatory bowel disease

Chi Chen
Department of Gastroenterology, Shanghai East Hospital, Tongji University School of Medicine, Shanghai, China

Introduction: Tuftsin is a natural tetrapeptide known to possess a wide spectrum of activities related primarily to the immune system function. The innate immune response impairment had been verified as an initial and crucial factor in the pathogenesis of IBD. In this study we compared the serum level of tuftsin between IBD patients and healthy subjects to see whether tuftsin activity is deficient in IBD. The serum concentration of proinflammatory cytokines (TNF-α – tumour necrosis factor-α; IFN-γ – interferon-γ) and amount of NK (natural killer) cells had been examined, respectively. By the investigation of comparing these results, we aimed to determine the immunomodulatory effect and mechanism of tuftsin in IBD.

Methods: 60 IBD patients (40 ulcerative colitis, 20 Crohn’s disease) and 30 healthy subjects had been recruited. The clinical activity of each patient was assessed by CDAI and UCAI. The level of serum tuftsin was measured by reverse-phase high-performance liquid chromatography (RP-HPLC). Enzyme-linked immunosorbent assay (ELISA) was used to detect the content of TNF-α and IFN-γ. The amount of NK cells was identified by flow cytometry (FCM).

Results: Patients had reduced tuftsin activity compared with controls (p < 0.01) and a lower NK cells count (p < 0.01). Tuftsin level was correlated with CDAI score (p = 0.002). Serum TNF-α and IFN-γ content both in CD and UC group significantly increased (p < 0.001), which was correlated with tuftsin activity (p < 0.001).

Discussion/Conclusion: Tuftsin activity was reduced in IBD which is contributed to impaired amount of NK cells and dysregulated cytokine production. Such an abnormality appears to be related to impaired innate immune function and activation of inflammation. The features of tuftsin, coupled with its low toxicity, make the peptide an attractive candidate for immunotherapy.
Colorectal and rectocolic reflexes in canines: Involvement of tone, compliance and anal sphincter relaxation

Ji-Hong Chen, MD, PhD; Jiande DZ Chen, PhD*
Division of Gastroenterology and Hepatology, Renmin Hospital of Wuhan University, Wuhan 430060, P. R. China
*Division of Gastroenterology, University of Texas Medical Branch, Galveston, TX 77550, USA

Introduction: Distention of the proximal colon may have inhibitory or excitatory effects on the rectum and vice versa. The reflexes between the proximal colon and the rectum are not well studied due to difficulties in accessing the proximal colon. The aim of this study was to investigate the reflex responses and their mechanisms between the proximal colon and the rectum in consideration of distention-related changes in tone and compliance of these organs as well as anal sphincter relaxation in a canine model.

Methods: Proximal colon/rectal tone, compliance and anal sphincter relaxation were investigated in six dogs chronically implanted with a proximal colon cannula in the fasting state and during proximal colon distention or rectal distention.

Results: It was found that: 1) rectal distention and proximal colon distention both significantly and substantially decreased the compliance of the opposite regions, and guanethidine abolished proximal colon distention-induced changes in rectal compliance; 2) rectal/proximal colon distension decreased proximal colonic/rectal tone and guanethidine abolished both of these inhibitory effects; 3) the anal sphincter was more sensitive to rectal distention than proximal colon distention; the minimal distention pressure required to induce anal inhibitory reflex was lower for rectal distention than proximal colon distention.

Discussion/Conclusion: It was concluded that distention-related changes in tone and compliance suggest the long inhibitory reflexes between the proximal colon and the rectum with the sympathetic involvement in rectal responses. The anal sphincter is more sensitive to the distention of the rectum than that of the proximal colon.
Gastric electrical stimulation reduces visceral sensitivity to gastric distention in healthy canines

Ji-Hong Chen, MD, PhD; Jiande DZ Chen, PhD*
Division of Gastroenterology and Hepatology, Renmin Hospital of Wuhan University, Wuhan 430060, P. R. China
*Division of Gastroenterology, University of Texas Medical Branch, Galveston, TX 77550, USA

Introduction: The aim of this study was to investigate the effects and mechanisms of gastric electrical stimulation (GES) on proximal stomach distention-induced visceral sensitivity.

Methods: Isobaric gastric distention was performed using a barostat system in 8 normal and 6 vagotomized dogs and animal behaviors were noted and graded. The normal dogs were studied in 4 sessions: control (no GES), short pulse GES, long pulse GES, and dual-pulse GES, and the vagotomized dogs were studied in three sessions: control (no GES), long pulse GES and guanethidine.

Results: It was found that: 1) proximal stomach distention-induced behavioral changes were mediated by vagal and sympathetic pathways. The total behavior score (TBS) was 40.6 ± 7.4 in the controls, 15.3 ± 8.9 in vagotomized dogs (P = 0.006 vs. control) and 8.8 ± 0.9 in the vagotomized dogs with guanethidine (P = 0.04 vs. vagotomy). The behavioral changes were mediated via the vagal pathway at distention pressures below 20 mmHg, but mediated via both the vagal and sympathetic pathways at distention pressures equal to and above 20 mmHg. 2) GES with long pulses or dual pulses but not short pulses reduced the distention-induced behavioral score (P = 0.003, P = 0.006 and P = 0.7, respectively) and the effects of GES of long pulses might be mediated via the vagal and sympathetic pathways.

Discussion/Conclusion: In conclusion, gastric distention-induced visceral sensitivity is mediated via the vagal pathway at low distention pressures but via both vagal and sympathetic pathways at high distention pressures. GES with long but not short pulses reduces distention-induced visceral sensitivity.
Traditional Chinese physician pattern of syndrome and correlation shown by the colonoscope of part of ulcerative colitis in Urumqi

Chen junling, Wang hongfeng
Hepatology Department of the Fourth Teaching Hospital of XinJiang Medical University, Urumqi 830054, China, Tel.: 13999279909

Introduction: By observing traditional Chinese physician pattern of syndrome and correlation shown by the colonoscope of part of ulcerative colitis in Urumqi, I hope this paper can provide powerful and objective index for the diagnosis and treatment of traditional Chinese physician as well as the clinical of medical doctor.

Method: Gather the ulcerative colitis patients' data from January to December of 2009 of the clinic service and sickroom from the First Attached Hospital of Xinjiang Medical College, People’s Hospital of Xinjiang Uygur Autonomous Region, Traditional Chinese Medical Hospital of Xinjiang Uygur Autonomous Region, a military district General Hospital, and Urumqi Traditional Chinese Medical Hospital. Then undergo traditional Chinese medical process of differentiation-classification, colonoscope classification, collect related data and analyse the statistic.

Results: The ulcerative colitis patients in Urumqi are mostly between the age of 30 and 39, account 31% of the general incidence rate, the average age of onset is 42.8, of these, patients' pathogenesis less than 5 years is the most, account 80%, more than 5 years only accounts 5.7%. Of the syndrome of deficiency, spleen deficiency is the most common thing, more than 58.5% of the patients manifest this to some degree. Of the sthenic syndrome, damp-heat syndrome is the most common thing, more than 66.5% of the patients manifest this to some degree. Of the Chinese Medical Science, endoretention of damp heat is the most common thing, account 27.14%. Of these, women most manifest the syndrome of stagnation of liver-QI with deficiency of the spleen and weakness of the spleen and stomach, men most manifest the syndrome of endoretention of damp heat. Of endoscopic classification I, endoretention of damp heat, stagnation of liver-QI with deficiency of the spleen and stagnation of vital energy and blood stasis are the most common syndrome. Obviously higher than YANG deficiency of spleen and kidney as well as deficiency of YIN-blood. Of endoscopic classification II, the rate of the syndrome of endoretention of damp heat, weakness of the spleen and stomach and stagnation of liver-QI with deficiency of the spleen are almost same. Of endoscopic classification III, weakness of the spleen and stomach is the most common syndrome.

Conclusion: The endoscopic classification and diagnosis and treatment of traditional chinese physician of part of ulcerative colitis patients in Urumqi have obvious correlation, so the endoscopic check of ulcerative colitis patients can be an elongation of inspection applied in clinical, can provide powerful and objective index for the diagnosis and treatment of traditional Chinese physician.
Structural shifts of gut flora in rat acute alcoholic liver injury and Jianpihuoxue decoction’s effect displayed by ERIC-PCR fingerprint

Yang CHENG1,2,3, Haihui WANG1, Yiyang HU1,2,3, Gaofeng CHEN1, Jian PING3, Jinhua PEN1, Qin FEN1

1Institute of Liver Diseases, Shuguang Hospital affiliated to Shanghai University of TCM (Shanghai 201203), China
2E-institutes of Shanghai Municipal Education Commission, China
3Key Laboratory of Liver and Kidney Diseases, Ministry of Education, China

Objective: To study the structural shifts of gut flora in rats with acute alcoholic liver injury (AALI), and the modification effect of Jianpihuoxue (JPHX) decoction on gut flora.

Method: Thirty-six Sprague Dawley rats were allocated to the control, AALI model and JPHX intervention groups randomly. Rats in AALI and JPHX groups were given ethanol by intragastric garage for 5 days; rats in JPHX group were administered JPHX decoction simultaneously. At the end of experiment, rats were sacrificed and blood and liver tissue samples were collected. Activities of serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), hepatic γ-glutamyltranspeptidase (γ-GT) and hepatic triglyceride (TG) amount were determined respectively. Plasma endotoxin level in portal vein was measured. Hematoxylin and eosin (HE) staining and oil O red staining were performed to determine pathological changes of liver tissues. Fresh rat fecal samples were collected too. Total DNA of gut flora were extracted from fecal samples by Bead-beating method and determined by ERIC-PCR fingerprint method. The similarity cluster analysis and principle component analysis were performed to analyze the ERIC-PCR fingerprint respectively.

Results: In AALI group, the ratio of liver/body weight, activities of ALT, AST and hepatic γ-GT, amount of hepatic TG were elevated significantly; and the results of HE and oil O red staining showed that fat deposited markedly in liver tissue. JPHX decoction alleviated hepatic biochemical indices and pathological changes significantly. Plasma LPS level in rat portal vein in AALI group increased significantly but that in JPHX group decreased significantly. The cluster analysis and principal component analysis of ERIC-PCR fingerprint showed that gut flora in AALI group changed markedly, and JPHX decoction could recover gut flora to some extent.

Conclusion: Structure of gut flora shift markedly during acute alcoholic liver injury, JPHX decoction had prevention effect through the modification of gut flora.

Key words: acute alcoholic liver injury; gut flora; Jianpihuoxue decoction; ERIC-PCR; fingerprint; cluster analysis; principle component analysis
Supported by Shanghai Rising-Star Program (07QA14052), E-institutes of Shanghai Municipal Education Commission (E03008); Innovative Research Team in Universities, Shanghai Municipal Education Commission; and Shanghai Leading Academic Discipline Project of Shanghai Municipal Education Commission.

Correspondence to:

Dr. Yang Cheng, No. 528 Zhangheng Road, Pudong Shanghai 201203, Institute of Liver Diseases, Shuguang Hospital affiliated to Shanghai University of TCM. E-Mail: chengyang@hotmail.com
Capsule enteroscopy diagnostic yield for chronic abdominal pain

J. Derova\textsuperscript{1}, A. Derovs\textsuperscript{2}, S. Sitkin\textsuperscript{3}, J. Pokrotnieks\textsuperscript{2}
\textsuperscript{1}Latvian Maritime Medical Centre, Riga, Latvia  
\textsuperscript{2}P. Stradin Clinical University Hospital, St. Petersburg, Russia  
\textsuperscript{3}II Methnikov St. Petersburg State Medical Academy, St. Petersburg, Russia

Introduction: Chronic abdominal pain is one of the controversial indications for video capsule endoscopy (VCE). Latvian experience shows that this indication could help gastroenterologists to put the right diagnosis and start proper treatment in time.

Aim of study: This study was designed to evaluate capsule endoscopy efficiency for revealing the cause of unclear chronic abdominal pain.

Methods: All the patients that undergo capsule endoscopy procedure were either from the P. Stradin Clinical University Hospital or Latvian Maritime Medical Centre and had unclear etiology anemia. All the patients had upper or/and lower endoscopy before VCE, but the reason was still unclear. Radiological methods such as small bowel follow through, CT, MRI also couldn’t put the diagnosis. The capsule endoscopy was performed using three systems: Given Imaging, Olympus Endocapsule, and OMOM Capsule Endoscope system. Specially designed software for each system was used to analyze the cases. 15 VCE with indication chronic abdominal pain of unclear etiology from June 2006 to January 2010 were observed.

Results: Total 15 VCE were performed (7 females and 8 males). Patients age was from 13 to 78 (average 49.27 \pm 16.15). 3 patients were examined using Given Imaging PillCam, 1 – using Olympus Endocapsule and 11 – using OMOM Capsule Endoscope. Capsule endoscopy results are summarized in the table below:

<table>
<thead>
<tr>
<th>Cause revealed</th>
<th>Cause possible</th>
<th>Cause unlikely</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crohn’s disease – 2</td>
<td>erythematous enteropathy – 1</td>
<td>duodenopathy – 2</td>
</tr>
<tr>
<td>Nematodes in small bowel – 1</td>
<td>erosive enteropathy – 3</td>
<td>duodenojejunalopathy – 1</td>
</tr>
<tr>
<td>NSAID enteropathy – 2</td>
<td></td>
<td>multiple nodular mucous uplifts – 1</td>
</tr>
<tr>
<td>terminal ileitis – 1</td>
<td></td>
<td>multiple phlebectasias – 1</td>
</tr>
<tr>
<td></td>
<td>40%</td>
<td>26.67%</td>
</tr>
<tr>
<td></td>
<td>26.67%</td>
<td>33.33%</td>
</tr>
</tbody>
</table>

Discussion/Conclusion: Our preliminary data shows that: 1) capsule endoscopy system is safe and informative procedure for finding the cause of unclear chronic abdominal pain; 2) possible cause of chronic abdominal pain was found in 66.67%, which shows high diagnostic yield of VCE for such indication.
Quality of bowel cleansing level before video capsule endoscopy, using most popular bowel cleansing scheme

A. Derovs¹, J. Derova², S. Sitkin³ J. Pokrotnieks¹
¹Latvian Maritime Medical Centre, Riga, Latvia
²P. Stradin Clinical University Hospital, St. Peterburg, Russia
³II Methnikov St. Petersburg State Medical Academy, St. Petersburg, Russia

Introduction: Although video capsule enteroscopy (VCE) has been shown to be superior to the other techniques for diagnosing small bowel lesions, its diagnostic value can be hampered by the presence of impure intestinal juice or air bubbles, which can influence the diagnosis by causing incomplete visualization of the intestinal mucosa. Unfortunately, no standardized protocol for preparation exists.

Aim of study: This study was designed to evaluate small bowel cleansing efficacy with most popular scheme.

Methods: All the patients that undergo the VCE had strict indications for VCE, such as obscure gastrointestinal bleeding, Crohn’s disease, hereditary polyposis syndromes, small-bowel tumor, celiac disease or unclear pain in stomach. All the patients had upper or/and lower endoscopy before VCE, but the reason was still unclear. VCE were performed using 3 capsule endoscopy technologies (Olympus Endocapsule, Given Imaging PillCam, OMOM Capsule Endoscope). All the patients were prepared for the examination using one of the schemes: 2 l of polyethylene glycol (PEG) prior the examination, 4 l PEG prior the examination or 24 h fasting prior the examination. Main scheme was 2 l of PEG the day prior the VCE. 4 l of PEG was chosen for those patients, who were suspected in delayed small bowel transit time. The scheme of 24 h fasting before the VCE was chosen in cases, when PEG was contraindicated. The effect of small bowel cleansing was evaluated using specially designed scheme: perfect (no air bubbles, no fluids), satisfactory (air bubbles and fluids hamper visualization of mucosa) and poor (because of air bubbles and fluids it was impossible to visualize the mucosa of small bowel). Specially designed questionnaire with 370 parameters (anamnesis, laboratory and other investigation results and VCE data) was filled in for each patient. All the questionnaires were entered into database. Statistical data analysis was performed using SPSS Windows ver. 16.0

Results: Total 165 VCE were performed. 126 patients (77 women and 49 men) were enrolled in the study. Patients' age was 13–79 (mean 44 ± 18). Our main scheme 114 pts. (90.5%) for small bowel cleansing was 2 l of PEG the day before procedure. The regimen with 4 l of PEG was applied for 4 pts. (3.2%). In 7 (5.6%) cases the scheme of 24 h fasting was applied. In 1 (0.8%) case instead of PEG, X-prep was given because of the allergy to PEG. The number of patient with “perfect” bowel cleansing level (BCL) was only in 28 (22.2%) cases. The number of patient with “satisfactory” BCL was in 92 (73%) case, “poor” BCL were 6 (4.8%). Statistical significance of bowel cleansing regimen impact on small bowel purity level was not observed.
Discussion/Conclusion: Sizeable amount of “satisfactory” BCL and relatively small amount of “perfect” BCL using the most popular bowel cleansing scheme in the world indicates existing problems with small bowel cleansing before VCE. New bowel cleansing schemes should be developed for use prior VCE to increase the amount of “perfect” BCL.
High depression and anxiety scores in a systematic review of psychological questionnaires in irritable bowel syndrome

C. Elliott\textsuperscript{1}, M.A. Kamm\textsuperscript{2}, D. Bullas\textsuperscript{3}, S.R. Gurmany\textsuperscript{3}, N. Arebi\textsuperscript{3}

\textsuperscript{1}Physiology, St. Mark’s Hospital, Harrow, London, United Kingdom
\textsuperscript{2}Gastroenterology, St. Vincent’s Hospital, Melbourne, Australia
\textsuperscript{3}Physiology, St. Mark’s Hospital, Harrow, London, United Kingdom

Introduction: Irritable bowel syndrome (IBS) is associated with psychological co-morbidity (PCM). Specific psychological questionnaires (PQ) have been used to define PCM prevalence and applied in therapeutic trials. Numerous questionnaires are available with emphasis on different psychological domains. PCM may indicate the need for psychological therapy.

Methods: Aims: 1) determine the types and frequency of PQ used to record PCM in IBS, 2) compare score differences between IBS and controls. A PubMed literature search (1980–2008) used search terms questionnaire/scores with a list of psychological conditions and IBS. Excluded studies: quality of life PQ, populations with primary psychological or psychiatric disorder, IBS treatment studies. For aim 2 only studies that reported controls scores were assessed. Results are expressed as mean scores and 95% confidence intervals (CI).

From a total 371 studies, 67 studies met the inclusion criteria. Fifty-three studies were analysed. A total of 46 different PQ were identified. The number of studies using each PQ is shown in parenthesis: Scl-90 (14), Hospital Anxiety and Depression Scale (HADS) (10), Eysenck Personality Inventory (EPI) (8), Diagnostic Interview Schedule (DIS- DSM-III-R) (8), Minnesota Multiphasic Personality Inventory (MMPI) (8), Short Form (SF-36) (7), Beck Depression Inventory (BDI) (7), Hamilton Depression Scale (HDS) (6), Spielberger State/trait Anxiety (SSTAI) (5). The PQ in the remaining 36 studies were infrequently used (1–3). Mean score differences between controls and IBS were greatest for depression (7.0) and anxiety (8.3) irrespective of PQ type (table). DIS. Scores for personality traits such as somatisation, obsessive compulsive and paranoid ideation by MMPI and EPI were only marginally greater for IBS than controls.
Discussion/Conclusion: 46 PQ have been used to describe IBS PCM. Control PQ scores are marginally lower than IBS patients for all domains except for depression and anxiety. These indicate that whilst PCM is common, depression and anxiety are the more marked manifestations of IBS. Psychological assessment in clinical practice should focus on eliciting these 2 conditions.

<table>
<thead>
<tr>
<th>Depression and anxiety scores compared to controls</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>mean IBS score (95% CI)</strong></td>
</tr>
<tr>
<td>-----------------------------</td>
</tr>
<tr>
<td>BDI</td>
</tr>
<tr>
<td>HDS</td>
</tr>
<tr>
<td>HADS (depression)</td>
</tr>
<tr>
<td>HADS (anxiety)</td>
</tr>
<tr>
<td>SSSI</td>
</tr>
<tr>
<td>STAI</td>
</tr>
<tr>
<td>SCL-90 Depression</td>
</tr>
<tr>
<td>SCL-90 Anxiety</td>
</tr>
</tbody>
</table>
NKX2-3 rs10883365 is associated with disease susceptibility to both Crohn’s disease and ulcerative colitis while IRGM rs13361189 variant allele increased the risk for Crohn’s disease in Eastern European patients

Peter Fuszekb, Tamas G. Tothb, Nora Meggyesiä, Lajos S. Kissb, Magdalena Koszarskaä, Martin Bortlikç, Dana Duricovaæ, Laszlo Lakatosd, Tamas Molnarä, Martin Leničekf, Libor Vítekf, Istvan Altorjayg, Maria Pappg, Zsolt Tulassayh Pal Mihellerh, Janos Pappö, Attila Tordaiä, Hajnalka Andrikovicsä, Milan Lukasö, Peter Laszlo Lakatosb, for the Hungarian IBD Study Groupä

ãDepartment of Molecular Diagnostics, Hungarian National Blood Transfusion Service, Budapest, Hungary
b1st Department of Medicine, Semmelweis University, Budapest, Hungary
cIBD Clinical and Research Centre, ISCare IVF and 1st Faculty of Medicine, Charles University in Prague, Czech Republic
d1st Department of Medicine, Csolnoky F. County Hospital, Veszprem, Hungary
e1st Department of Medicine, University of Szeged, Szeged, Hungary
fInstitute of Clinical Biochemistry and Laboratory Diagnostics, 1st Faculty of Medicine, Charles University in Prague, Prague, Czech Republic
g2nd Department of Medicine, University of Debrecen, Debrecen, Hungary
h2nd Department of Medicine, Semmelweis University, Budapest, Hungary
Jahn Ferenc Hospital. Budapest, Hungary

& further Hungarian IBD Study Group members are: Semmelweis University, 1st Department of Medicine, Budapest: Simon Fischer, Henrik Csaba Horvath, Barbara Lovasz, Zsuzsanna Vegh; Csolnoky F. County Hospital, 1st Department of Medicine, Veszprem: Zsuzsanna Erdelyi, Gabor Mester, Tunde Pandur; Erzsebet Hospital, 1st Department of Medicine, Budapest: Agota, Kovacs, Laszlo Bene; University of Szeged, 1st Department of Medicine, Szeged: Ferenc Nagy, Klaudia Farkas; University of Debrecen, 2nd Department of Medicine, Debrecen: Karoly Palatka, Zsuzsanna Vitalis; Semmelweis University, 2nd Department of Medicine, Semmelweis University, Budapest: Laszlo Herszenyi

Introduction: Sequence variants in the autophagy gene IRGM and NKX2-3 have been reported to contribute to Crohn’s disease (CD) susceptibility while ECM1 to ulcerative colitis (UC) in genome-wide association scans in North America and Western Europe. The aim of this study was to investigate variants of the above genes and examine genotype-phenotype relationships in an independent Eastern European IBD cohorts.

Methods: 1707 Hungarian and Czech subjects were analysed (CD: 810, age: 37.1 ± 12.6 years, duration: 10.7 ± 8.4 years and UC: 428, age: 43.7 ± 15.0 years, duration: 12.6 ± 9.9 years, and 469 healthy controls). IRGM rs13361189, NKX2-3 rs10883365 and ECM1 rs13294 polymorphisms were tested by LightCycler allele discrimination method. Detailed clinical phenotypes were determined by reviewing the medical charts.
Results: NKX2-3 rs10883365 variant allele was associated with increased risk for both CD (p = 0.009, OR: 1.24, 95% CI: 1.06–1.48) and UC (p = 0.001, OR: 1.36, 95% CI: 1.13–1.63), while variant IRGM allele increased the risk for CD (p = 0.029, OR: 1.36, 95% CI: 1.03–1.79). In contrast, ECM1 rs13294 was not associated with either CD or UC. In CD, presence of the variant IRGM allele was associated with colon only location (in carriers: 25% vs. wild-type: 17.1%, p = 0.02, OR: 1.62, 95% CI: 1.07–2.44). In UC, homozygous carriage of the ECM1 variant allele was associated to cutaneous manifestations (11.5% in homozygotes vs. 3.7% in other patients, p = 0.002, OR: 3.36, 95% CI: 1.48–7.63). In addition, carriage of the variant alleles did not predict use of or resistance to steroids, azathioprine or need for or short term efficacy of infliximab, need for surgery or smoking habits.

Discussion/Conclusions: We confirmed that NKX2-3 and IRGM are susceptibility loci for IBD in Eastern European patients. Further studies are needed to confirm the reported phenotype-genotype associations found in this study.

Key words: CD; UC; NKX2-3; IRGM; ECM1; genetics; phenotype; pharmacogenetics
Increased intestinal permeability to iohexol as a marker of disease activity in patients with inflammatory bowel disease

V. Gerova¹, D. Svinarov², S. Stoynov¹
¹Clinic of Gastroenterology, University Hospital Queen Joanna, Sofia, Bulgaria
²Central Laboratory of Therapeutic Drug Monitoring and Clinical Pharmacology, University Hospital Alexandrovska, Sofia, Bulgaria

**Aim:** To study the intestinal permeability (IP) and its relationship to the disease activity in patients with inflammatory bowel diseases (IBD) – Crohn's disease (CD) and ulcerative colitis (UC).

**Materials and methods:** 58 patients with active IBD (32 with CD and 26 with UC) and 25 healthy controls consented to participate in the study. The clinical activity of CD was estimated using Crohn’s Disease Activity Index (CDAI) and the endoscopic activity of UC using the Mayo scoring system. IP was assessed using of a contrast medium iohexol (omnipaque), which was administrated orally (25 ml, 350 mg/ml) 2 hours after breakfast. Six hours later serum iohexol concentrations (SelOH-6 mg/l) were determined by a validated high-performance liquid chromatography technique.

**Results:** In comparison to the control group, IP (assessed by SelOH-6 mg/l) was significantly higher in patients with CD (2.63 ± 2.18 vs 1.11 ± 1.10 mg/l) and UC (2.49 ± 2.80 vs 1.11 ± 1.10 mg/l), (p < 0.05). Increased IP was established in 50.0% CD pts, in 30.8% UC pts and in 8% controls. A significant positive correlation was found between IP and CDAI (r = 0.74; p < 0.05). In UC group, the patients with severe endoscopic activity showed significantly higher SelOH-6 mg/l than the cases with mild and moderate activity (3.68 ± 3.18 vs 0.92 ± 0.69 mg/l), (p < 0.05)

**Conclusion:** IP is increased in patients with IBD, more often in CD. Serum levels of iohexol appear to be a reliable disease marker as they reflect increased IP, which is related to disease activity.
Proliferating cell nuclear antigen (PCNA) is associated with dysplasia in ulcerative colitis

Katarzyna Guzińska-Ustymowicz, Anna Pryczynicz, Marek Ustymowicz, Marcin Sokolowski, Andrzej Kemona
Department of General Pathomorphology, Medical University of Białystok, Poland

**Introduction:** The probability of developing cancer in ulcerative colitis is 5-fold greater than in the general population. Detected numerous groups of dysplasia may prevent the development of cancer by execution a total colectomy.

**Methods:** The study included a group of 19 patients with ulcerative colitis, who was classified histologically as: positive for dysplasia (10 patients) and negative for dysplasia (9 patients). The expression of PCNA protein was assessed by means for immunohistochemical method using monoclonal anti-PCNA antibody (clone PC10, Dako). PCNA expression was determined using the semiquantitative method and assessed as weak (lack of reaction or reaction present in < 40% cells) and strong (reaction visible in ≥ 40% cells).

**Results:** Protein expression in cells that do not show dysplasia in ulcerative colitis was strong in 1/19 (5.3%) patients and weak in 18/19 (94.7%) patients. By contrast, in dysplastic cells in ulcerative colitis PCNA protein expression was strong in 8/10 (80%) patients, and weak in 2/10 patients (20%). Overall assessment of PCNA expression in both the non dysplastic and dysplastic cells in ulcerative colitis shows that a strong expression of PCNA protein correlate to the presence of dysplasia (p = 0.001).

**Conclusion:** PCNA expression is associated in formation of dysplastic changes in ulcerative colitis. Increased proliferation of dysplastic cells may predispose to the occurrence of mutations and increase the risk of cancer.
The natural history of adult Crohn's disease in China

Jing Hu, Qiao Mei, Jianming Xu
Department of Gastroenterology, the First Affiliated Hospital, Anhui Medical University, Hefei 230031, China

Introduction: Crohn's disease is a chronic inflammatory granulomatous process that usually involves different sites in the intestinal tract. Long-term studies on the natural history have been described in many countries. However, the natural history of Crohn's disease in China and risk factors necessitating surgery have not been thoroughly described.

Methods: From 2000 to 2005, we identified 104 Crohn's disease patients in Anhui province, with a follow-up time $\geq$ 4 years.

Results: The most frequent disease location at diagnosis was the terminal ileum (59%). In our follow-up, 41% patients have disease extension. Complicated behavior was observed in 31% of patients at diagnosis and 49% at follow-up. Cumulative incidence of surgery were 15% at 3 years and 34% at 5 years from diagnosis. Azathioprine was introduced earlier in the course of disease in patients not undergoing surgery than in patients requiring surgery.

Discussion/Conclusion: Crohn's disease was characterized by frequent occurrence with time, of a severe phenotype with extensive, complicated disease. Immunosuppressive therapy may improve the natural history of this disease and decrease the need for performing surgery.
Study on the correlation of colonic pathologic changes due to ulcerative colitis and tongue proper, tongue four and pulse condition

Professor Jie Han
Henan College of TCM Zhengzhou, Henan 450000, China

Introduction: The objective of the study was to explore the correlations of colonic local lesions due to ulcerative colitis (UC) and tongue proper, tongue four and pulse conditions. According to the analysis of symptoms and signs based on the theories of TCM.

Methods: 120 cases with UC were clarified and divided into three groups of different types: the damp-heat due to hypofunction of spleen (40 cases, group A), deficiency of both spleen and kidney (40 cases, group B), and intestinal damp-heat (40 cases, group C). The colonoscopic findings and the tongue pulse findings of the 3 groups were compared and analyzed and their correlations were studied.

Results: The tongue pulse expressions of the patients with UC are actually the general reaction of colonic local pathologic changes.

Discussion/Conclusion: It is concluded that better diagnosis and treatment may be achieved just on the basis of the analysis of both colonoscopic findings and the tongue pulse findings.
The estimation of late rectal mucosal damage after conformal radiotherapy for prostate carcinoma

Piotr Kędzierawski, Tomasz Wollny, Andrzej Salata
Regional Cancer Center, Kielce, Poland

Introduction: Radiotherapy is a commonly used method in therapy of patients with localized prostate cancer. The aim of the study was the estimation of the late rectal mucosal damage in patients after radical conformal radiotherapy because of localized prostate cancer performed by flexible rectosigmoidoscopy.

Methods: Flexible rectosigmoidoscopy was performed on 36 patients. Patients were treated between 2000 and 2003. The median follow up was 88 months after 3-D planned conformal radiotherapy of prostate cancer. The dose received was 68–70 Gy conventionally fractionated. Rectal mucosa was estimated according to the own scale: grade 0 – none, grade I – not bleeding angiectasia, grade II – bleeding angiectasia, grade III – ulceration, grade IV – necrosis and A – abnormalities on anterior rectal wall, B – abnormalities less than 50% of rectal circumference and on the anterior rectal wall, C – abnormalities more than 50% of rectal circumference and on the anterior rectal wall.

Results: Total dose of radiotherapy was effective and all examined patients were alive with normal level of PSA. In 8 patients (22%) there were no observed changes on rectal mucosa. Twenty four patients (66%) had grade I rectal damage (21/24 grade IA and 3/24-grade IC). Grade II was found in 4 (11%) patients. There were not observed grades III and IV.

Discussion/Conclusion: Rectosigmoidoscopy offers the possibility of detecting signs of tissue dysfunction below the level of subjective symptoms. Conformal radiotherapy used for patients with localized prostate cancer was safe and effective; all examined patients are alive with normal level of PSA. There were no serious late damages of rectal mucosa.
The clinical and molecular features of ulcerative colitis related colon cancer

Jingnan Li, Weiyang Zheng Jiaming Qian
Peking Union Medical College Hospital, Beijing 100730, China

Introduction: Long-standing ulcerative colitis (UC) has been associated with a high risk of developing colorectal cancer (CRC). The clinical features and the carcinogenesis pathways in UC associated CRC are thought to be different from sporadic CRC. The aims of this study were to analyze the clinical features and determine the differences in expression of oncogenic proteins in UC-related colon cancer

Methods: The clinical features, pathology, treatment, and prognosis were summarized in 6 cases of UC-associated CRC in Peking Union Medical College Hospital from 1984–2008. 34 cases of UC were studied in which there were 16 colectomy specimens and 18 colon endoscopy biopsy specimens, and they were divided into 3 groups by the duration of colitis (0–8 years: 15 cases, 9–15 years: 14 cases, > 16 years: 5 cases). 15 non-UC colectomy specimens with tubulovillous adenoma and 12 colectomy specimens with sporadic CRC were also studied, 6 normal colon mucosa specimens obtained by endoscopic biopsy as a control. The protein expression of APC, β-catenin, P53 and Wnt-1 were detected by immunohistochemistry. K-ras mutation was detected by microdissection and PCR-sequencing. This study was approved by the local institutional review board and all patients provided signed informed consent.

Results: CRC developed in 1.1% of UC patients. Females were more commonly affected than male patients, and the age of diagnosis was younger than in sporadic CRC. 83.3% (5/6) UC-related CRC suffered UC with long duration and extensive colitis. Carcinoma occurred in the rectum in 66.7% of cases (4/6). The pathology always was adenocarcinoma. The prognosis was poor. The proteins APC, β-catenin, P53 and Wnt-1 were overexpressed in UC-related cancer, colon cancer and adenoma. The expression level of APC, β-catenin and Wnt-1 in the UC-related cancer was higher compared to their level in colon cancer and tubulovillous adenoma. But the expression of the p53 decreased in UC. The data also indicated that the protein levels of APC, β-catenin and Wnt-1 were increased with increasing duration of colitis. The rate of K-ras mutation in UC-associated CRC was significant lower than sporadic CRC (16.7% 1/6 vs. 58.3% 7/12)

Discussion/Conclusion: The UC-associated CRC was less happened in UC patients, and the long duration and extent of colitis were the main clinical features. The proteins APC, β-catenin, P53 and Wnt-1 are overexpressed in UC, and the risk is elevated depending upon the duration of the colitis. It also suggests that the molecular mechanism of the neoplastic transformation in UC maybe involved Wnt signal pathway, and β-catenin plays more important role than p53 but Kras mutations are uncommon.
Prevention of colonic fibrosis by taurine in rats with colitis induced by 2,4,6-trinitrobenzene sulphonnic acid

Lin lin, Cheng jiafei, Ning Yueji, Zhang Wei, Zhang Hongjie
Department of Gastroenterology, the First Affiliated Hospital of Nanjing Medical University, Nanjing 210029, P. R. China

Background/Aim: Over one-third of patients with Crohn’s disease would develop intestinal stricture, however, no effective preventive measures or medical therapies are available. Taurine has an antifibrotic effect on a number of organs, but its role in colonic fibrosis remains uncertain. The aim of this study was to investigate the effect of taurine on colonic fibrosis in rats with colitis induced by 2,4,6-trinitrobenzene sulphonnic acid (TNBS) and its mechanism.

Methods: Thirty-two SD rats were randomly divided into normal control group, model group, and low-dose and high-dose taurine groups (400 mg/kg and 800 mg/kg taurine, respectively). Rats in normal control group were administrated with 0.9% NaCl solution enema, and rat colitis model was induced by TNBS enema in the latter three groups. Morphology and disease activity index (DAI) was evaluated, colitis scores of macroscopic and histologic was performed, and colon length and weight were also measured. Levels of hydroxyproline, collagen type I, transforming growth factor-beta1 (TGF-β1), and Smad3 protein and mRNA in colon tissues were examined.

Results: Compared with control group, colon length of model group decreased and colon weight increased obviously ($P < 0.01$); DAI, macroscopic score and histologic score raised significantly ($P < 0.01$); markedly high levels of hydroxyproline, collagen type I, TGF-β1 and Smad3 were discovered ($P < 0.01$). Intervention with taurine ameliorated the above indexes remarkably, especially with high-dose taurine. In this group, colon length increased and colon weight decreased ($P < 0.01$); DAI, macroscopic and histologic scores reduced ($P < 0.05$, $P < 0.01$, $P < 0.01$, respectively); a low level of hydroxyproline contents was observed ($P < 0.05$) in colon tissues, with an evident decrease in expression of collagen type I, TGF-β1 and Smad3 ($P < 0.01$).

Conclusions: Taurine is effective in prevention of colon fibrosis induced by TNBS in rats, whose antifibrotic mechanism seems to be mediated by the down regulation of TGF-β1 and the inhibition of TGF-β/Smad3 pathway. These findings may give a window into the intervention of Crohn’s disease with colon fibrosis.
The clinical value of miniature ultrasonic probes on diagnosis and treatment of digestive tract diseases

Penfei Liu
Jiangyin People’s Hospital of Jiangsu Province, China

Objective: To investigate the clinical value of miniature ultrasonic probes (MUP) in the diagnosis and treatment of digestive tract diseases.

Methods: 537 patients who were indicated for endoscopic ultrasonography (EUS) underwent EUS with 7.5–20 MHz MUP and double-cavity electronic endoscope. According to the diagnoses of MUP, those patients who presented the indication of treatment were treated by endoscopic resection or surgical excision respectively. The postoperative histological results were compared with the preoperative diagnoses of MUP. A follow-up with MUP was periodically made for a few patients without endoscopic resection or surgical excision.

Results: Among the 537 patients the diagnosis of gastrointestinal submucosal lesions was made in the 256 cases, polyp in 56 cases, inflammatory prominence in 37 cases, extrinsic compression 53 cases, digestive tract cancer 50 cases, peptic ulcer 17 cases, cholecystolithiasis 11 cases, chronic pancreatitis in 8 cases, and achalasia 2 cases and 47 cases were diagnosed as normal. After examination of MUP, 220 patients were treated by endoscopic resection or surgical excision respectively. The postoperative histological results of 211 patients were completely consistent with the preoperative diagnosis of MUP, and diagnostic accuracy of MUP was 95.9%. The result of follow-up with MUP indicated that gastrointestinal leiomyoma, lipoma, phlebangioma and cyst were unchanged within 1–2 years. The patients who were treated by endoscopic resection or centesis showed no complication.

Conclusion: EUS with MUP is a valuable method in diagnosis of gastrointestinal submucosal lesions, staging of digestive tract cancer and diagnosis of biliary-pancreatic diseases. It plays a very important role for making scientific, effective, safe and economic therapeutic plan.
The study of intestinal mucosal permeability of ulcerative colitis patients

Liu Xiaochang, Mei Qiao, Xu Jianming, Jin Juan, Xia Quan, Xu Dujuan, Hu Jing
The First Affiliated Hospital, The Key Laboratory of Digestive Diseases of Anhui Province, Hefei 230032, China

Introduction: To estimate the change of intestinal mucosal permeability of UC patients by HPLC (high-performance liquid chromatography)-RI method and investigate the sensitivity of intestinal mucosal permeability to reflect the disease activity of UC patients.

Methods: Detected the lactulose and mannitol in urine of 15 UC patients and 15 healthy people after they took orally the lactulose and mannitol test solution by HPLC-RI method and calculated the ratio of them. Compared the change of intestinal mucosal permeability and analysed the sensitivity of the lactulose/mannitol ratio, ESR and CRP reflecting the disease activity of UC patients.

Results: The lactulose/mannitol ratio in 15 UC patients was 0.494 ± 0.190, it was significantly higher than that in 15 healthy people (0.039 ± 0.014, P < 0.05). The result indicated that the intestinal mucosal permeability of UC patients was significantly higher than that of the healthy people. There was a strong correlation between the intestinal mucosal permeability and Sutherland DAI of UC patients. The ESR, CRP were normal in UC patients with the lesion in the left side colon, while ESR, CRP were increased in UC patients with the lesion in the whole colon (P < 0.05).

Conclusion: The intestinal mucosal permeability of UC patients increased significantly than that of healthy people. The intestinal mucosal permeability could reflect the disease activity of UC patients and the sensitivity was higher than that of ESR and CRP.
Effects of military training on food intake-related changes of automatic nervous system in new college students

Xin Liu, Zhixin Li, Qian Zhang, Cuizhen Zhang, Jihong Chen, MD PhD
Division of Gastroenterology, Renmin Hospital of Wuhan University, Wuhan 430060, P. R. China

Introduction: The aim of this study was to investigate the effects of military training on food intake-related changes of automatic nervous system in new college students.

Methods: Twenty healthy new college students who had a four weeks’ military training were enrolled in this study, 8 hours training everyday. HRV were measured by using the GE SEER MC electrographic recording Holter at 3 time points: before the training, the end of the second week and the end of the fourth week, preprandially and postprandially. Frequency domain indices were analyzed including very low frequency (0.003–0.04 Hz), low frequency (0.04–0.15 Hz), high frequency (0.15–0.4 Hz) and the LF/HF ratio.

Results: 1) After the military training, the preprandial VLF, LF and HF indices were decreased compared with that before training; LF/HF ratio had no change (figure 1); 2) During the training, no differences of VLF, LF and HF were found between preprandial and postprandial, LF/HF didn’t show any changes (figure 2).

Discussion/Conclusion: The military training has an effect on the indices which reflect vagal and sympathetic activity, but it doesn’t change the vagal-sympathetic balance.
Foxp3⁺ IL-17⁺ T cells in inflammatory intestinal mucosa show inflammatory features

Zhanju Liu¹, Jingling Su¹, Xingpeng Wang¹, Ping-Chang Yang²
¹Department of Gastroenterology, the Shanghai Tenth People’s Hospital, Tongji University, Shanghai, China
²Department of Pathology and Molecular Medicine, McMaster University, Hamilton, ON, Canada

**Background:** Published data indicate the enhancement of numbers of Foxp3⁺ CD4⁺ CD25⁺ T cells, IL-17⁺ cells and immune inflammation can co-exist in the intestine, such as in inflammatory bowel disease (IBD) intestinal mucosa. Whether these cells play a role in the pathogenesis of IBD is unknown. This study aimed to characterize the IL-17⁺ Foxp3⁺ T cells in the intestinal mucosa with immune inflammation.

**Method:** Colonic biopsies were collected from 59 IBD patients and examined by immunohistochemistry. An IBD mouse model was developed to examine the induction of IL-17⁺ Foxp3⁺ cells in the intestinal mucosa.

**Results:** IL-17⁺ Foxp3⁺ cells were abundantly localized in colonic mucosa of IBD biopsies, but were seldom seen in normal controls. The results indicate that the number of Foxp3⁺ T cell does increase in IBD intestinal mucosa, but most of them (close 90%) are also IL-17-positive. In trinitrobenzene sulfonic acid (TNBS)-induced colitis, the number of Foxp3⁺ IL-17⁺ T cells in colonic mucosa was significantly more than that in naïve mice. Exposure to microbial product-primed DC facilitated the expression of IL-17 in Foxp3⁺ T cells, in which DC-derived IL-6 played a critical role. The Foxp3⁺ IL-17⁺ T cells do not suppress antigen-specific CD4⁺ T cell activities. The microbial antigen-specific Foxp3⁺ IL-17⁺ T cells released proinflammatory cytokines TNF-α and IL-17 upon exposure to the specific microbial antigen. Passive transfer with Foxp3⁺ IL-17⁺ T cells resulted in IBD-like colitis in recipient mice.

**Conclusions:** CD4⁺ Foxp3⁺ IL-17⁺ T cells in colonic mucosa with immune inflammation have inflammatory features and are capable of initiating immune inflammation in the intestine.

Key words: intestine; inflammatory bowel disease; dendritic cell; lymphocyte; flagellin

Supported by the Natural Science Foundation of China (#30971358)
Downregulation of survivin by RNAi inhibits the growth of human gastric carcinoma cells SGC7901

LU Qi-ming¹, MIAO Guo-ying²
¹Department of Digestion, Gansu Province People Hospital, Gansu, Lanzhou 730000, P. R. China
²Clinical School of Lanzhou University, Gansu, Lanzhou 730000, P. R. China

Objective: To investigate the inhibitory effect of small interfering RNA on the expression of survivin and cell growth in human gastric carcinoma cell line SGC-7901.

Methods: Small interfering RNA was transfected into SGC-7901 cells to knockdown survivin expression. mRNA and protein levels of survivin were detected by reverse transcription-polymerase chain reaction (RT-PCR) and Western blot. Cell growth inhibition was determined by methyl thiazolyl tetrazolium (MTT) assay. The effect of survivin siRNA on cell cycle distribution and cell apoptosis was assayed by flow cytometry (FCM).

Results: RNA interference could efficiently and stably suppress survivin expression in SGC-7901 cells. Downregulation of survivin resulted in significantly inhibition of tumor cells growth in vitro. At 24 h, 48 h, 72 h after the transfection growth inhibitory rates were significantly higher in specific survivin siRNA group than control. The apoptosis rate was 3.56% after treatment of specific survivin siRNA, and G0/G1 phase arrest was shown.

Conclusion: Downregulation of survivin resulted in significantly inhibition of tumor growth in vitro. Inhibiting the expression of survivin can induce apoptosis of SGC-7901 cells the use of survivin specific siRNA deserves further investigation as a novel approach to cancer therapy.

Key words: gastric carcinoma; surviving; RNA interference; apoptosis; gene expression
Practices of using methotrexate as monotherapy and in combination with azathioprine in patients with ulcerative colitis

P. Makarchuk
State Scientific Center for Coloproctology, Moscow, Russia

For the period from 2002 to 2008 in the State Scientific Center for Coloproctology (Moscow) 74 patients with ulcerative colitis were treated with methotrexate, and for 14 patients the treatment combined methotrexate and azathioprine. All of them suffered from total lesion of the large intestine and severe form of hormone resistant ulcerative colitis, in 60 of the patients – it was a chronic, recurrent form. The average age of the patients was 32.4 ± 3.6 years old. The duration of the disease was from 8 months up to 5 years.

All patients were also undergoing hormone therapy with prednisolone in doses of 2 mg/kg of the body mass. Methotrexate was prescribed in doses of 25 mg per week, azathioprine – 2.5 mg/kg of the body mass. The duration of the methotrexate therapy was one year. In cases of combined therapy patients were treated with methotrexate and azathioprine for one year and then received a monotherapy with azathioprine for up to two years.

The effectiveness of the treatment was estimated on the basis of the clinical endoscopic data. The control colonoscopy was made within 3–6 months after the initiation of the treatment. The condition of the remission was considered as the absence of blood in the patients’ stool, stool frequency of up to 3 times during the day and absence of inflammatory changes in the large intestine mucose membrane as per the endoscopic data.

Out of 74 patients that received methotrexate 61 (82.4%) overcame the hormone resistance, and it was managed to achieve remission. 13 patients (11.6%) due to ineffectiveness of the therapy were operated on after the second week of treatment with methotrexate.

Out of 61 patients that achieved remission, 25 (40.9%) had the remission period of more than 1 year. The rest 36 (59.1%) had the acute condition of the ulcerative colitis within 5–8 months after the beginning of the treatment. By that time all patients were treated only with methotrexate (prednisolone was excluded). It was possible to stop the development of the acute condition in 21 (58.3%) patients with additional therapy of 5-ASA preparation, in 13 patients (36.1%) with the resumption of the hormone therapy and 2 (5.6%) patients underwent surgery due to the inefficiency of the therapy.

The clinical response appeared at the second week from the start of the therapy and was proclaimed in reduction of the frequency of the stool. No patients had the reduction of leukocytes, thrombocytes and erythrocytes. It is worth mentioning that 6 patients showed irrelevant raise of the transaminase levels (ALT, AST) up to 50 u/1 in the forth month of the therapy.
Out of 14 patients that received combined therapy of methotrexate and azathioprine, 12 (85.7%) managed to achieve remission that lasted for more than 1 year. Two (14.3%) patients were operated on due to ineffectiveness of treatment.

Two patients out of this group at the process of the treatment had leucopenia, after 2 months of therapy – leukocytes levels dropped to $1.9 \times 10^9/l$. For these patients the doses of methotrexate were reduced to 12.5 mg per week. The control blood tests in a month’s time showed that the leukocytes levels were normal.

During the combined treatment with methotrexate and azathioprine, in two months time the pancytopenia was revealed in one patient: leukocytes – $1.2 \times 10^9/l$, thrombocytes – $90 \times 10^9/l$, erythrocytes – $1.6 \times 10^9/l$. The therapy was stopped for one month and then resumed with less doses of methotrexate of 12.5 mg per week, which was done after the normalization of the laboratory tests data.

Thereby, the use of methotrexate in combination with azathioprine can overcome hormone resistance and induce remission in ulcerative colitis patients. The effectiveness of methotrexate therapy is comparable with combined therapy (methotrexate and azathioprine) and is 82.4% and 85.7% correspondingly.

However, the ulcerative colitis recurrence during the year when treated only with methotrexate as compared to the combined therapy (methotrexate and azathioprine) constitutes 60% of patients. At the same time the cytostatic effect at combined therapy is shown in 14.3% patients.
Improved quality-of-life in Crohn’s disease after the intake of a probiotic

P. Nikolov, D. Panova
St. Ivan Rilsky University Hospital, Clinic of Gastroenterology, Sofia, Bulgaria

Introduction: The general well-being in patients with inflammatory bowel disease (IBD) can be seriously impaired depending on disease course and therapy. It can be easily evaluated with the validated quality-of-life questionnaire (IBDQ) of McMaster University. The aim of this study was to evaluate the changes in IBDQ before and after the intake of a probiotic.

Methods: 30 patients with IBD (8 men, 22 women, mean age 41.6 ± 14, 22–69 years) – 15 with Crohn’s disease (CD) and 15 with ulcerative colitis (UC) received probiotic (Lactobacillus bulgaricus ATCC 21815) for 28 days. The quality-of-life was evaluated by IBDQ on day 0 and day 28.

Results: Before the probiotic intake the total IBDQ (tIBDQ) score and the emotional health subscore (EH) were significantly lower in CD than in UC: 155 ± 38.6 vs. 183.4 ± 30.8 (p = 0.035) and 4.6 ± 1.2 vs. 5.6 ± 1, respectively. After 28 days of probiotic intake in CD patients there was a significant increase in tIBDQ from 155 ± 38.6 to 168.3 ± 33.3 (p = 0.016), EH from 4.6 ± 1.2 to 5 ± 1.2 (p = 0.031) and systemic symptoms subscore from 4.6 ± 1.2 to 5 ± 1 (p = 0.038). No significant changes were observed in the bowel symptoms and social functions subscores. UC patients showed a mild increase in tIBDQ from 183.4 ± 30.8 to 189.3 ± 22.8 and all subscores but the changes were not statistically significant (p > 0.05). After the probiotic intake there is no difference between CD and UC in tIBDQ and all subscores (p > 0.05).

Discussion/Conclusion: There was an improved quality of life in patients with CD but not in UC after the intake of a probiotic. Larger randomized controlled trials are needed to elucidate the effects of probiotics in IBD.
Alterations of CRP in patients with inflammatory bowel disease after the intake of a probiotic

P. Nikolov
St. Ivan Rilsky University Hospital, Clinic of Gastroenterology, Sofia, Bulgaria

Introduction: C-reactive protein (CRP) is a potent predictive factor and marker of inflammation in inflammatory bowel disease. Patients with Crohn’s disease (CD) have a stronger CRP response than the ones with ulcerative colitis (UC). In CD the disease phenotype has no influence on CRP levels. CRP rates in UC at diagnosis are related to the extent of the disease. The aim of our study was to monitor the changes of serum CRP in CD and UC patients before and after the intake of a probiotic.

Methods: 30 patients with IBD (8 men, 22 women, mean age 41.6 ± 14, 22–69 years) – 15 with Crohn’s disease (CD) and 15 with ulcerative colitis (UC) received probiotic (Lactobacillus bulgaricus ATCC 21815) for 28 days. The serum CRP was investigated on day 0 and day 28.

Results: Before the probiotic intake the mean CRP levels in serum of CD and UC were almost equal: 5.8 ± 13.6 vs. 5.6 ± 11.4 mg/l respectively (p > 0.05). After 28 days of probiotic intake there was a mild elevation of mean CRP from 5.8 +/- 13.6 to 10.2 ± 22.4 mg/l but it is not significant (p = 0.074). In UC there was a mild decrease in CRP from 5.6 ± 11.4 to 3.2 ± 3.2 mg/l but it was not significant (p = 0.326). After the probiotic intake there in no statistical difference between mean CRP in CD and UC (p > 0.05).

Discussion/Conclusion: There was a mild elevation of mean CRP in CD but a decrease in UC after the intake of a probiotic. It’s a matter of debate whether these changes are only fluctuations or a result of the probiotic bacteria. Larger randomized controlled trials are needed to elucidate the effects of probiotics on intestinal inflammation and CRP in IBD.
Diagnostic criteria of IBD

Qin Ouyang, L.-Y. Xue
Department of Gastroenterology, West China Hospital, Sichuan University Chengdu, China

With a significant increase in the incidence and prevalence of inflammatory bowel disease (IBD), the diagnosis of both ulcerative colitis (UC) and Crohn's disease (CD) become much more complex, which has attracted GI clinician's close attention. A correct diagnosis of the disease is not only the primary request for clinical management, but also the prerequisite for all clinical research. I will discuss clinical characteristics, diagnostic difficulties, and diagnostic criteria of IBD management consensus from Western and from our country. Finally, to further discuss the criteria required to apply the suggested diagnosis of IBD used in our hospital.

Compared to the West, in China, IBD are mild to moderate cases with different distribution and extent of disease. A number of diseases mimic clinical presentation of IBD which makes the differentiation difficult, such as infectious colitis and intestinal tuberculosis are more prevalent in this area. Both medical staff and patients lacking experience in IBD will increase the difficulty of the diagnosis. A correct diagnosis of IBD needs the cooperative work from clinicians, endoscopist, radiologist and pathologist. Clinicians should communicate with endoscopist, radiologist and pathologist closely for improvement of diagnostic ability. As the diagnosis of IBD is basically exclusive and histological decisive, most of the diagnosis could not be confirmed. In the suggested diagnosis group, careful analyze the items is crucial for the degree of confirmation. Follow-up study could make more definite diagnosis of IBD, especially for highly suggested diagnosis cases.

Following diagnostic criteria of IBD is important for uniform clinical description, epidemiological investigation and cooperative clinical trials etc. The currently used diagnostic criteria need to be further elaborated with meticulous description for better usage. The investigation on diagnostic markers from serum, feces and tissue will be helpful for better diagnostic practice. Turning back to practice, their cumulative nature in the diagnosis of IBD should be appreciated.
The role of complementary alternative medicine in inflammatory bowel disease – Focus on Traditional Chinese Medicine in UC

Yan Pan, Qin Ouyang, Xi Chen, Chunyan Ye
Department of Gastroenterology, West China Hospital, Sichuan University, Chengdu 610041, China

The conventional therapy for inflammatory bowel disease (IBD) is 5-aminosalicylic acid (5-ASA), glucocorticosteroids (GCS) and immunosuppressors (IS). Recently, biological agents have achieved great success with good prognosis, but totally unsatisfactory especially of the side effects, costly and long-term medication that limit the acceptability by the patients. Therefore many of our patients choose complementary alternative medicine (CAM) instead. The early reports from literatures were 4–13% of CAM users on IBD, but recently increased to 34–47%. In a national survey from Germany, 50% of IBD patients had experiences with CAM reflecting a chronic, costly, refractory and complicated nature of this disease.

As defined by the National Center for Complementary and Alternative Medicine (NCCAM), USA, the term “alternative” implies that these interventions are substituted for allopathic or Western medicine. “Complementary” suggests that these practices complement or are combined with conventional healthcare. According to the NCCAM, CAM is classified into five categories. Traditional Chinese Medicine (TCM) was classified into Alternative Medical Systems as major component of CAM. Hereby an analysis of Traditional Chinese Medicine in the Treatment of Ulcerative Colitis from Chinese Literatures is presented.

The objective of our study was to investigate current status of ulcerative colitis (UC) treatment from Chinese literatures during 1989 to 2003 and to evaluate the role of traditional Chinese medicinal (TCM) and Western medicines (WM) with principles of evidence-based medicine (EBM). Most clinical trials were TCM and combination of TCM and WM (70.1%) only a few were WM only. Although therapeutic effects were extremely good from the literature the most of them had rather low reasoning intensity and a lot of them were descriptive studies. TCM plays an important role in inducing and maintaining remission of UC as a CAM with satisfactory effects, at least from patient viewpoint found in the Chinese literature, but safety data and mechanism of the role will need to be investigated thoroughly with modern pharmaceutical methodology.

The results of a recent clinical trial and animal experience with BA WEI XI LEI SAN will also be reported.
Capsule enteroscopy small bowel transit time doesn't correlate with vital signs

J. Pokrotnieks¹, J. Derova², S. Sitkin³, A. Derovs¹
¹P. Stradin Clinical University Hospital, Riga, Latvia
²Latvian Maritime Medical Centre, Riga, Latvia
³II Methnikov St. Petersburg State Medical Academy, St. Petersburg, Russia

Introduction: The impact of small bowel transit time (SBTT) on diagnostic yield during capsule endoscopy (VCE) is very significant. Delayed small bowel transit time because of the dysmotility can considerably affect the rate at which the capsule moves from stomach to caecum.

Aim of study: This study was designed to evaluate possible correlations between patient vital signs (height, weight, waist perimeter, body mass index (BMI)) and capsule small bowel transit time.

Methods: All the patients had strict indications for capsule endoscopy. Upper or/and lower endoscopy and radiological investigations (SBFT, CT angiography, MRI) were performed before VCE. Body mass index were calculated using the standard formula (body mass index is defined as the individual's body weight divided by the square of his/her height). Database and statistic calculations were performed using SPSS ver. 16. Kendall’s τb coefficient was used to calculate statistical significance.

Results: In total from database of 165 patients, 126 cases were analyzed. From them 77 (61.1%) were females and 49 (38.9%) males. Patients’ age were from 13 to 79 (mean 42 ± 18). Patients’ heights were from 150 to 189 cm (mean 167 ± 8). Patients’ weights were from 28 to 113 kg (mean 65 ± 17.8). Patients’ waist perimeters were from 52 to 120 cm (mean 88.5 ± 15.1). Patients’ BMI were from 12.44 ± 39.06. Capsule working time were from 377 to 631 (mean 494 ± 38.7%). Stomach transit time were from 2 to 441 (mean 33 ± 54). Small bowel transit time was from 39 to 502 min. (mean 284.66 ± 95.49). In 24 cases capsule did not reach colon. Neither a partial correlation with control parameters like age or sex nor a bivariate correlation has been found.

Discussion/Conclusion: From our trial, we can conclude that small bowel transit time does not depend from height, weight, waist perimeter and BMI.
Comparative studies on the PCNA expression in inflammatory bowel diseases and colorectal cancer

Anna Pryczynicz, Katarzyna Guzińska-Ustymowicz, Marek Ustymowicz, Marcin Sokolowski, Andrzej Kemona
Department of General Pathomorphology, Medical University of Białystok, Poland

Introduction: The proliferating cell nuclear antigen (PCNA) is a protein also known as cyclin. PCNA is a polymerase-associated protein and is synthesized in early G1 and S phases of the cell cycle. But PCNA protein has a lower specificity in determining cell proliferation because it also participates in the repair of DNA. The aim of this study was to observation of PCNA expression changes in Crohn’s disease, ulcerative colitis and colorectal adenocarcinoma.

Methods: PCNA protein expression was analyzed immunohistochemically using monoclonal antibody anti-PCNA (clone PC10, Dako). Expression of PCNA protein in ≥ 40% of the cells was classified as positive.

Results: Positive expression of PCNA protein was present in 5/10 (50%) cases of Crohn's disease, in 15/19 (78.9%) cases of ulcerative colitis and in 33/55 (60%) with colorectal adenocarcinoma.

Conclusion: Increased PCNA expression in ulcerative colitis can lead to malignant transformation as a result of the abnormal cell division. These studies confirm that patients with Crohn's disease have a less risk of colorectal cancer that that of patients with ulcerative colitis.
Results of surgery in carcinoma rectum with sphincter preservation

Manish Sahni, MBBS, DNB (Surgery final yr); Satish Jain, MS, FICS, FAIS, M-ASCO (USA); Kuljinder S. Sodhi, MS, DNB, MCh (Surgical Oncology)
Mohan Dai Oswal Cancer Hospital, ludhiana, India

Introduction: Sphincter preservation following anterior resection with TME has been the standard treatment for selected cases of cancer rectum. We conducted a prospective study for Ca rectum patients in which anterior resection was carried out.

Methods: 35 patients (histologically proven) cases of carcinoma rectum are included in this study operated between January 2005 to January 2009 for anterior resection and follow-up was done till Jan 2010.

Results: This study revealed a male predominance with bleeding per rectum the most common presentation (71%). 65% patients had undergone circular stapled anastomosis and 35% patients with hand-sewn anastomosis. Dukes B and Dukes C each being (44%) is the histopathological staging. Postoperative complications being wound infection (11%), anastomotic leak (14%), rectal stenosis (11% – all in patients with stapled anastomosis). Postoperative mortality being (8%) due to sepsis. The local recurrence rate was 11%

Discussion/Conclusion: Colorectal cancer is the most common cancer of GIT. CT scan abdomen remains the investigation of choice for its staging and treatment. Anterior resection is associated with the risk of anastomotic leak. Patients undergoing circular stapled anastomosis have slight more chances of postoperative rectal stenosis as compared to hand-sewn anastomosis. Adjuvant treatment with radiotherapy and chemotherapy have definite role in Dukes B and Dukes C patients.
Delayed gastric emptying in Indonesian population with reflux esophagitis

David Samosir*, L.A. Lesmana†, Murdani Abdullah†
*Estomihi Hospital, Medan, Indonesia, †Faculty of Medicine, University of Indonesia

Introduction: Numerous studies have demonstrated inconsistent results on the role of gastric emptying in reflux esophagitis due to their various study methods. In Indonesian population, evaluation of gastric emptying by standard scintigraphic method in patients with gastroesophageal reflux disease (GERD) has never been performed. The aim of our study was to observe the delayed gastric emptying in patients with reflux esophagitis as well as to recognize the proportion of GERD patients who have delayed gastric emptying in Indonesian population by using standard scintigraphic method.

Methods: Patients with heartburn and/or regurgitation in the last six-month period were included in the study. After endoscopic examination of upper gastrointestinal tract, scintigraphic examination was performed in appropriate to Consensus Recommendation for Gastric Emptying Scintigraphy with standard 99Tc-labeled egg-white meal of 255 kcal. Delayed gastric emptying (gastric retention) was defined to be > 90% at 1 hour, > 60% at 2 hours and > 10% at 4 hours.

Results: Twenty-three patients with reflux esophagitis were compared to 23 subjects with non-erosive reflux disease (NERD). Subjects with reflux esophagitis demonstrated slower gastric emptying compared to subjects with NERD at 1 hour (p < 0.05), 2 hours (p < 0.05) and 4 hours (p < 0.05). Gastric retention > 10% at 4 hours was found in 6% patients with GERD (2 patients with reflux esophagitis and 1 patient with NERD).

Discussion/Conclusion: Although the number of patients who had delayed gastric emptying in our study is relatively lesser than data from Western countries, but by using standard technique, we found that the gastric emptying in patients with reflux esophagitis is significantly slower than patients with NERD.
Crohn’s disease in the Endoscopic Unit, Division of Gastroenterology, Department of Internal Medicine, Cipto Mangunkusumo General Hospital, Jakarta in the year 2007–2008

Marcellus Simadibrata¹, Dolly Dolven Kansera², Jane Estherina², Nata P.H. Lugito², Rizky Yarantradhani², Fransiska Hardi², Nur Ista², Murdani Abdullah¹, Achmad Fauzi¹, Daldiyono Hardjodisastro¹, A. Aziz Rani¹, Ening Krisnohani³, Diah Rini Handjani³

¹Division of Gastroenterology, Department of Internal Medicine, Faculty of Medicine, University of Indonesia, dr. Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia
²Department of Internal Medicine, Faculty of Medicine, University of Indonesia, dr. Cipto Mangunkusumo Hospital, Jakarta, Indonesia
³Department of Anatomical Pathology, Faculty of Medicine, University of Indonesia, dr. Cipto Mangunkusumo Hospital, Jakarta, Indonesia

Introduction: The prevalence of Crohn’s disease is 35–100/100,000 for Caucasian populations in northern Europe and North America. In South America, Asia, and Africa these diseases remain uncommon but appear to be increasing. Within geographic areas, ethnic and racial variations exist in the incidence of Crohn’s disease. The aim of this study was to reveal the incidence and demographic data of Crohn’s disease patients.

Method: This study was done retrospectively from medical records of patients that underwent colonoscopy at Endoscopic Unit, Gastroenterology Division, Department of Internal Medicine, Cipto Mangunkusumo General Hospital, Jakarta and histological evaluation in Department of Anatomic Pathology, Faculty of Medicine University of Indonesia in the year 2007–2008. We identified patients based on sex, age, clinical complaints, colonoscopy description.

Results: There were 921 patients that underwent colonoscopy from January 2007–December 2008, and 19 patients (2.1%) with clinical complaints colonoscopy description and pathological findings suggestive of Crohn’s disease. There was no sex preponderance. The mean age was 47.7 years with a peak age at presentation was 50–60 years. Diarrhea (42.1%), lower gastrointestinal bleeding (36.8%), abdominal pain (10.5%) and upper gastrointestinal bleeding (5.3%) were the main clinical complaints. In colonoscopic findings the involvement of isolated left colon was 26.3%, isolated right colon was 10.5%, pancolitis was 57.9%, ileitis was 5.3%, ileocolitis was 36.8% and skip lesion in 1 patient (7.1%).

Conclusion: The incidence of Crohn’s disease in our study was 2.1% with no sex preponderance, mean age of presentation was 47.7 years, and diarrhea as the main clinical complaints. In colonoscopy pancolitis was the dominant findings.

Key words: Crohn’s disease; incidence; sex; age; clinical complaints; colonoscopy description
Evaluation of Ki-67 and PCNA expression in Crohn’s disease

Marcin Sokołowski, Katarzyna Guzińska-Ustymowicz, Anna Pryczynicz, Marek Ustymowicz, Andrzej Kemona
Department of General Pathomorphology, Medical University of Białystok, Poland

Introduction: Ki-67 and PCNA are proteins involved in cell cycle. The aim of this study was comparison of expression of these two proteins as markers of cell proliferation in Crohn’s disease.

Methods: The study was conducted in a group of 12 patients with Crohn’s disease. Dysplastic changes were present in 5 cases. Immunohistochemical investigations were carried out using antibody against Ki-67 and PCNA. PCNA and Ki-67 expression were determined using the semiquantitative method. Expression for PCNA was absent (lack of reaction or reaction in < 40% cells), weak (reaction in 40–60% cells), average (reaction in 61–80% cells) or strong (reaction in 81–100% cells). Expression for Ki-67 was absent (lack of reaction or reaction in < 10% cells), weak (reaction in 10–40% cells), average (reaction in 41–70% cells) or strong (reaction in 71–100% cells).

Results: Cells without dysplasia in Crohn's disease showed a lack of protein expression of Ki-67 in 8/12 cases and poor in 4/12 cases, while the PCNA protein showed only weak expression in 100% (10/10) of cases. The dysplastic cells expressing Ki-67 was on average 2/5 cases and strong in 3/5 cases, while the protein showed strong PCNA expression in 100% (5/5) cases.

Conclusion: Dysplastic cells show a greater expression of Ki-67 protein and PCNA than nondysplastic cells. PCNA protein appears to be a better marker to distinguish dysplastic epithelium from nondysplastic.
Clinical study on effect of compound glutamin entersolube capsule combined clysis therapy on ulcerative colitis

TAN Hua, SUN Man-yi, YANG Jian, et al.
Department of Gastroenterology, People Hospital of Tianjin, Tianjin 300121, China

Introduction: To observe the effect and safety of compound glutamine entersolube capsule combined clysis therapy on active ulcerative colitis (UC).

Methods: One hundred and sixty-eight patients with active UC were divided randomly into the treatment group (n = 86, compound glutamine entersolube capsule combined with Solu-Medrol™ for clysis) and the control group (n = 82, Solu-Medrol™ singly used for clysis), and the efficacy of treatment and the changes of the principal symptoms were evaluated before and after treatment.

Results: The total effective rate in the treatment group was 94.19%, and that in the control group was 82.93%, while the difference in the two groups was significant ($P < 0.05$). The symptoms of blood in stool and abdominal pain were improved and UCAI was smaller after treated in both the treatment group and the control group, and the difference in the two groups were significant ($P < 0.01$, $P < 0.001$). The improvement of blood in stool, time of disappearance of grumous pus blood in stool and UCAI after treated in the treatment group were superior to those in the control group, and the difference were significant ($P < 0.05$, $P < 0.005$, $P < 0.005$). Clysis cannot be performed in two cases of the treatment group, with no adverse reaction.

Discussion/Conclusion: The effect of compound glutamine entersolube capsule combined with glucocorticoids for clysis on active UC was obviously superior to that of glucocorticoids singly used in the near future, with no adverse reaction.
Epidemiological prospective study in inflammatory bowel disease in Aljarafe region (Seville)

Hospital San Juan Dios del Aljarafe, Seville, Spain

Objective: To study the incidence of inflammatory bowel disease (IBD) in the Aljarafe region (Seville) and describe the clinical and epidemiological features in this disease.

Methods: Prospective study in our health area (with 257,628 population). We registered all new patients over 14 years of age, with IBD that were diagnosed in the five consecutive years following the opening of our hospital (January 2004–December 2008). We analyzed the annual median incidence, sex, age distribution, phenotype, and location of the disease.

Results: We included 176 patients: 67 with ulcerative colitis (UC) and 109 with Crohn’s disease (CD). The rate of annual median incidence adjusted by 105 patients between 14 and 75 years was 6.72 for UC and 10.7 for CD. Sex distribution was 1.17 without significant difference with an average age at diagnosis of 35.6 ± 14.6 years. At the time of diagnosis, patients with CD were younger than UC patients (23.6 ± 5.1 years versus 40.15 ± 15.6 years; p < 0.05).

Endoscopic extension in UC patients was: rectal in 28.86%, 41.7% in left colon, and 31.35% pancolitis.
In CD patients, ileal affectation predominated in 45.8%, followed by ileo-colonic in 39.9%, and colonic in 14.6%. Perianal disease was observed in 19 patients and extracolonic affectation in 7 patients. The behaviour was inflammatory in 63.3% of the patients, estenotic in 8.25% and fistulous in 28.45%.

Conclusions:
1. In our area, the incidence of CD is superior to the habitual incidence in Northern European countries, while UC incidence is significantly lower.
2. CD mainly affects young people, while UC predominates in middle age persons without significant difference in sex distribution.
3. There is a greater disparity among age in UC patients, than CD patients, likely due to the two peaks of incidence in CU.
4. At diagnosis, UC is more frequently localized in left colon, with sigma-rectum predominance, while in CD, the more frequent location is ileal (without significant difference) with inflammatory behaviour (p < 0.05).
Clinical and epidemiological characteristics of Crohn’s disease, depending on age at onset

Dr. José Manuel Hospital San Juan de Dios del Aljarafe Bormujos, Seville, Spain

Aims: To describe the prevalence, the clinical and epidemiological characteristics, and the differences in evolution and complications in patients diagnosed with Crohn’s disease (CD) before and after 50 years of age.

Patients and methods: All the patients diagnosed with CD in our centre from January 2004 to December 2009 were included prospectively. They were subdivided into two groups: E1 (less than 50 years old) and E2 (50 years old or more). We compared the two groups with respect to gender and age, symptoms at onset, extent and phenotype of the disease, evolution, prevalence of complications, and the need for immunomodulatory and surgical treatment and hospitalization.

Results: The sample was of 190 patients: 168 patients in E1 (88.4%) with a gender distribution ratio of 1.7F/1M; and 22 patients (11.6%) in E2, with a distribution of 0.7F/1M.
At diagnosis, the extent of CD in E1 and E2 was colonic in 11.3% and 31.8%, ileal in 47% and 40.9%, and ileocolonic in 41.7% and 27.3% respectively.
The prevalence of perianal fistula (PAF) in E1 was 36%, against 0% in E2.
The frequency of presenting symptoms such as diarrhoea, weight loss, abdominal pain, and rectorrhagia was similar in the two groups, with a higher frequency of anaemia in young patients, although the differences were not significant.
The distribution by phenotypes was fistulising 31.6%, mixed 9.5%, stenosing 8.9%, and inflammatory 50% in E1; and 91% inflammatory, 4.5% stenosing, 4.5% mixed, and no case of pure fistulising in E2.
In their evolution, 57% of E1 patients needed immunomodulatory treatment to control the disease, and 17.26% needed biological treatment; against 36.4% and 4.5%, respectively, in E2.
The need for hospitalization during the study period was 48.8% in E1, against 31.8% in E2; with some type of surgical operation being needed by 25% in E1 and 13.5% in E2.

Conclusions:
1. CD presents a higher incidence in E1, similarly to other series reported, before the age of 50; and is more frequent in men younger than 50 years old and in women after that age, the difference being statistically significant.
2. In E1, the higher incidence of CD is in men, with the opposite trend in E2.
3. Conditions affecting the terminal ileum is more frequent in young patients than in E2, the difference being significant (p < 0.05%).
4. There are no significant differences in the onset of symptoms between the two groups. PAF is present in 21.4% of young patients, and non-existent in patients of more than 50 years old in our sample.
5. CD in young patients shows a clearly more aggressive behaviour, as measured by the need for immunosuppressive treatment, biological treatment, and surgical operations.
6. The fistulising phenotype in E1 is 31.6%, and non-existent in E2
7. The need for hospital admission to control the disease is greater in E1, although the difference is not statistically significant.
Duodenal histologic alterations in lactose intolerance

Hospital San Juan de Dios del Aljarafe Bormujos, Sevilla, Spain

Objectives: Investigate the presence of histological lesions in intestinal mucosa in patients with clinical suspicion of lactose intolerance (LI) and their follow up.

Methods: Prospective and descriptive study including patients with symptoms compatible with LI. Subjects age 14 to 65 years during the course of six months (June 1–December 31, 2008). We analyzed tolerance to lactose by glucemic curve test and breath hydrogen tests, after an overload of lactose (50 g); establishing the diagnosis in patients with compatible symptoms and at least one positive test. We did histological studies of the second and third portion of the duodenal mucosa and determined antibodies associated with celiac disease (CD) and anti-gliadin and transglutaminase antibodies (IgA, IgG and total IgA and IgG).

We analyzed age, sex, prevalence of antibodies for CD, histological alterations (Marsh score) in duodenal mucosa, and tolerance to lactose.

Results: We included 63 patients, with a male:female ratio of 1:2.1, and a mean age of 36.2 ± 12.35 years.

In 47.6% of the patients, we confirmed lactose intolerance. Of those, 20 were female and 10 male, without a significant difference, probably due to the male-female proportion of our sample. We did not find significant difference in the age of either group.

In 26.5% of the patients with LI, we found histological alterations suggestive of celiac disease, allowing confirmation of this disease. Contrarily, in 73.5% patients showed a primary lactose intolerance.

Conclusions:

1. There was no significant difference with regard to sex or age distribution in our patients with LI.
2. In 26.5% of the patients, we found histological alterations suggestive of celiac disease, allowing confirmation of this disease. Contrarily, in 73.5% patients showed a primary lactose intolerance.
3. The negative prevalence of antibodies for CD in adults does not exclude the existence of histological alterations in duodenal mucosa nor a CD diagnosis. Therefore, we find the differential diagnosis in patients with LI justifiable.
Serum lipopolysaccharide-binding protein and soluble CD14 are markers of disease activity in patients with Crohn’s disease

Tamas G. Toth¹,5, Peter Fuszek¹, Lajos Sandor Kiss¹, Karoly Palatka², Istvan Altorjay², Peter Antal-Szalmas³, Eszter Palyu², Miklos Udvardy², Tamas Molnar⁴, Klaudia Farkas⁴, Janos Papp¹, Maria Papp², Peter Laszlo Lakatos¹
¹1st Department of Medicine, Semmelweis University, Budapest, Hungary
²2nd Department of Medicine, University of Debrecen, Debrecen, Hungary
³Department of Clinical Biochemistry and Molecular Pathology, University of Debrecen, Debrecen, Hungary
⁴1st Department of Medicine, University of Szeged, Szeged, Hungary
⁵SztJanos Hospital, Budapest, Hungary

Background: In inflammatory bowel disease (IBD), enhanced inflammatory activity in the gut is thought to increase the risk of bacterial translocation and endotoxemia. In the present study, we aimed to investigate the association between serum levels of lipopolysaccharide-binding protein (LBP), soluble CD14 (sCD14) and clinical disease activity, high-sensitivity C-reactive protein (hs-CRP), anti-microbial serology profile, NOD2/CARD15 status and clinical phenotype in a large cohort of Hungarian Crohn’s disease (CD) patients.

Methods: 214 well-characterized, unrelated, consecutive CD patients (m/f: 95/119, age: 35.6 ± 13.1 years, duration: 8.3 ± 7.5 years) and 110 healthy controls were investigated. Sera were assayed for LBP, sCD14, hs-CRP, ASCA IgG/IgA and anti-OMP IgA antibodies. NOD2/CARD15 variants were tested. Detailed clinical phenotypes were determined by reviewing the patients’ medical charts.

Results: Serum LBP level was significantly higher (p < 0.0001 for both), while sCD14 was lower (p < 0.0001) in both active and inactive CD compared to the controls. The accuracy of hs-CRP (AUC = 0.66), sCD14 (AUC = 0.70), and LBP (AUC = 0.58) was comparable for identifying patients with active disease. There was a significant correlation between LBP (p < 0.001), sCD14 (p = 0.015) and hs-CRP levels but not with anti-microbial seroreactivity or NOD2/CARD15 genotype. In inactive CD, LBP was associated with penetrating disease. In a Kaplan-Meier analysis and a proportional Cox-regression analysis, LBP (p = 0.006), sCD14 (p = 0.007) and previous relapse frequency (p = 0.023) were independently associated with time to clinical relapse during a 12-month follow-up period.

Conclusion: Serum LBP and sCD14 are markers of disease activity in CD with a similar accuracy as hs-CRP. In addition, LBP, sCD14 and high frequency of previous relapses were independent predictors for medium-term clinical flare-up.
**Ki-67 overexpression in Crohn’s disease, colitis ulcerosa and colorectal adenocarcinoma**

Marek Ustymowicz, Anna Prynyczynic, Katarzyna Guzinska-Ustymowicz, Andrzej Kemona  
Department of General Pathomorphology, Medical University of Białystok, Poland

**Introduction:** Ki-67 is a marker for cell proliferation and is present in the cell nucleus in G1, S, G2, mitosis and absent in inactive and resting cells in G0 phase. Ki-67 index is very useful for a prognostic factor in many cancers. Therefore the object of this study was to estimate expression of Ki-67 protein in inflammatory bowel diseases and correlate to its expression in colorectal adenocarcinoma.

**Methods:** The expression of Ki-67 was analyzed in 12 patients with Crohn’s disease, 19 patients with colitis ulcerosa and 55 patients with colorectal cancer. The protein expression was evaluated by immunohistochemical reaction using antibody for Ki-67. Expression of Ki 67 protein in ≥ 20% of the cells was classified as positive.

**Results:** Positive expression for Ki-67 was observed in 2/12 (16.6%) cases with Crohn’s disease, in 12/19 (63.2%) cases of colitis ulcerosa and in 31/55 (56.4%) cases of colorectal cancer.

**Conclusion:** These investigations suggest that increased cell proliferation in patients with colitis ulcerosa is associated with higher risk of developing cancer.
Therapeutic effect of CXCR4 antagonist AMD3100 on experimental colitis induced by DSS in mice

Fangyu Wang, Xianming Xia
Department of Gastroenterology and Hepatology, Jinling Hospital, School of Medicine, Nanjing University, Nanjing 210002, China
E-Mail: wangfy65@gmail.com

Background: The CXCL12/CXCR4 chemokine axis has been proved to involve in several inflammatory diseases such as rheumatoid arthritis, acute lung injury, and sepsis. Recent studies demonstrated that CXCL12 and CXCR4 were constitutively expressed on human intestinal epithelial cells, lamina propria T cells, and peripheral blood T cells, and the expression was increased in patients with ulcerative colitis (UC). Blockade of CXCR4 significantly ameliorate murine experimental colitis, suggested a possible role of this chemokine axis in intestinal inflammatory response. Whether the CXCL12/CXCR4 chemokine axis takes role in epithelial apoptosis and barrier function, however, needs to be further clarified.

Aim: To examine effect of a CXCR4 antagonist on DSS-induced colitis in mice. To further elucidate the role of the CXCL12/CXCR4 interaction in colonic inflammation, we also investigated the CXCR4 antagonist on isolated peripheral blood mononuclear cells (PBMCs).

Materials and methods: Mice were given 5% DSS in drinking water for 7 days. CXCR4 antagonist AMD3100 was obtained from Sigma (St. Louis, MO, USA). Twenty-five micrograms of AMD3100 dissolved with 200 µl of phosphate-buffered saline (PBS) or 200 µl of PBS alone was administered intraperitoneally once a day during the study period. At day 8, segments of the colons were removed for subsequent assays. Morphology, colonic cytokines, myeloperoxidase (MPO) activity (indicator of inflammatory infiltration), gut permeability, and epithelial apoptosis examinations were all performed.

To further elucidate the role of the CXCL12/CXCR4 interaction in colonic inflammation, we also investigated the CXCR4 antagonist on migration and cytokine production of isolated peripheral blood mononuclear cells (PBMCs). To evaluate whether AMD3100, the CXCR4 antagonist, could block PBMCs migration, we performed an in vitro PBMCs chemotaxis assay. To mimic the in vivo inflammatory response, the PBMCs were pre-activated with PHA. The IOD values were employed to assess the number of migrated PBMCs.

Results: Seven days after administration of DSS in mice, the colonic mucosa showed presence of congestion, erosion, and hemorrhagic ulcerations. Histological findings demonstrated remarkable epithelial destruction, inflammatory infiltration, crypt distortion, and submucosal edema. The histological score in mice with DSS-induced colitis was significantly higher than that in control mice, and treated with AMD3100 markedly reduced histological score in mice with colitis.

Colonic TNF-α, IL-6, and IFN-γ levels were significantly elevated at 7 days after induction of colitis, as compared with control mice; treated with AMD3100 markedly decreased colonic cytokines production in mice with colitis.
The mucosal-to-serosal passage of FD4 was low in control mice, and the calculated clearance was $9.10 \pm 1.10 \text{ nl/min/cm}^2$. DSS-administrated mice demonstrated a marked increase in gut permeability, the calculated clearance reaching $24.18 \pm 1.83 \text{ nl/min/cm}^2$. In AMD3100 treated mice, there was a significantly reduction of permeability, and the calculated clearance was $14.71 \pm 1.43 \text{ nl/min/cm}^2$ vs. colitis group, $p < 0.05$).

Sporadic apoptotic cells were observed in the colon from control mice (apoptotic cells were $1.25 \pm 0.12$ per field). The number of apoptotic cells in the colon was markedly increased 7 days after induction of colitis, the apoptotic bodies mainly localized in the epithelium (apoptotic cells were $11.98 \pm 0.81$ per field). However, the presence of apoptotic cells was significantly decreased in the colon from AMD3100 treated mice (apoptotic cells were $4.23 \pm 0.28$ per field, vs. colitis group, $p < 0.05$).

CXCL12 treatment significantly increased the migration of PBMCs, as compared with control group, the IOD values were $79.68 \pm 3.76$, $51.28 \pm 2.97$, respectively ($p < 0.05$), and the migration of PBMCs were significantly inhibited by AMD3100 pre-treated (IOD values $53.27 \pm 3.70$, vs. CXCL12 group, $p < 0.05$).

**Conclusion:** These results suggest that the CXCR4 antagonist may have a therapeutic effect on experimental colitis, and further proved that CXCL12/CXCR4 chemokine axis should play an important role in the pathogenesis of UC.
The role of enteral nutrition in adult Crohn’s disease patients

Lei Wang, Jizhong Guo, Guoqiang Zhang
Department of Digestion, the People’s Hospital of Wuxi Affiliated to Nanjing Medical University, Wuxi 214023, China

Background: There is limited information on the nutrition impact of enteral nutrition (EN) in adult Crohn’s disease (CD).

Aim: This study was performed to examine if EN can improve nutrition status, induce remission, maintain remission.

Methods: 32 patients with histologically and endoscope proven CD were eligible for the study between 2008 and 2010. The parameters of number of leukocytes, sedimentation, haemoglobin levels, albumin level, C-reactive protein, body mass index (BMI), disease activity index (CDAI/AI), and the number of hospital days were analyzed in the 18 EN patients and 14 controls (tradition diet treatment) in the first day, three and six months after.

Results: The duration of the application of EN was 15.5 ± 4 days. The analysis of these parameters has shown that there is no statistically significant difference in the number of hospital days in both groups, but analysis of the disease activity (CDAI/AI) has shown that EN patients were in a more severe stage. The EN group had a higher increasing trend in the BMI and albumin level compared with the control group. The significant decreasing trend in the parameters of inflammation activity can be found in the EN group. The relapsing rate of CD in EN group was lower than in the control group, but the difference was not statistically significant. CONCLUSIONS: EN may play a role in Crohn’s disease patients. The advantages were shown to induce clinical remission, maintain remission, reduce inflammation activity, and improve nutrition status.

Key words: Crohn’s disease; adults; nutrition therapy; enteral nutrition
The curative effect of moderate and severe ulcerative colitis treated by mesalazine combined with Tripterygium hypoglaucum Hutchins

WANG Long, XIANG Yong Sheng, JIANG Rui, LIU Chang-qing
Department of Digestive Diseases, Jingmen No. 1 People's Hospital, Hubei Province, Jingmen, China

Introduction: To evaluate the curative effect of ulcerative colitis treated by mesalazine combined with Tripterygium hypoglaucum Hutchins.

Methods: 40 patients with moderate and severe ulcerative colitis were divided into 2 groups randomly. A group is control group, 20 patients, mesalazine was given orally as 4 g/d, four times a day; B group is experimental group, 20 patients, mesalazine was given orally as 4 g/d, four times a day, combined with Tripterygium hypoglaucum Hutchins given orally as 0.9 g/d, three times a day for 8 weeks.

Results: The remission rates of experimental group and control group were 84.4% and 63.2% respectively. The difference was significant (P < 0.05). There is no marked difference on bad reaction between both groups (P > 0.05).

Discussion/Conclusion: The effect of mesalazine combined with Tripterygium hypoglaucum Hutchins was higher than that of mesalazine alone for the patients with moderate and severe ulcerative colitis and long-term therapeutic effect was very good.
The frequency and function of Th-17 cells producing IL-17A in inflammatory bowel disease

Yi Wang, Xueping Liu, Zhibin Zhao, Junhao Chen, Chenggong Yu
Department of Gastroenterology, the Affiliated Drum Tower Hospital of Nanjing University Medical School, Nanjing 210008, P. R. China

Introduction: Inflammatory bowel disease (IBD) is an autoimmunity disease characterized by relapsing inflammation of gastrointestinal tract. Th-17 cells that secret IL-17A is closely related to autoimmunity diseases. The aim of this study was to investigate the relationship between Th-17 cells and IBD.

Methods: The Th-17 cell proportion in peripheral blood and biopsy specimens from patients with IBD was analyzed by flow cytometry and immunohistochemistry, respectively. Real-time polymerase reaction was used to examine IL-17A mRNA expression and concentration of IL-17A in serum was detected by enzyme-linked immunosorbent assay (ELISA). In vitro IL-17A function analysis was performed and the expression of intercellular adhesion molecule-1 (ICAM-1) on T lymphocyte was examined by flow cytometry.

Results: The Th-17 cell proportion was significantly increased in both peripheral blood and biopsy specimen compared with that in healthy controls. IL-17A mRNA and serum IL-17A were both significantly increased in IBD patients. Moreover, we found recombinant IL-17A induces ICAM-1 expression in T lymphocyte.

Discussion/Conclusion: There is an expanded Th-17 cell population in peripheral blood and biopsy specimens from patients with IBD. The secretory IL-17A induces lymphocyte infiltration and sequential damages in inflamed mucosa (no data in results section). These results may suggest a potential role of Th17 cell in IBD pathogenesis.
The prevalence status of inflammatory bowel disease in China

Yufang Wang, Qin Ouyang, Renwei Hu
West China Hospital of Sichuan University, Chengdu Sichuan Province, China

Introduction: The epidemiology and phenotype of IBD in the Chinese population is not well-known. The purpose of this study was to collect the epidemiologic data of IBD in China.

Methods: A long-term literature review was performed through the CBM database from January 1989 to December 2007. A clinical analysis of hospitalized IBD from 23 medical centers in 11 cities over China during 1990–2003 was also completed in China.

Results: The literature review showed that the number of IBD cases reported has been increasing progressively in China within the past 19 years. 3100 cases of UC and 515 cases of CD were collected from the retrospective nationwide survey in China. Conservative speculative data from these cases indicated the prevalence of UC and CD to be 11.6/100,000 and 1.4/100,000 respectively. The data also showed 5-fold increases in hospitalized cases in the past 5 years compared with that of the first 5 years. There are some notable epidemiological differences between Chinese IBD with Caucasian IBD including the lack of familial clustering, male predominance, a relatively later onset of illness with no second peak age occurrence after 50 years, a milder clinical course, less extraintestinal manifestations and complications.

Discussion/Conclusion: The data indicate a true increase of IBD in China with a lot of complicated clinical problems, which offers potential opportunities to study the disease prospectively and identify the etiologic factors, also better management for this disease in China.
Human intestinal lamina propria CD4\(^+\)CD25\(^++\) T regulatory cells (Treg) can be expanded in vitro with retention of potent suppressor function

Zhonghui Wen\(^1\), Qin Ouyang\(^1\), Gail West\(^2\), Claudio Fiocchi\(^2\)
\(^1\)West China Hospital of Sichuan University, Chengdu Sichuan Province, China
\(^2\)University Hospitals of Cleveland, Cleveland, OH, USA

**Introduction:** CD4\(^+\)CD25\(^++\) Treg represent a minute portion of peripheral CD4\(^+\) T cells, but they exert a potent regulatory function on systemic immune homeostasis. Such function is also essential in the gut mucosa, especially for IBD patients.

**Methods:** From control and IBD patients, CD4\(^+\) T-cells were isolated from PBMC and LPMC by negative selection with magnetic beads, separated into CD4\(^+\)CD25\(^++\) and CD4\(^+\)CD25\(^-\) subsets by fluorescence-activated cell sorting, and expanded with anti-CD3\(^+\) anti-CD28 and IL-2. The function of fresh and cultured CD4\(^+\)CD25\(^++\) cell was tested by the proliferation of lymph cells.

**Results:** In control, 1.6 ± 0.4% of CD4\(^+\) T cells from the peripheral circulation were CD4\(^+\)CD25\(^++\) (n = 11), while in the lamina propria 0.6 ± 0.7% of CD4\(^+\) T cells were CD4\(^+\)CD25\(^++\) (n = 20) (p < 0.01). Freshly isolated peripheral blood CD4\(^+\)CD25\(^++\) cells suppressed proliferation of autologous CD4\(^+\)CD25\(^-\) cells by 87 ± 11% (68–95%; n = 5), and LPMC CD4\(^+\)CD25\(^++\) cells suppressed autologous CD4\(^+\)CD25\(^-\) cells by 63 ± 22% (40–90%; n = 5) (p < 0.05). After culture, both blood and lamina CD4\(^+\)CD25\(^++\) cells were highly viable. Lamina propria CD4\(^+\)CD25\(^++\) cells expanded 6–7 folds, which is less than blood CD4\(^+\)CD25\(^++\) cells. Expanded CD4\(^+\)CD25\(^++\) cells inhibited proliferation of fresh CD4\(^+\) T-cells, by 82 ± 19% (n = 4) for PBMC and 79 ± 13% (n = 2) for LPMC.

**Discussion/Conclusion:** CD4\(^+\)CD25\(^++\) Tregs from intestinal lamina propria are significantly fewer than in the circulation, but they are displaying strong suppressor function too. Mucosal Treg can be expanded in culture with retention of function capacity, allowing a better evaluation of their functional properties under normal, inflammatory and immune-mediated conditions.
Hypoxia in perspective from inflammatory bowel disease to colorectal cancer – Study of hypoxia-inducible protein. EPO serum levels as prognostic marker of survival of colorectal cancer patients

Andrzej Wincewicz, Adam Pietrzykowski, Luiza Kanczuga-Koda, Marek Baltaziak, Urszula Sulkowska, Mariusz Koda, Waldemar Famulski, Stanislaw Sulkowski
Departments of Pathology and Medical History, Maria Sklodowska-Curie Memorial Bialystok Center of Oncology and Medical University of Bialystok, Technical Support, Bialystok, Poland

Introduction: Colorectal cancers are sometimes proceeded by inflammatory bowel disease and are usually infiltrated by lymphocytes with chronic inflammation at tumour borders. Inflammation and colorectal cancer are oxygen consuming. Colorectal cancer is also associated with haemorrhages, subsequent anaemia as well as invading tumour growth also utilize great amount of oxygen in the battle with immune system. Hypoxia renders production of erythropoietin (EPO), which was shown to be generated by colorectal cancers.

Methods: ELISA kits were applied to evaluate preoperative serum levels of EPO in samples from 106 colorectal cancer patients. EPO levels were split into two groups: one of patients with the serum EPO levels below mean value of 7.6 mIU/ml for control group of 16 volunteers and the other one group with higher serum levels of EPO. Kaplan Meier plot was used for statistics.

Results: Patients with higher EPO levels were characterized by significantly shorter overall survival than patients with lower levels of the marker (p < 0.02). Validity of the test was further confirmed in this study group by checking up for significantly poor prognostic impact of higher grading (p < 0.042) and nodal metastagenicity (p < 0.009).

Discussion/Conclusion: Hypoxic environment of colorectal cancer is manifested by excess of circulating EPO. Endogenous serum high EPO levels are markers of poor prognosis in colorectal cancers. The use of recombinant EPO should be cautiously considered as there is strong ground to suspect that endogenous EPO could affect tumour growth in an analogous manner to resuming population of erythrocytes in cases of colorectal cancer related anaemia.
A case-control study on dietary and living style factors for the development of inflammatory bowel disease in Hunan province

Wu xiaoping, Mo yaxian, Liu xiaowei
The Second Xiangya Hospital of Central South University, Changsha 410011, China

Objective: A matched case-control study on the living styles, dietary habit was performed to evaluate the risk factors of IBD (inflammatory bowel disease, IBD) diagnosed in Hunan province.

Methods: A matched case-control (1:1) study was designed. The IBD patients and the healthy control were matched both in sex and age. One hundred and twenty-four IBD patients (103 UC, 21 CD) together with 124 matched healthy subjects were included. A questionnaire was used to collect related information from the patients and controls. SPSS13.0 was applied to the whole statistics process. The related statistics methods were chi-square test, t test conditional logistic regression and Cox regression model.

Results: The age distribution of IBD patients was mainly in 30 to 40. Conditional logistic regression analysis indicated that occupational tensity (OR: 1.169, 95% CI: 1.383–3.401), fried food intake (OR: 1.729, 95% CI: 1.006–2.970) played a significant role in the pathogenesis of IBD (P < 0.05). Nevertheless, smoking (OR: 0.571, 95% CI: 0.329–0.990) is a protective factor for UC (P < 0.05).

Conclusions: Occupational tensity and fried food intake are probably the risk factors of IBD. Smoking is probably a protective factor of UC. The living environment of patients, intake of alcohol, tea, capsicum chilli and smoked food are probably not the risk factors of IBD.
Expression of proteinase-activated receptor-2 in intestinal mucosa of patients with ulcerative colitis

Wu Zheng-xiang
Department of Gastroenterology, the First Affiliated Hospital, Anhui Medical University Hefei, Hefei 230001, China
Telephone: 13866184276

**Introduction:** To investigate the expression of proteinase-activated receptor-2 (PAR-2), the change of mast cells (MC) in intestinal mucosa of patients with ulcerative colitis, and the possible roles of PAR-2 and MC in the pathogenesis of UC.

**Methods:** UC tissues were obtained from 32 patients undergoing colonoscopy. Normal human colon tissues were obtained from 15 healthy adult volunteers. Semi-quantitative reverse transcription polymerase chain reaction (RT-PCR) was used to determine the expression of PAR-2 mRNA. Immunohistochemistry was used to determine the expression of PAR-2 protein and the number of MC.

**Results:** Expression of PAR-2 in mRNA and protein level in mucosa of UC was significantly higher than that of healthy control. The overexpression of PAR-2 mRNA was positively correlated to the severity of UC (P < 0.01). The number of mast cells with UC was significantly higher than of the healthy control group (P < 0.01). Immunohistochemistry showed PAR-2 protein was localized in colonic epithelial cells, crypt surface and inflammatory cells of lamina propria in UC. Patients with inflammation grade III, IV exhibited significant higher expression of PAR-2 and the number of MC than those with inflammation grade I, II (P < 0.05). The expression of PAR-2 in protein was also positively correlated with the number of mast cell (r = 0.78, P < 0.01).

**Discussion/Conclusion:** The occurrence of UC correlates with the increased expression of PAR-2 and number of mast cells. These results indicate that the activation of PAR-2 through tryptase released from mast cells might be involved in the pathogenesis of UC.
Effect of total glucosides of paeony on oxazolone-induced colitis in mice

Junying Xiang¹, Renwei Hu², Qin Ouyang²
¹Affiliated Hospital of North Sichuan Medical College, Nanchong Sichuan Province, China
²West China Hospital of Sichuan University, Chengdu Sichuan Province, China

Introduction: To investigate the effect and mechanisms of total glucosides of paeny (TGP) on oxazolone induced colitis in mice.

Methods: Forty eight mice were randomized into 6 groups (n = 8): normal control group, model control group, SASP group, TGP low dose group, TGP medium-dose group and TGP high-dose group (60, 120 and 240 mg/kg x day). Except the mice in normal control group, all mice were induced by oxazolone enema. Disease activity index (DAI) was observed every day. At the four day after enema, all the mice were scarified and all colonic mucosa was collected for further studies. The tumor necrosis factor (TNF)-α level of the colon mucosa was measured by ELISA, and the colonic expression of NF-κB p65 was detected by western blot analysis.

Results: In comparing with normal control group, the DAI score and TNF-α level of the model group was significantly increased (p < 0.05), and similar to that of TGP low dose group (p > 0.05). In comparing with the model group, the DAI score and TNF-α level of the TGP medium dose group and TGP high dose group was significantly decreased (p < 0.05). The expression of NF-κB p65 protein of model group was significantly higher than those of normal control group, SASP group, TGP medium dose group and TGP high dose group (p < 0.01), but similar to those of TGP low dose group (p > 0.05).

Discussion/Conclusion: TGP possesses anti-inflammatory effects upon the mice with oxazolone-induced colitis by inhibiting the activation of NF-κB and the production of TNF-α.
Role of endoscopy and histopathology in distinguishing between Crohn’s disease and intestinal tuberculosis in Kunming, China

Yuliang Xiao¹, Yinglei Miao¹, Yan Du² and Ping Pu³
¹Department of Gastroenterology, ²Department of Clinical Laboratory, ³Department of Pathology, the First Affiliated Hospital of Kunming Medical College, Kunming, Yunnan Province, China

Introduction: To evaluate clinical values of endoscopy and histopathology in diagnosing intestinal tuberculosis and Crohn’s disease and characterize distinctive diagnostic features of intestinal tuberculosis and Crohn’s disease in surgically resected specimens.

Methods: All surgically resected enterocolonic cases previously diagnosed as either CD or intestinal tuberculosis were reviewed to compare the clinical, endoscopic and morphologic aspects, and were determined the points of differentiation in the First Affiliated Hospital of Kunming Medical College. Histological parameters selected were assessed retrospectively in a total 60 cases (half were CD and another were intestinal tuberculosis).

Results: The sensitivity, specificity and accuracy of endoscopy in diagnosing Crohn's disease were 80%, 25.6% and 49.3%, respectively, which of intestinal tuberculosis were 86.7%, 46.1% and 63.7%. The characteristic histological parameters of intestinal tuberculosis were confluent granulomas often accompanying with caseating necrosis and stenosal submucosa. However, the features of CD were non-caseating necrosis granulomas, submucosal edema, knife-like fissuring ulceration and prominent lymphoid aggregates. All the same, histopathology similarities between CD and intestinal tuberculosis were found, such as chronic non-specific inflammation of intestinal wall, ulceration, collections of epithelioid histocytes, microgranulomas and transmural inflammation.

Discussion/Conclusion: Although typically diagnostic features of CD and intestinal tuberculosis were found, the clinical, endoscopical values were still limited. And the final differential diagnosis depends largely on pathology in Kunming, China.
Follow-up of surgical treatment for ulcerative colitis

Yang xuesong, Li Ruyuan, *Fu Wei
Department of Gastroenterolog, *Department of General Surgery, Peking University 3rd Hospital, Beijing, 100191, China

Introduction: To evaluate the current status and long-term prognosis of surgical treatment for ulcerative colitis (UC).

Methods: Retrospectively review the hospitalized UC cases and follow up who underwent surgery for UC during 1986-2009 in PKU 3rd hospital.

Results: Among 303 UC admitted, there were 13 cases (male/female 7:6) received surgery, accounted for 4.29% of total UC (13/303) and 18.3% of severe cases (13/71). The average age of UC onset and while received operation was 22.7 (17–49)/34.2 (17–54) years old respectively. The interval between diagnosis and operation was from 4 months to 11 years. All 13 cases were severe UC with entire colon involved. Seven were at the first onset and 6 in chronic persistent or recurrent condition, both could not get or maintain remission by SASP/5-ASA and steroid/immunosuppressor. Two experienced emergent operation for bleeding or perforation. The surgical pattern included proctocolectomy, total or subtotals colectomy, caecum-rectal anastamosis with or without ileal pouch. There were 9 patients received ileal ostomy and 2 left with permanent ostomy. Seven of the 13 patients underwent more than 2 times surgery for UC. One had rectal-vaginal fistulation. Within 4–23 years follow-up, 4 of 7 patients who had the rectum remnant suffered from UC relapse and had to be on oral or suppository 5-ASA. Two experienced incomplete intestinal obstruction.

Discussion/Conclusion: The outcome and prognosis of surgery for UC is associated with the time and pattern of operation.
The relationship between tumor necrosis factor-α and ulcerative colitis

YANG Youlin
The First Affiliated Hospital of Harbin Medical University Heilongjiang Province, Harbin 150001, China

Introduction: Some research data indicate that alterations in cytokine synthesis may play an important role in the pathogenesis of ulcerative colitis (UC). The different production of cytokines has been linked to single nucleotide polymorphisms in gene promoter regions, signal sequences and gene introns.

Objective: To investigate the gene polymorphisms and serum levels of tumor necrosis factor-α (TNF-α) in UC patients, then to explore the relationship of TNF-α and UC.

Methods: The genotypes of TNF-α in 60 UC patients and 60 normal controls were determined by polymerase chain reaction-sequence specific primers (PCR-SSP). The serum levels of TNF-α were measured by enzyme-linked immunosorbent assay (ELISA).

Results: The genotype frequency and allelic frequency of TNF-α-308 in UC patients had no significant differences compared with those in normal controls ($P > 0.05$). The genotype of TNF-α-308GG in UC patients with pancolitis was significantly higher than that in proctitis and left-sided colitis ($P < 0.05$). The serum levels of TNF-α in UC patients were significantly higher than those normal controls ($P < 0.05$) but no significant difference was observed in UC patients with different genotypes ($P > 0.05$) while the results in normal controls were opposite ($P < 0.05$).

Discussion/Conclusion: The gene polymorphisms of TNF-α-308 may not be correlated with the susceptibility of UC. Genotype of TNF-α-308GG may correlate with the extent of the disease. Genotypes of TNF-α may be the determinants of their corresponding serum levels in healthy adult people, however, the serum levels in UC patients were also influenced by other factors simultaneously.
Diagnosis of obscure gastrointestinal hemorrhages with capsule endoscopy in the different ages

Bing-ling ZHANG, Chun-xiao CHEN, You-ming LI
Department of Gastroenterology, The First Affiliated Hospital, College of Medicine, Zhejiang University, Hangzhou 310003, China

Introduction: To demonstrate the clinical efficacy of capsule endoscopy (CE) diagnostic imaging in the identification of obscure gastrointestinal hemorrhages and investigate the characteristic of lesions in different ages.

Methods: 385 patients of obscure gastrointestinal hemorrhages included in this study were recruited from June 2003 to November 2009 from the First Affiliated Hospital of Zhejiang University, Zhejiang, China. All of them divided into the group of old age (> 65 years), the group of middle age (41–65 years) and the young (17–40 years) were examined with CE. Diagnostic data were collected for analysis.

Results: The detective rate of CE in the old age, the middle age and the young is 66.94%, 62.29% and 61.80%, respectively (P > 0.05). While, the diagnostic rate of CE is 48.76%, 45.14% and 53.59%, respectively (P > 0.05). The main lesions found by CE were vascular anomalies, small intestinal tumors, and Crohn’s disease, non-specific enteritis and small intestinal ulcer, et al.

Discussion/Conclusion: CE shows high diagnostic value in obscure gastrointestinal hemorrhages in different ages. In different ages, the main cause of intestinal bleeding is different. The three main lesions detected by CE in the old age were vascular anomalies, small intestinal tumors and small intestinal ulcer. Which in the middle age were small intestinal tumors, vascular anomalies and non-specific enteritis and in the young were Crohn’s disease, small intestinal tumors and non-specific enteritis.
The effect of military training impact on freshmen’s electrogastrogram (EGG)

Qian Zhang, Zhixin Li, Cuizhen Zhang, Xin Liu, Jihong Chen, MD PhD
Division of Gastroenterology, Renmin Hospital of Wuhan University, Wuhan 430060, P. R. China

Introduction: Electrogastrogram can be altered by the autonomic nervous balance which would be changed by military training.

Methods: 20 freshmen were choosed randomly and had tests before, during or after the military training (named group 1, group 2 and group 3) with Medtronic Polygram Net. The indexes were analysed automatically which include dominant frequency and power and percentage of normal gastric slow wave at fast or postprandial (preDF, preDP, preN%, posDF, posDP, posN%).

Results:
1. posDP is over preDP in group 1; there is no difference between preDP and posDP in group 2 and group 3 (P > 0.05) (Table 1).
2. posDF are faster than preDF in group 2 and group 3 (3.07 ± 0.2 vs. 2.87 ± 0.2, P < 0.001 and 3.08 ± 0.2 vs. 2.9 ± 0.3, P < 0.001).
3. Both posDF in group 2 and group 3 are faster than group 1 (Table 2).
4. There is no difference of N% between each group, also preN% and posN% in each group (P > 0.05) (Table 3).

Discussion/Conclusion: Military training increases posDF compensatorily and it has no impact on N%.

Table 1: DP changes

<table>
<thead>
<tr>
<th></th>
<th>preDP</th>
<th>posDP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group1</td>
<td>47.3 ± 5.0</td>
<td>50.9 ± 6.0* P = 0.023</td>
</tr>
<tr>
<td>Group2</td>
<td>48.6 ± 7.5</td>
<td>49.9 ± 5.6</td>
</tr>
<tr>
<td>Group3</td>
<td>47.4 ± 6.3</td>
<td>50.7 ± 5.9</td>
</tr>
</tbody>
</table>

Table 2: DF changes

<table>
<thead>
<tr>
<th></th>
<th>preDF</th>
<th>posDF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group1</td>
<td>2.895 ± 0.187</td>
<td>2.937 ± 0.211</td>
</tr>
<tr>
<td>Group2</td>
<td>2.867 ± 0.157</td>
<td>3.072 ± 0.202 XP &lt; 0.05</td>
</tr>
<tr>
<td>Group3</td>
<td>2.850 ± 0.260</td>
<td>3.083 ± 0.195 § P &lt; 0.05</td>
</tr>
</tbody>
</table>

Table 3: N% changes

<table>
<thead>
<tr>
<th></th>
<th>preN%</th>
<th>posN%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group1</td>
<td>84.650 ± 16.140</td>
<td>85.830 ± 14.052</td>
</tr>
<tr>
<td>Group2</td>
<td>87.167 ± 14.986</td>
<td>83.911 ± 14.005</td>
</tr>
<tr>
<td>Group3</td>
<td>87.811 ± 15.529</td>
<td>84.616 ± 17.855</td>
</tr>
</tbody>
</table>
Expression and clinical significance of GAFP and COX-2 in the colonic mucosa of patients with ulcerative colitis and irritable bowel syndrome

Zhong Ying-qiang, Yan Rong
Department of Gastroenterology, The Second Affiliated Hospital, Sun Yat-sen University, Guangzhou 510120, China

Objective: To investigate expressions and significances of GFAP and COX-2 in ulcerative colitis (UC) and irritable bowel syndrome (IBS).

Methods: Expressions of COX-2 and GFAP of 30 cases with UC and 60 cases with IBS were detected by two-step immunohistochemistry (IHC). The clinical data of patients were recorded.

Results: The positive rate of COX-2 expression was 83%, 93%, 100% and 76%, and higher positive rate was 33%, 57%, 83% and 13%, and IHC score was 2.97 ± 1.40, 3.57 ± 1.36, 4.83 ± 1.44 and 2.36 ± 1.13 in IBS-C, IBS-D, UC and the control respectively (P < 0.05). The positive rate of GFAP was 83%, 100%, 100% and 100%, and higher positive rate was 37%, 73%, 57% and 63%, and IHC score was 3.13 ± 1.48, 4.33 ± 1.24, 3.83 ± 1.23 and 4.17 ± 1.26 in IBS-C, IBS-D, UC and the control respectively (P < 0.05). There were correlation between expressions of COX-2 or GFAP and illness course, severity of IBS. The relationship between expressions of COX-2 or GFAP and clinical grade, endoscopic grade of UC.

Conclusions: Expression of COX-2 is weakly in the control, IBS and strongly in UC irrespectively, which is relation with illness course and severity of IBS, and with clinic grade of UC. Expression of GFAP is strongly in the control, IBS-D and moderate UC, but weakly in IBS-C and severe UC, which is relation with constipation degree and clinic grade of UC, and illness course and severity of IBS-C.

Key words: COX-2; GFAP; irritable bowel syndrome; ulcerative colitis; immunohistochemistry
HIV protease inhibitors induce gut microbial translocation and systemic inflammation by disrupting intestinal epithelial barrier integrity through activating the ER stress response

Huiping Zhou, Yi Huang, Xiaokun Li, Elaine Studer, William M. Pandak, Phillip B. Hylemon
Department of Microbiology & Immunology and Medicine/GI Division, Virginia Commonwealth University, USA

Introduction: HIV protease inhibitors (PIs) have been successfully used in highly active anti-retroviral therapy (HAART) for HIV infection. However, accumulating clinical evidence indicates that HAART has changed the clinical profile of HIV infection from a sub-acute lethal disease to a chronic ambulatory disease. There is increasing evidence that microbial translocation across the gut and subsequent activation of the systemic inflammatory response play critical roles in HIV-1 disease progression. Although HAART significantly reduced HIV-1-induced gut microbial translocation, the plasma levels of bacterial DNA remain elevated even in patients, whose virus had been reduced to undetectable levels for several years, suggesting that drug-induced intestinal injury contributes to the increase of gut permeability and chronic inflammation in HIV patients under HAART. However, the cellular/molecular mechanism remains to be identified.

Methods: We have previously shown that activation of ER stress response represents an important cellular mechanism underlying HIV PI-induced inflammatory response. In the present study, we examined the effect of HIV PIs on gut microbial translocation and systemic inflammation in wild type and CHOP-/- mice by measuring serum endotoxin and inflammatory cytokine levels after 4-week treatment.

Results: The results indicate that ritonavir and lopinavir, the two most commonly used HIV PIs in the clinic, significantly increased gut microbial translocation and IL-6 levels in wild type mice, but amprenavir, which does not activate ER stress response, had no effect. However, in CHOP-/- mice, both ritonavir and lopinavir failed to increase serum endotoxin and IL-6 levels.

Discussion/Conclusion: These results suggest that activation of ER stress plays a critical role in HIV PI-induced microbial translocation and systemic inflammation. The burden of gastrointestinal complications in HIV-1 patients is expected to increase as the number of patients living with HIV continues to rise. This study provides important information for the future development of new preventive and therapeutic strategies to reduce HAART-associated complications.
The quantitative analysis of the contrast-enhanced ultrasonography in colorectal carcinomas

Hua Zhuang M.D., Zhi-gang Yang, Ph.D., M.D.

Introduction: Contrast-enhanced ultrasonography has been applied in many clinical areas, but few studies have addressed colorectal cancer. This study is to investigate the feasibility of the contrast-enhanced ultrasonography with the technique of pulse inversed harmonic imaging under low mechanical index to assess microcirculation of colorectal neoplasms and to describe the perfusion features of the cancer.

Methods: The contrast-enhanced ultrasonography of colorectal cancer was performed with the technique of pulse inversed harmonic imaging under low mechanical index in 64 patients, which were subdivided into three subgroups according to the location of the tumor (left-side colon, right-side colon and rectum). The normal intestinal wall of the same study cohort served as control. Repeatability of the measurement of perfusion, the arrival time (AT), time-to-peak (TTP), area under the curve (AUC), peak (PI) and baseline (pre-injection) intensities (BI) were evaluated in the colorectal tumor and normal intestinal wall. Contrast-enhanced intensity (PI minus BI) was calculated. Mean values of the parameters were compared between the carcinoma and the normal wall, between the adenocarcinoma and adenoma, between tumors with and without lymph-node metastases, between the early and advanced adenocarcinoma, and between the low and middle differentiated adenocarcinoma. ROC analysis was performed to determine the cutoff value of area under the curve to discriminate the microcirculation of the adenocarcinoma from that of normal intestinal wall.

Results: Good intra-observer agreements were confirmed in perfusion parameter measurements in both normal stomach and the cancer. Area under the curve was significantly increased in colorectal cancer compared with normal intestinal wall. 112.0 dBsec of AUC was employed as the cutoff value to discriminate the microcirculation of the tumor from that of normal colorectal wall with a sensitivity of 81.03%, and a specificity of 51.02%. There were no significant differences of any perfusion parameters in other comparisons.

Discussion/Conclusion: The contrast-enhanced ultrasonography with pulse inversed harmonic imaging under low mechanical index is a feasible technique for quantifying tumor vascularity and angiogenesis in colorectal cancer. AUC was significantly increased in the colorectal cancer and the cutoff value of 112.0 dBsec of AUC could discriminate the microcirculation of the cancer and the normal colorectal wall.
The amount of alcohol consumption negatively impacts short-term mortality in patients with alcoholic hepatitis: Clinical implications

Jose Altamirano¹, Fatima Higuera³, Andres Duarte-Rojo⁴, Manuel Martinez, Luis Herrera⁴, Juan G. Abraldes¹, Laura Zapata², Marlene Domínguez¹, Pere Ginès¹, Juan Caballería¹ and Ramón Bataller¹

¹Liver Unit, Hospital Clinic i Provincial de Barcelona, IDIBAPS, CIBERehd, University of Barcelona, Barcelona, Spain
²Gastroenterology Unit, Research Department, Hospital Juarez de México, Mexico
³Gastroenterology Unit, Hospital General de Mexico OD, Mexico
⁴Gastroenterology Unit, Instituto Nacional de Ciencias Médicas y Nutrición 'Salvador Zubirán', Mexico
⁵Gastroenterology Unit, Hospital Universitario 'Dr. José E. González' U.A.N.L., Mexico

Introduction: The prognostic stratification of patients with AH is essential for clinical decision-making. We developed the ABIC score, which stratifies patients with low, moderate and high risk of death. Our aims were to validate the performance of the ABIC score in a different cohort and to investigate if the amount of alcohol consumption impacts short-term mortality.

Methods: One hundred and ninety-two patients with full criteria of AH of 4 hospital centers were included (2006–2008). Epidemiological, clinical and analytical data were recorded and the amount of alcohol consumption (g/day) was obtained by a direct questionnaire. The accuracy of different scores to predict short-term mortality (90-days) was compared through the analysis of the area under the ROC curve (AUROC). The prognostic stratification of the ABIC score was evaluated by the Kaplan-Meier method. The identification of prognostic factors of short-term mortality was done by multivariate logistic regression analysis.

Results: The 90 days overall mortality was 50%. The AUROC for the different scores were: Maddrey's DF 0.79; MELD score 0.83; Glasgow score 0.77 and ABIC score 0.82. The ABIC score allowed an accurate discrimination of 3 distinct prognosis subgroups with 14% (low), 50% (moderate) and 80% (high) mortality at 90 days (p < 0.001). The independent prognostic factors were: age, creatinine, bilirubin, leukocytes count and alcohol consumption > 120 g/day. Importantly, the amount of alcohol consumption was an independent prognostic factor related with mortality (patients with > 120 g/day had a 64% mortality rate at 90 days) and was particularly strong among patients with moderate risk of death (30% vs. 62% risk of death, p = 0.02)

Discussion/Conclusion: The ABIC score is useful for the prognostic stratification of patients with AH. An amount of alcohol consumption > 120 g/day has a negative impact on patient mortality. Policies aimed at decreasing alcoholic consumption may have beneficial effects in patients with a high risk at developing AH.
Hepatitis B virus genotypes and subtypes among chronic hepatitis B, liver cirrhosis and hepatocellular carcinoma patients in Pekanbaru, Indonesia

A. Arfianti¹, Andi Zainal², Rita Endriani³, Fauzia Andrini³
¹Department of Medical Biology, Faculty of Medicine, University of Riau, Pekanbaru, Indonesia
²Department of Internal Medicine, Faculty of Medicine, University of Riau/Arifin Ahmad General District Hospital, Pekanbaru, Indonesia
³Department of Microbiology, Faculty of Medicine, University of Riau, Pekanbaru, Indonesia

Introduction: HBV is currently classified into 8 of genotypes (A to H) and 4 of HBsAg subtypes which are adw, ayw, adr, and ayr. Previous studies showed that HBV genotypes and subtypes showed a distinct geographic and ethnic distribution. Additionally, HBV genotypes may influence the clinical manifestation of chronic hepatitis B infection, development of HCC and response to antiviral treatment. The aim of the present study was to investigate the distribution of HBV genotypes and subtypes among different clinical status of chronic hepatitis B in Pekanbaru.

Methods: HBV genotypes were examined based on homology of S gene from this study with those of GenBank Database. Gene S was generated by amplification using polymerase chain reaction (PCR) method, followed by DNA sequencing using dye-labelled terminator method.

Results: A total of 52 of chronic hepatitis B sera was examined in this study, including 10 of HBsAg-positive blood donors, 12 of chronic hepatitis B active patients, 10 of liver cirrhosis patients and 20 of HCC patients. The results showed that there was no significant difference in the distribution of HBV genotypes and subtypes among blood donors, chronic hepatitis B active patients, liver cirrhosis patients and HCC. However, the distribution of HBV genotype was significantly different between cirrhotic-HCC patients and non cirrhotic-HCC patients. Genotype C was predominantly detected among cirrhotic-HCC patients (88.9%), while genotype B was mostly identified among non cirrhotic-HCC patients (72.7%) (p = 0.01).

Discussion/Conclusion: Genotype C was predominant among cirrhotic-HCC patients and might be associated with the development of cirrhotic and noncirrhotic-HCC.
Value of large volume paracentesis in management of ascitic patients with acute variceal bleeding

Abdallah Bahnacy and Magdy Alserafy*
Internal Medicine Department, Menoufiya and Cairo* University, Egypt

**Introduction:** The effect of large volume paracentesis on portal venous pressure as well as portal venous blood flow and the clinical outcome had been studied in two groups of patients with tense ascites and acute variceal bleeding.

**Methods:** After resuscitation injection sclerotherapy was done for all patients followed by large volume paracentesis for group I. Abdominal sonography was done for all patients with Doppler study of the portal vein. Measurement of portal vein diameter (PVD) and portal venous blood flow (PVBF) was done on admission, after sclerotherapy and after paracentesis.

**Results:** PVD was 15.6 ± 1.6 in group I versus 15.4 ± 1.3 in group II and PVBF was 15.6 ± 1.2 cm/sec. in group I versus 15.8 ± 1.7 in group II; this was not significant. After paracentesis PVD and PVBF was decreased significantly 13.8 ± 2.6 mm and 14.8 ± 2.6 cm/sec. versus 15.6 ± 1.6 and 15.6 ± 1.2, respectively.

**Discussion:** We found that PVD and PVBF were not significantly different between both groups neither on admission nor immediately after sclerotherapy. On the other hand these values decreased significantly in group I after paracentesis. These results conclude that large volume paracentesis in cirrhotic patients with tense ascites can participate in reduction of portal pressure. We recommend to do large volume paracentesis in combination with sclerotherapy in treatment of variceal bleeding in those patients.

Key words: portal hypertension; variceal bleeding; ascites
State hepatobiliary system in children with obesity and metabolic syndrome

T.A. Bokova
The Moscow Regional Research Clinical Institute of M. F. Vladimirsky, Moscow, Russia

**Purpose:** To study of hepatobiliary system in children with obesity and metabolic syndrome (MS).

**Materials and methods:** The study involved 200 obese children aged 3 to 16 years: 102 boys and 98 girls. 53% of children identified signs of MS (WHO, 1999). Non-alcoholic fatty liver disease (NFLD) was diagnosed in 54% of children, in 41% identified changes of the gallbladder (GB) wall, in 4% of the stones and 2% biliary sludge were found in the GB. Even in 18% of patients was determined by a lot of loose sediment in the GB. Waist size in children as with NFLD so with cholelithiasis was greater than in children without modification of hepatobiliary tract: 102.0 ± 12.17 and 94.2 ± 12.9 cm (p < 0.005) and 113.5 ± 14.8 and 97.3 ± 12.2 cm, respectively (p < 0.005). Patients with NFLD in contrast to children without her GPT/ALT level was higher (45.1 ± 10.8 and 23.01 ± 11.1 U/L, respectively, p < 0.005), uric acid (432.1 ± 82.3 and 359.1 ± 84.5 mmol/l, p < 0.005), fibrinogen (4.3 ± 0.7 and 3.47 ± 0.55 g/l, p < 0.005), insulin (163.4 ± 103.2 and 114.1 ± 80.7 pmol/l, p < 0.005) and HOMA (5.28 ± 3.74 and 3.39 ± 1.98, p < 0.005). The level of insulin and HOMA was higher in children with changing wall GB: insulin they amounted to 188.4 ± 78.2 pmol/l in children with intact GB – 161 ± 44.3 pmol/l (p < 0.005), HOMA – 6.1 ± 0.5 and 3.9 ± 2.7, respectively (p < 0.005). NFLD was detected in 66.4% of children with MS and 39% of children without MS (p < 0.005), anomalies of GB in 45% and 20% (p < 0.005), change the wall GB in 46% and 35%, sediment in GB in 21% and 14% (p < 0.005), cholelithiasis in 8% and 4.5% of children respectively (p < 0.005).

**Conclusions:** The results indicate etiopathogenetic relationship pathology of hepatobiliary tract and disorders of glucose and lipid metabolism in childhood.
Effects of ursodeoxycholic acid in treatment of children with metabolic syndrome

T.A. Bokova
The Moscow Regional Research Clinical Institute of M. F. Vladimirsky, Moscow, Russia

Purpose: To study the effects of therapy with ursodeoxycholic acid (UDCA) children with metabolic syndrome (MS).

Materials and methods: The study involved 106 children with MS (WHO, 1999) aged 10 to 16 years. In 57% of them registered 4–5 signs of MS and in 35% registered more than 5 signs, in 8% of children were incomplete MS. Non-alcoholic fatty liver disease (NFLD) identified in 66.4% of children, in 18% of them showed signs of steatohepatitis. In 46% of children showed changes of the gallbladder (GB) wall. Cholelithiasis identified in 8% of children. Also lot of friable sediment in the GB defined in 21% of children. The analysis of treatment of 13 children with MS and pathological hepatobiliary system, which in addition to diet therapy received UDCA (Ursofalk®) 10–12 mg/kg/day for 3 months, and six of them for 6 months.

Results: Against the background of therapy has decreased the level of GPT\ALT from 31.8 ± 17.8 to 14.7 ± 8.1 U/l (p < 0.005) and GOT\AST from 29.3 ± 8.5 to 23.3 ± 3.9 g/l. Decreased body-mass index (BMI) with 29.9 ± 5.4 to 26.1 ± 4.1 kg/m², HOMA with 5.3 ± 2.8 to 2.1 ± 0.8 units (p < 0.005), insulin levels with 154.4 ± 70.8 to 65.1 ± 20.4 pmol/l (p < 0.005), glucose with 5.3 ± 0.7 to 4.9 ± 0.8 mmol/l. All patients had improved performance lipidogrammy: reduced cholesterol levels with 4.9 ± 0.6 to 4.5 ± 0.7 mmol/l, triglycerides from 1.5 ± 0.5 to 1.2 ± 0.6 mmol/l, low density lipoprotein cholesterol from 3.2 ± 0.5 to 2.6 ± 0.6 mmol/l, increased levels of high density lipoprotein cholesterol from 1.15 ± 0.2 to 1.22 ± 0.2 mmol/l, with the most significant change in these parameters was noted after 6-month course of therapy.

Conclusions: The use of UDCA in treatment of children with MS improves indices of glucose and lipid metabolism.
The value of MESO (MELD/Na index) scoring system in predicting prognosis of patients with cirrhosis

Chen Lihong, Hu Naizhong, Wang yalei
Department of Gastroenteropathy, the First Affiliated Hospital of Anhui Medical University, Hefei 230022, China

Introduction: To evaluate the value of MESO scoring system in predicting the prognosis of patients with decompensated cirrhosis.

Methods: We present a retrospective cohort study of 190 decompensated cirrhotic hospitalized patients, calculate CTP, MELD, MESO score of each patient using the information collected at the time of admission to our hospital respectively and evaluate the three scoring systems' capacity for predicting the prognosis of cirrhotic patients using the receiver characteristic curve and the area under the curve. Meanwhile, investigating the association between the outcome of patients and MESO index within a single CTP class.

Results: The time of admission as the start-point, and mortality or the time when our reseach end as the end-point. Follow-up time ranges from 2 days to 734 days. 47 (24.74%) patients died within the first 3 months, MESO and MELD of 3-month death group are significantly more than that of 3-month survival group (P < 0.05); MESO predicts the 3-month prognosis more efficiently than MELD and CTP do. Youden index are 49.11%, 48.96% and 31.60% respectively; AUC are 0.83, 0.81, 0.75 (P < 0.05) respectively. Mortality in the group of MESO index more than 1.6 is higher than that in the group of MESO index less than 1.6 (P < 0.05) within a single CTP class.

Discussion/Conclusion: MESO is a useful prognostic predictor for short- and mediate-term prognosis in decompensated cirrhotic patients, and better than MELD and CTP. Combination of MESO and CTP scoring system can predict the outcome of patients with cirrhosis more efficiently within a single class.
The clinical analysis of 82 patients with drug-induced liver injury

CONG Chun-li, SU Bing-zhong
Affiliated Hospital, Inner Medical College, Hohhot 010050, China

Objective: To study and investigate the management of our hospital inpatients with drug-induced liver injury (DILI), to evaluate the efficacy and safety of ursodeoxycholic acid (UDCA) in the treatment of the drug-induced liver injury with acute cholestasis.

Methods: From 2006 to 2010 in our hospital 82 patients were diagnosed as DILI based on their medication history, clinical manifestation, liver function and other laboratory tests. The drugs suspected to induce liver injury were listed, in 82 patients with DILI, 37 men, 45 females, age from 20 to 71 years old. The patients were randomly divided into the treatment group and the control group. The treatment group was given UDCA besides basic therapy, the control group was only treated with conventional therapy.

Results: DILI could be classified as acute hepatocellular injury (32.9%), acute cholestasis (41.4%) and mixtures (25.7%). Most patients recovered rapidly after stopping the relevant medicine, but the mortality rate was 4.87% (4/82), especially the patients had basic liver diseases. The drugs most commonly causing DILI were antituberculosis drugs (29.6%) and Chinese traditional medicine (25.1%). After 4 weeks treatment the effective rate in the treatment group was significantly higher than that in control group (83.5% vs. 58.3, p < 0.05).

Conclusions: The number of patients with DILI was increasing in last few years. Antituberculosis drugs and Chinese traditional medicine may be the main causes of DILI. Combined therapy with UDCA was more effective in improving the symptom and liver function of patients with cholestasis DILI.
Clinical features and effects of ursodeoxycholic acid on Chinese patients with primary biliary cirrhosis

Duan WJ, Ou XJ, Zhang FK, You H, Ma H, Jia JD
Department of Hepatology, Beijing Friendship Hospital, Capital Medical University, Beijing 100050, China.

Introduction: To observe the clinical features and effects of ursodeoxycholic acid on liver biochemical parameters in Chinese patients with primary biliary cirrhosis.

Methods: From 1999 to 2009, 203 patients diagnosed with PBC at the Beijing Friendship Hospital, were reviewed. To evaluate the effects of ursodeoxycholic acid (UDCA), patients treated with UDCA were followed every three months.

Results: Antimitochondrial antibody-negative (n = 14)/positive (n = 96) patients were remarkably similar in terms of clinical manifestations, liver biochemistry indexes and the frequency of antinuclear antibodies. 90 patients treated with UDCA (13–15 mg/kg/d) for 3–72 months. After therapy of UDCA, serum concentration of alkaline phosphatase, γ-glutamyl aminotranspeptidase, alanine and aspartate aminotransferase were significantly decreased, reaching statistical significance at all time points of treatment (P < 0.05). However, there were no significantly changes in serum concentration of TBIL and CHE during the follow up.

Discussion/Conclusion: Antimitochondrial antibody-negative/positive PBC patients showed no significant difference in clinical manifestations and laboratory tests. Treatment with UDCA is associated with a marked improvement in serum biochemical markers of cholestasis such as alkaline phosphatase, γ-glutamyl aminotranspeptidase, as well as in serum alanine and aspartate aminotransferases.
Frequent hypermethylation of the 14-3-3 sigma gene in human hepatitis B virus-related hepatocellular carcinoma

Yu-Feng Gao, Qian Su, Jia-Bin Li, Xu Li
Department of Infectious Diseases, The Second Affiliated Hospital of Anhui Medical University, Hefei 230032, Anhui Province, China

Introduction: 14-3-3 sigma is one isoform of the 14-3-3 family, and it has been most directly linked to carcinogenesis and tumor progression. To detect the methylation status of 14-3-3 sigma gene in hepatitis B virus (HBV)-related hepatocellular carcinoma (HCC) and to investigate the relationship between the hypermethylation of 14-3-3 sigma gene and the development of HCC.

Methods: Using methylation-specific PCR (MSP) to detect methylation status of 14-3-3 sigma gene in samples of excised 45 paired specimens of carcinoma and adjacent non-tumorous liver tissues from HCC patients, 6 normal liver tissues also detected.

Results: Among the 45 HBV-related HCC patients, 14-3-3 sigma gene methylation was detected in 91.1% of the HCC tissues, and in adjacent non-tumorous liver tissues covered 73.3%. But in 6 normal liver tissues, nonmethylation specific fragments were detected ($\chi^2 = 21.633, P = 0.000 < 0.05$).

Discussion/Conclusion: Hypermethylation of 14-3-3 sigma gene is frequent in HBV-related HCC, probably occur at the early stage of hepatocarcinogenesis. We predict it may act as diagnostic marker to detect early period of HBV-related HCC.
Small intestinal dysmotility and bacterial overgrowth in patients with liver cirrhosis

V. Gerova, S. Stoynov
Clinic of Gastroenterology, University Hospital Queen Joanna, Sofia, Bulgaria

Aim: To assess small intestinal motility and the prevalence of small intestinal bacterial overgrowth (SIBO) and to analyze its relationship with the etiology of the disease and severity of liver dysfunction in patients with liver cirrhosis (LC).

Materials and methods: The study included 43 patients with LC (25 alcohol- and 18 viral-induced) and 10 healthy controls. According to Child-Pugh classification 7 of the patients were with class A, 14 class B and 22 class C. Oro-caecal transit time (OCCT) and SIBO were measured indirectly by lactulose breath test.

Results: In 4 of the patients no peak of H$_2$ was recorded. Prolonged OCCT was established in 74.3% of patients and in 10% of healthy subjects (p < 0.05). In comparison to controls, LC patients had significantly prolonged OCTT (123.33 ± 27.31 vs 87.01 ± 11.59 min) and higher basal breathed H$_2$ (15.85 ± 8.77 vs 6.24 ± 3.39 ppm), p < 0.05). Of the 39 patients with LC, 12 (27.9%) had SIBO as compared to none of the healthy controls. All cirrhotics with SIBO had delayed small bowel transit. SIBO was significantly higher in patients with ascites (35.7%) than in those without ascites (13.3%) and among patients with Child-Pugh class C (36.4%) than in those with B (21.4%) or class A (14.3%) (p < 0.05). SIBO was documented in 83.3% of the alcohol- and only in 16.7% of the viral-induced LC (p < 0.05). There were no data of spontaneous bacterial peritonitis in our patients.

Conclusion: Abnormal small bowel motility and SIBO are common in patients with LC. SIBO is more frequent in the cases with alcoholic etiology and advanced liver dysfunction. Future larger trials are needed to establish the exact role of these alterations in patients with LC.
Attenuation of hepatic triglyceride accumulation and insulin resistance in ob/ob mice by macrophage (Kupffer cell)-specific overexpression of cholesteryl ester hydrolase

Shobha Ghosh, Jinghua Bie, Bin Zhao
Department of Internal Medicine, VCU Medical Center, Richmond, VA 23298-0050, USA

Introduction: Neutral cholesteryl ester hydrolase (CEH) releases free cholesterol from cellular cholesteryl ester (CE) stores and reduces cellular CE burden. Macrophage specific transgenic expression of CEH not only results in attenuated diet-induced atherosclerosis in ldlr deficient mice and improved insulin sensitivity in this model but also reduces systemic inflammation. In the present study we tested the hypothesis that CEH over-expression mediated reduction in inflammation will attenuate hepatic lipid accumulation.

Methods: We crossed CEH transgenic mice with leptin deficient ob/ob mice and littermates (ob/ob or ob/obCEHTg) were fed 0.2% cholesterol containing chow diet for 4 weeks. Insulin sensitivity was determined by intra-peritoneal glucose tolerance test. At the time of necropsy, liver was fixed for histological analyses and also used to extract lipids.

Results: There was no significant difference in the body weight or visceral adipose tissue mass between the two genotypes. However, there was a significant decrease in hepatic triglyceride (31.78 ± 4.16 vs 23.45 ± 4.23 ug/mg, p = 0.006) as well as total cholesterol accumulation (26.59 ± 3.02 vs 13.58 ± 1.42 ug/mg, p = 2.9E-6) in ob/obCEHTg mice indicating attenuation of hepatic steatosis. Figure 1 shows representative H&E stained liver sections showing decreased lipid accumulation (white areas) in ob/obCEHTg. Consistent with decreased lipid accumulation in the liver, ob/obCEHTg were more insulin sensitive as assessed by improved glucose tolerance test.

Discussion/Conclusion: These studies demonstrate that by regulating macrophage (Kupffer cell) cholesterol homeostasis, CEH regulates hepatic steatosis and provide evidence for cross-talk between Kupffer cells and hepatocytes in regulating hepatic lipid metabolism.
Figure 1

**Transgenic Expression of CEH reduces Hepatic Lipid Accumulation**

**Histological Analyses**

**A: H&E Stained Liver Sections**
- *ob/ob*
- *ob/obCEHTg*

**B: Magnified Images of Single Cells**
- *ob/ob*
- *ob/obCEHTg*
Beta lipoprotein faster migration is sensitive parameter for acute and chronic active hepatitis

Dr. Kareem Hameed Hassan
Basra General Hospital, Basra, Iraq

Introduction: Unfortunately no attention had been given to the speed of lipoproteins migration. Beta lipoprotein migration (BLM) had not been reported clearly, nor have detailed studies of lipoproteins migration been described. In the presenting investigation paper electrophoresis was used to characterise (BLM) in acute and chronic active hepatitis.

Methods: The series included 48 patients with biopsy proven chronic active hepatitis (CAH), 36 patients with acute hepatitis and 21 non-affected control subjects. Rotten methods of Baghdad Medical City laboratories were used to estimate serum concentration of protein, AST, ALT, alkaline phosphatase and bilirubin. electrophoretic separation of serum lipoproteins was carried out on 32 cellulose acetate plates (hellena 76 x 60 m). A constant potential of 220 volts was applied for 25 minutes, staining of strips was carried in oil O staining solution. Mill metric measurement (peak scale x 7) was used to measure BLM, beta lipoprotein faster migration (BLFM) was estimated according to the simple equation:

$$BLFM = \frac{\text{patient BLM}}{25 \text{ min}} - \frac{\text{control subject BLM}}{25 \text{ min}}$$

Serum bilirubin of the studied cases was used to test sensitivity of (BLFM) in expressing the severity of liver injury.

Results: In acute hepatitis the highest mean BLM (2.6 mm/25 min) was evident in severe cases belong to the highest bilirubin group (30–40 mg/100 ml), while the least mean BLM (0.928 mm/25 min) was evident in cases of mild severity which belong to bilirubin group (2–10 mg/100 ml) and the difference was significant (p < 0.001). In the chronic cases the least mean BLM (0.56 mm/25 min) was evident in the group with bilirubin level less than (2 mg/100 ml), while the highest mean BLM (3.05 mm/25 min) was in the group with highest bilirubin level (20–30 mg/100 ml) and the difference was significant (p < 0.001).

Discussion/Conclusion: The major conclusion of this study is that acute and CAH resulted in remarkable faster migration of beta lipoproteins. BLM is sensitive parameter for acute and CAH, it is simple and reliable test for diagnostic and prognostic purposes, especially for CAH patients with normal serum bilirubin and enzymes. It is of marked prognostic value in patients with hepatic coma. Lipoprotein composition abnormalities and charges defect are proposed to be the cause for BLM, a concept which can be utilized for trials for management of hepatic coma.
The role of TGF-βs expressed by biliary epithelial cells in the pathogenesis of cholestatic liver disease

HE yao, CHEN bai-li, YANG rong-ping, ZENG zhi-rong, REN ming
Department of Gastroenterology, the First Affiliated Hospital of SUN Yat-sen University, Guangzhou, 510080, China

Objective: From our previous study we proved that proliferation of biliary epithelial cells (BDECs) play a key role in the pathogenesis of BDL induced liver cholestasis, but the final mechanism is still unclear. Therefore, we designed this study to investigate the change of liver histology, proliferation of BDECs, and expression of TGF-βs in different stages of liver cholestasis.

Methods: 1) Rat cholestatic livers were induced by common bile duct ligation (BDL) and separated into 3 groups, namely control group (D0), 7 days after BDL group (D7), and 18 days after BDL group (D18). 2) Histological changes of livers in different groups were evaluated based on Knodell HAI score. 3) Real time PCR was used to detect the expression of TGF-βs in liver tissue and isolated BDECs in different groups. 4) Statistically analyzing the correlation between Knodell HAI score and the levels of TGF-β1 mRNA. 5) In vitro study was performed to investigate the effect of TGF-β1 on an immortalized mouse intrahepatic biliary epithelial cell line (mIBEC).

Results: 1) Knodell HAI score and the proliferation of intrahepatic bile ducts increased as the liver cholestasis aggravated. 2) The levels of TGF-β1, TGF-β2, and TGF-β3 mRNA were significantly up-regulated in liver tissues and BDECs as the liver cholestasis aggravated. 3) Positive correlation was found between Knodell fibrotic score and the levels of TGF-β1 mRNA in liver tissues and BDECs (r = 0.9376, P < 0.05 and r = 0.9682, P < 0.01). 4) In vitro study showed that TGF-β1 inhibited the proliferation of mIBEC.

Conclusions: 1) Liver injury and the levels of TGF-βs mRNA expression increased as liver cholestasis aggravated. 2) The interaction of TGF-β1 and BDECs plays an important role in the pathogenesis of BDL induced cholestatic liver disease. 3) Up-regulated expression of TGF-β1 mRNA in the proliferated BDECs participates in the formation of BDL induced cholestatic liver fibrosis.

Key words: biliary epithelial cell; TGF-β; cholestatic liver disease; rat
Analysis of risk factors of patients with chronic liver failure complicated invasive fungal infections

HU Ai-rong, TAN Jun
Ningbo Infectious Diseases Hospital, Ningbo, Zhejiang Province 315016, China

Introduction: To evaluate the risk factors of chronic liver failure (CLF) complicated invasive fungal infections (IFI) and prevention and treatment.

Methods: The risk factors of 52 patients with CLF complicated IFI were analyzed retrospectively and were compared with those not complicated IFI. Risk factors were analyzed by chi-square test, logistic regression test and Ridit test.

Results: In 52 patients with CLF complicated IFI, there were 69 fungal infections in different tissue and organs, the most were in lungs, but other tissue and organs especially intestinal tract and abdominal cavity infections were rising. Candida albicans infections were the most, but cryptococcus neoformans infections and aspergillus infections were rising. The risk factors included species of bacteria infections, serum total bilirubin, hospital days, times of antibiotics using, invasive operation, species of antibiotics and degrees of ascites. The mortality of patients with CLF complicated IFI were much higher than those not complicated IFI.

Conclusion: Patients with CLF complicated IFI have poor progress and prognosis. The effective prevent methods are treating primary disease actively, reducing hospital days, detecting patients’ body fluids closely, identifying source of infection as early as possible, using antibiotics correctly, reducing or avoiding invasive operation, using immunomodulators and disinfecting air regularly.

Key words: chronic liver failure; invasive fungal infections; risk factors
Short-term efficacy and safety of standard interferon with a low accelerating dosage regimen in HCV-related decompensated cirrhotics

JI Fanpu, DENG Hong, CAI Zhifang, XUE Hongan, TIAN Changyin
Department of Infectious Disease, the Second Affiliated Hospital of Xi'an Jiaotong University, Xi'an, China

Introduction: Patients with HCV-related decompensated cirrhotics are associated with a poor prognosis and are difficult to treat in view of concerns about the efficacy and safety of interferon-based therapy. Nevertheless, antiviral therapy might have a substantial benefit in these patients as it potentially minimizes disease progression and prevents recurrence after liver transplantation. We evaluated the short-term efficacy and safety of standard interferon with a low accelerating dosage regimen (LADR) in combination with ribavirin in these patients in 24 weeks.

Methods: Twelve patients with HCV-related decompensated cirrhotics were prospectively investigated. All patients had clinical complications of cirrhosis and were interferon naive. The Child-Pugh stage was A in four patients, B in five and C in three, the score was 7.8 ± 2.0. HCV-genotype distribution was 1b (n = 8), 2a (n = 3) and 1 (n = 1). Patients received 0.9–1.5 MU/2d standard interferon-α2b with increasing dose regimen and weight-based ribavirin (800–1000 mg/d) for 48 weeks.

Results: All patients had adverse events such as weary, weight loss, fever, anorexia, nausea, neutropenia, anemia and thrombocytopenia. Severe adverse events occurred in three patients including variceal hemorrhage, thrombocytopenia (11 x 10^9/L) accompanied by gum, nasal mucous membrane and skin bleeding and severe hemolysis (HGB 43 g/L) accompanied by spontaneous bacterial peritonitis, massive ascites. Adverse events caused treatment withdrawal in two cases. On-treatment respond (OTR) was obtained in 8 subjects (67%) in 24 weeks. Compared with baselines, the levels of serum ALT, ALB, PTA, and Child-Pugh score were significantly improved (P < 0.05) and decreased in the level of serum TBIL (P > 0.05) in patients with OTR.

Discussion/Conclusion: Standard interferon with LADR in combined with ribavirin in treatment of patients with HCV-related decompensated cirrhotics is effective and 67% patients obtain OTR in 24 weeks. Adverse events are common, a close monitoring is necessary during antiviral therapy.
Waist-to-hip ratio is a superior predictor for non-alcoholic fatty liver disease

JIANG Li, CHEN Xue-wan, ZHENG Rui-dan, CHEN Jie, MENG Jia-rong, LU Lun-gen
*Research and Therapy Center for Liver Diseases, the 175th Hospital of PLA, Zhangzhou 363000, China
Department of Gastroenterology, First Affiliated People’s Hospital of Shanghai, Jiaotong University, Shanghai 200080, China
Corresponding author: ZHENG Rui-dan, LU Lun-gen, E-Mail: zhengruidan@tom.com

Objective: To investigate the most effective anthropometric index as a predictor for non-alcoholic fatty liver disease (NAFLD).

Method: This retrospective case-control study was comprised of 127 patients from Centers for Liver Disease in Southeast Hospital Affiliated to Xiamen University. Liver ultrasound B scans and liver biopsy were analyzed for each patient. 77 patients were diagnosed as NAFLD, and 50 patients were diagnosed as non-NAFLD. Data of height, weight, waist circumference, hip circumference, waist-to-hip ratio (WHR), waist-to-height ratio (WHR) were collected from each patient. Risk factors were determined by Mantel-Haenszel chi-square test and analyzed using logistic regression models and empirical receiver-operating characteristic curves.

Results: Compared with non-NAFLD group, NAFLD group has significantly higher BMI ($t = 8.541$, $P < 0.001$), WHR ($t' = 10.783$, $P < 0.001$) and WHtR ($t' = 9.113$, $P < 0.001$). Moreover, BMI ($\chi^2 = 25.017$, $P < 0.001$), WHR ($\chi^2_{MH} = 56.793; P < 0.001$) and WHtR ($\chi^2_{MH} = 42.695; P < 0.001$) are also risk factors of NAFLD examined by M-H chi-square test. A Linear forward binary logistic regression was performed to evaluate the relationship between NAFLD and its related factors. BMI ($\text{OR}_j = 11.757$) and WHR ($\text{OR}_j = 3.094$) were chosen as predictors for NAFLD, reaching an overall predicting percentage as 85%. Receiver-operating characteristic curves showed that BMI, WHR, WHtR and WC had area under curves as 0.854, 0.916, 0.878 and 0.876, respectively. Therefore, WHR values most for diagnosing NAFLD. Especially when choosing 0.891 as the cutoff point, the sum of sensitivity and specificity maximizes.

Conclusion: WHR serves as the most effective anthropometric index for predicting NAFLD.

Key words: non-alcoholic fatty liver disease, predictors; body mass index; waist-to-hip ratio; waist-to-height ratio; waist circumference

基金项目: 上海市科学技术委员会 (054119618); 漳州市科技局基金 (Z04094)
*作者简介: 蒋瓅, 女, 现厦门大学预防医学系2006级本科生
通讯作者: 郑瑞丹, 陆伦根. E-Mail: zhengruidan@tom.com
Abdominal ultrasound accurately detects complications in patients with hepaticojejunooanastomosis

I. Kajzrlíková, P. Vitek, J. Chalupa
Beskydy Gastrocentre, Department of Internal Medicine, Hospital Frydek-Mistek, Czech Republic

Introduction: Hepaticojejunooanastomosis is a surgical replacement of the biliary tract. The most frequent indications for this procedure are biliary duct injuries, other benign biliary tract stenoses, biliary tumors, choledochal cysts and biliary atresia in children. The main complication of this method is stenosis of the anastomosis, which usually presents as a recurrent cholangitis, cholestasis with development of jaundice and elevation of cholestatic liver enzymes.

Methods: We retrospectively reviewed the cases of eight patients with a history of hepaticojejunooanastomosis for benign disorder with a view to the role of ultrasound examination in their follow-up. In all patients the diameter of anastomosis was measured and presence of biliary duct dilation, aerobilia, hepaticolithiasis, retained drains, absceses and free fluid in abdominal cavity were looked for.

Results: All eight patients had hepaticojejunooanastomosis-related complications during the follow up. The most frequent complication was cholangitis in 8 patients, followed by development of hepaticolithiasis in 2 patients a spondylodiscitis in one patient. Abdominal ultrasound was used as a primary diagnostic modality in the follow up of all patients. When a complication was suspected, it was followed directly by an invasive therapeutic method (PTD, ERC, CT-guided drainage), in four patients there were further non-invasive diagnostic tests indicated. Further non-invasive tests have not brought any new information, they only confirmed the ultrasound findings. If the clinical picture, laboratory tests and ultrasound examination were taken together, we were able to accurately detect complications in all patients.

Discussion/Conclusion: According to our results we can conclude that abdominal ultrasound is an accurate method for the detection of hepaticojejunooanastomosis-related complications and should be preferred in the surveillance of these patients.
The correlation between liver stiffness and serum markers of fibrosis in patients with chronic hepatitis B

V. Kawengian¹, B.J. Waleleng¹, N. Tendean Wenas¹, L. Rotty¹, M. Abdullah², A.A. Rani²
¹Division of Hepatology, Department of Internal Medicine, University of Sam Ratulangi/Prof. dr. R.D. Kandou Hospital, Manado, Indonesia
²Division of Gastroenterology, Department of Internal Medicine, Faculty of Medicine, University of Indonesia/dr. Cipto Mangunkusumo Hospital, Jakarta, Indonesia

Introduction: A progression of liver fibrosis is very important to determine the treatment and the prognosis of chronic hepatitis B. The gold standard for assessing fibrosis stage is liver biopsy. However, it is limited by invasiveness and patient discomfort. In addition to liver biopsy and Fibroscan, liver fibrosis stage could be predicted by an inexpensive routine laboratory test that is serum markers of fibrosis (APRI, Forns index, FIB-4). The aim of the study was to determine the correlation between Liver Stiffness (LS) and APRI, Forns index, FIB-4 in patients with chronic hepatitis B.

Methods: Twenty chronic hepatitis B patients were recruited into this cross sectional study. LS were evaluated using Fibroscan. Serum markers of fibrosis including APRI, Forns index, FIB-4 was examined using ELISA. Statistical analysis was performed using SPSS.

Results: The study population included 20 patients, consisted of 9 males (45%) and 11 females (55%). The youngest age was 18 years and the oldest was 68 with a mean age of 43.45 years and standard deviation (SD) of 14.862. Based on the statistical analysis by using Spearman’s rho correlation test, there was a significant correlation (p = 0.001) between LS and APRI, LS and Forns index, LS and FIB-4. The r value for LS and APRI, LS and Forns index, LS and FIB-4 were 0.677; 0.794; 0.796, respectively. The greatest r value was FIB-4.

Conclusions: These were a strong correlation between liver stiffness and serum markers of fibrosis.

Key words: liver stiffness; APRI; Forns index; FIB-4; hepatitis B
Stimulation of human hepatic stellate cells by cytochrome P4502E1-mediated oxidative stress

LI Jing, LIU Tian-hui, YOU Hong, XU You-qing
Department of Internal Medicine, Beijing Tiantan Hospital, Capital Medical University, Beijing 100050, China

Introduction: To explore the stimulation of human hepatic stellate cells by cytochrome P4502E1-mediated oxidative stress.

Methods: We had steadily transfected a recombinant eukaryotic expression plasmid PCI-CYP2E1 and PCI-neo to HepG2, named HepG2/CYP2E1 and HepG2/PCI. We examined the expression of mRNA and protein of HepG2/CYP2E1, compared with HepG2/PCI and HepG2. We examined the level of MDA in culture medium of HepG2/CYP2E1, compared with HepG2/PCI and HepG2. LX2 were co-incubated with HepG2/CYP2E1, HepG2/PCI and HepG2. After 48 hours, the level of hydroxyproline in culture medium was examined. And the cells were lysated and total RNA and protein were extracted with the TRIzol reagents and protein lysis respectively. COL-1 and MMP2 mRNA levels were detected by RT-PCR and analyzed semi-quantitatively, PICP proteins were measured by ELISA method. Zymography was performed to investigate MMP2 enzymatic activities.

Results: Compared with HepG2 and HepG2/PCI, the level of MDA excreted from HepG2/CYP2E1 could significantly increase (P < 0.01). After co-incubated for 48 hours, COL-1 mRNA had no difference among the groups. PICP protein, excreted by LX2 co-incubated with HepG2/CYP2E1, significantly increased (P < 0.01). MMP2 gene expression and enzymatic activities of MMP2 showed by zymography had no difference among the groups.

Discussion/Conclusion: CYP2E1 could induce oxidative stress. CYP2E1 could up-regulated LX2 to excret hydroxyproline. CYP2E1 had no effect on COL-1 mRNA, but it could up-regulated PICP protein expression. CYP2E1 had no effect on MMP2 mRNA level and enzymatic activities of MMP2.
The role and clinical significance of hepatic stellate cells in hepatocellular carcinoma

Li Liang, Yang Ling, Ye Jin, Wang Baoyong, Zhou Wen, Hou Xiaohua
Department of Gastroenterology, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, Hubei 430022, China
Correspondence should be addressed to: Yang Ling: yang_ling@yahoo.com.cn

Introduction: To investigate the role and status of hepatic stellate cells in primary hepatocellular carcinoma and analysis their clinical significance.

Methods: Immunofluorescence, RT-PCR and Western Blot were used to test the expression of α-SMA, CD133 and p75NTR in 30 specimens of hepatocellular carcinoma tissue and paired normal tumor-adjacent tissue.

Results: The expression of α-SMA and CD133 mRNA and protein in 30 cancers are obviously higher than in tumor-adjacent tissue, which have statistical significance (p < 0.05) and the expression of α-SMA and CD133 have positive correlation with tumor differentiation and AFP level. The expression of p75NTR in cancer is lower than in tumor-adjacent tissue, which has statistical significance. The expression of p75NTR has negative correlation with tumor differentiation.

Discussion/Conclusion: There are CD133 positive hepatic stellate cells found in hepatocellular cancer and their numbers in cancer are obviously more than those in tumor-adjacent tissue, which have statistical significance (p < 0.05) and the expression of CD133 positive HSC have positive correlation with the grades of tumor malignancy. HSC have the ability of vicious transformation besides self-repair, proliferation and differentiation. So we could figure that hepatic stellate cells might have some characteristics of cancer stem cells and play certain part in tumorigenesis and metastasis. The expression of p75NTR, as the surface antigen of HSC, decreased in hepatocellular cancer. We might conclude that p75NTR might mutate during the course of vicious transformation and lose the ability of regulate cell apoptosis. We firgue that p75NTR might be a potential tumor suppressor gene therefore.
Adjuvant gene therapy followed by orthotopic liver transplantation (OLT) for hepatocellular carcinoma (HCC) beyond the Milan criteria – A prospective study

Li Lixin
Beijing Transplantation Center, ChaoYang Hospital, Beijing, P. R. China

Introduction: Liver transplantation is the only curative treatment for patients with cirrhosis and unresectable hepatocellular carcinoma (HCC) without extrahepatic dissemination. Patients undergoing liver transplantation for hepatocellular carcinoma within the Milan criteria (single tumour \( \leq 5 \text{cm} \) in size or \( \leq 3 \) tumours each \( \leq 3 \text{cm} \) in size, and no macrovascular invasion) have an excellent outcome. However, survival for patients with cancers that exceed these criteria remains poor. In patients with hepatocellular carcinoma (HCC) exceeding the Milan criteria, the recurrence rate after liver transplantation is over 50%. The aim of this study was to explore the survival of patients with tumours that exceed the Milan criteria after ADV-TK therapy is an established adjuvant treatment in cancer. To assess whether the criteria could be less restrictive, enabling more patients to qualify as transplant candidates.

Methods: Between January 2003 and September 2006, 56 patients with HCC beyond the Milan criteria participated in the study over a follow-up period of 62 months. Among those patients, 16 received OLT only, 40 received OLT combined with ADV-TK therapy. All HCC patients enrolled in this study exceed the Milan criteria, no metastasis in lungs or bones detected by CT or MRI scan.

Results: The 2 groups were comparable in all clinicopathologic parameters. The overall survival in the OLT plus ADV-TK therapy group was 67.8% at four years, and the recurrence-free survival in the same group was 69.5%, both being significantly higher than those in the transplantation only group. The patients with vascular invasion received OLT plus ADV-TK therapy seemed to postpone recurrence time when compared with the patients received OLT only, but no significant difference of overall survival rates was detected between two groups. In no-vascular invasion subgroup, the overall survival and recurrence-free survival were both 100% in patients received OLT plus ADV-TK, significantly higher than those in patients received LT only. Macrovascular invasion is strongly associated with high rates of recurrence and diminished survival after LT.

Discussion/Conclusion: Locoregional ADV-TK therapy may have some role for reducing the dropout rate before transplantation. Adjuvant ADV-TK therapy to the patients with primary liver carcinoma exceeding Milan criteria could increase the survival rate, reduce the possibility of tumor recurrence, especially to HCC patients with no-vascular invasion. The ADV-TK therapy of the HCC patients exceeding Milan criteria is safe, feasible and acceptable. We propose the current criteria for OLT based on tumor size may be expanded while OLT plus ADV-TK therapy.
Analysis of 42 potential antiviral resistance mutation sites of HBV reverse transcriptase in chronic HBV infection patients with nucleos(t)ide treatment

Li Xiao-Guang, Xu Jie, Li Tong, Yang Jing-Xian, Liu Bao-Ming, Li Lu
Peking University Third Hospital and Peking University Health Science Center, 100191 Beijing, China

Introduction: Serum samples of 60 chronic hepatitis B patients with nucleos(t)ide analogue (NA) treatment from one hospital in Beijing, China were obtained from January 2008 to December 2009. The genotypic resistance of hepatitis B virus (HBV) was characterized.

Methods: Full-length HBV reverse transcriptase (RT) sequences were amplified, sequenced and analyzed, on which NA resistant (NAr) mutations at 42 potential antiviral resistance mutation sites.

Results: Among 60 HBV isolates, 16 (26.67%) and 44 (73.33%) were genotype B and C, respectively; and 34 (56.67%) harboured NAr mutations. The mutations including classical resistance mutations (rt80, rt169, rt180 rt181, rt204, rt236) and no-classical resistance mutations (rt38, rt53, rt124, rt126, rt128, rt134, rt191, rt207, rt214, rt221, rt224, rt229, rt238, rt242). In classical resistance mutations, rtM204I/V, rtL80I/V and rtL180M mutations were detected at the more frequency among 60 isolates. In no-classical resistance mutations, rt124, rt134, rt191, rt224, rt229, rt238 mutations more than others.

Discussion/Conclusion: More than half of the studied population harboured NAr HBV with complicated mutation patterns. The evolution and clinical impacts of the most prevalent rtM204 mutations and the no-classical NAr mutations rt191 and rt229 are of interest for further investigation.
Expression of leptin and its correlation with component of extracellular matrix in hepatic fibrosis

Lu Cuihua, Xu Jing, et al.
Department of Gastroenterology, The Affiliated Hospital of Nantong University, Nantong 226001, China

Objective: To investigate the expression of leptin in hepatic fibrosis of rat and its correlation with I,III collagen.

Methods: Liver fibrosis models were made by injection with 60% CCl₄. The expression of leptin and chief component of extracellular matrix collagen I and III were assayed by reverse transcription polymerase chain reaction, Western blot and immunohistochemistry, respectively.

Results: Immunohistochemistry: The expression of leptin, collagen I and collagen III were slight in normal liver tissues. In the model groups, the expression began to increase at the end of the 2nd week after injection with CCl₄. The common area of the expression of leptin, collagen I and collagen III were detected mainly in central veins, portal tracts, and proliferative portal space. The expression of them were found obviously higher at 4th, 6th week after injection with CCl₄. The expression of them were enhanced gradually during the experimental hepatic fibrosis, a positive correlation was found between the expression of leptin and collagen I, collagen III (P < 0.05). RT-PCR: Leptin mRNA was found in the fibrotic liver tissue induced by CCl₄ injection and its expression was found obviously higher than those in normal rats (P < 0.05). Expression of these mRNA were detected little in normal liver tissues, and was found obviously higher at 2nd, 4th, 6th weeks after CCl₄ injection. The expression of leptin and I, III collagen were enhanced obviously during the experimental hepatic fibrosis, a positive correlation was found between the mRNA expression of leptin and I, III collagen (P < 0.05).

Conclusion: In the process of hepatic fibrosis induced by CCl₄ injection in rats, expression of leptin, I, III collagen are increased with the development of hepatic fibrosis. An positive correlation was between the expression of leptin and collagen I, III. So, leptin probably participate the synthesis of ECM in hepatic fibrosis.
Liver injury in experimental sepsis: The late phase effects of hyperbaric and normobaric oxygen therapies

Department of Internal Medicine, Intensive Care Unit of Internal Medicine, Department of Physiology, Gulhane School of Medicine, Ankara, Turkey

Background and aims: The liver is one of the most frequently affected sites in sepsis. Hyperbaric oxygen (HBO) therapy reverses many pathogenic events involved in the mechanism of sepsis. However, its use in an intensive care unit is currently not available. Some studies have reported normobaric oxygen (NBO) treatment as an alternative to HBO with similar effects. In the present study, the effect of HBO versus NBO treatment on tissue oxidative stress parameters and histological injury was compared in a rat sepsis model.

Methods: Forty 40 male Wistar rats were divided into four with 10 animals in each group. Group 1 = sham, group 2 = sepsis plus cefepim (control), group 3 = sepsis plus cefepim plus HBO, group 4 = sepsis plus cefepim plus NBO. Sepsis was induced via intraperitoneal (i.p.) viable Escherichia coli injection. All treatments were started six hours after the induction of sepsis. Cefepim was administered i.p. HBO was administered 90 min b.i.d at 2.4 atm. NBO was administered 90 min b.i.d with 5 l/min oxygen at 1 atm. All animals were killed by the 5th day of treatment.

Results: Liver tissue malondialdehyde and superoxide dismutase levels were lower in group 3 (0.33 ± 0.05 mmol/g protein, 47.88 ± 9.34 U/g protein) and group 4 (0.39 ± 0.09 mmol/g protein, 70.48 ± 11.48 U/g protein) compared to group 2 (0.43 ± 0.11 mmol/g protein, 61.39 ± 14.88 U/g protein). Glutathione peroxidase level was higher in all sepsis groups with no difference in between. Tissue myeloperoxidase (MPO) level was increased in all sepsis groups but it was relatively lower in HBO treated group 3 (12.53 ± 2.54 U/L) compared to NBO treated group 4 (14.65 ± 2.42 U/L). It was similar in groups 2 and 3 (13.30 ± 2.77 U/L). Histopathological results in liver were not different after addition of either HBO or NBO to cefepim in sepsis induced groups.

Conclusions: In rat sepsis, oxidative liver injury is reduced after HBO administration but not after NBO. Both options have no effect over antbiotherapy in terms of histological recovery. The role of bedside NBO as an alternative to HBO therapy needs more research.
The role of heme oxygenase-1 on nutritional steatohepatitis in mice

Yue-Min Nan, Rong-Qi Wang, Wen-Juan Wu, Bao-Li Liang, Su-Xian Zhao, Na Fu, Jun Yu
Department of Traditional and Western Medical Hepatology, Third Hospital of Hebei Medical University, 139 Ziqiang Road, Shijiazhuang 050051, P. R. China
Tel: (86)-311-88602151, Fax: (86)-311-87023626, E-Mail: nanyuemin@163.com

Introduction: There are an overwhelming number of studies postulating a protective role of the upregulation of the microsomal enzyme, heme oxygenase-1 (HO-1) in oxidant-induced tissue injury. However, its protective effect on non-alcoholic steatohepatitis (NASH) is not clear. This study aimed to elucidate the effect and the mechanism of HO-1 on NASH in mice.

Methods: C57BL/6J mice were fed with a methionine-choline deficient (MCD) diet for four weeks to induce steatohepatitis. HO-1 inducer hemin, HO-1 inhibitor zinc protoporphyrin IX (ZnPP-IX) and/or an adenovirus vector that expressed HO-1 (Ad-HO-1) were respectively intraperitoneal injected three times per week. Hepatocyte apoptosis was assessed by the TUNEL assay, the mRNA and protein expression of apoptosis related genes, hepatic inflammatory factors were assayed by RT-PCR and Western blot.

Results: MCD feeding mice showed increasing serum ALT and AST, progressive hepatic injury including hepatic steatosis and inflammatory infiltration. TUNEL-positive hepatocytes were markedly increased in NASH confirming the occurrence of apoptosis. Hepatic steatosis, hepatocyte apoptosis and necroinflammation were attenuated by administration of hemin and/or Ad-HO-1. This effect was associated with increase of HO-1 protein and activity, downregulation of sterol regulatory element binding protein isoform-1c (SREBP-1c), suppressed expression of cytochrome P450 (CYP2E1), lowered activity of nuclear factor kappa B (NF-κB) and cytochrome C (Cyt-C), up-regulated anti-apoptotic gene Bcl-2 and down-regulated pro-apoptotic gene Bax. A contrary effect was observed in mice injected with ZnPP-IX.

Discussion/Conclusion: The present study provided a morphological and molecular biological evidence for the protective role of HO-1 in ameliorating hepatic steatosis, hepatocyte apoptosis and necroinflammation in experimental nutritional steatohepatitis.
Viral hepatitis in patients with chronic renal insufficiency on hemodialysis

O.B. Nepesova, A.G. Japarova, H.E. Blum
Turkmen State Medical Institute, Ashgabat/Turkmenistan
Department of Medicine II, University Hospital Freiburg, Germany

Introduction: Viral hepatitis is one of the major problems of internal medicine and infectious diseases worldwide. Viral hepatitis acquired by contamination is an important issue in hemodialysis units, especially HBV and HCV infection. Chronic hepatitis B and C carry a high risk of progression to liver cirrhosis and hepatocellular carcinoma that are associated with significant morbidity and mortality.

Methods: We examined 50 patients with chronic renal insufficiency in the Department of Hemodialysis in the Treatment Consultation Centre of Turkmenistan. The following examinations were performed: ultrasound, routine laboratory analyses, and serological markers of viral hepatitis, including HBsAg, anti-HBs, HBeAg, anti-HBc, and anti-HCV.

Results: Evidence for infection with HBV or HCV was found in 20 out of 25 patients (80%). Chronic hepatitis B was detected in 6 out of 25 (24%) and chronic hepatitis C was detected in 12 out of 25 patients (48%). Mixed infection was detected in 2 out of 25 (8%). Reduced total protein was found in 37 out of 50 patients (74%), elevated ALT levels were found in 12 out of 50 patients (24%), a reduced level of hemoglobin and number of erythrocytes, respectively was detected in 43/50 patients (86%).

Discussion/Conclusion: Overall, HBV and HCV infection was documented in patients on chronic hemodialysis. Therefore, patients with chronic renal insufficiency should regularly be monitored for infection with HBV and/or HCV. Further, the observation of highest hygienic standards as well as HBV vaccination are major issues in hemodialysis units.
Adipose tissue-derived MSCs are an eligible option to human hepatocytes

A.K. Nüssler¹, C. Seeliger¹, M. Culmes¹, L. Schyschka¹, U. Stöckle¹, N. Nüssler², M. Schoenberg³, S. Ehnert¹
¹Technical University Munich, MRI, Department of Traumatology, Munich, Germany
²Klinikum Neuperlach, Department of General Surgery, Munich, Germany
³Rotkreuz Hospital, Department of General Surgery, Munich, Germany

Introduction: Due to limited human primary hepatocyte availability, researchers trying to find alternatives based on stem cell technology using adult stem or precursor cells (mesenchymal stem cells (MSCs), fat tissue (Ad-) or liver). Reduced expression of hepatocytic-markers and drug metabolizing capacity, and limited amount cells generate in a reproducible manner are major drawbacks. Aim of this study was to contrast metabolic capability and pluripotency of Ad-MSC with human hepatocytes.

Methods: Ad-MSCs and hepatocytes were isolated according ethical guidelines of MRI. For hepatic differentiation several supplement combinations were used. The generated hepatocyte-like cells were stained for Glycogen, Glucose-6-phosphatase (G6P) and neutral lipids, and analyzed for glucose and urea metabolism as well as phase I and II drug metabolizing enzyme activities. Expression of pluripotency markers was detected by RT-PCR. Differentiated and non-differentiated cells were injected into mice and tracked by immunohistochemistry.

Results: During differentiation Ad-MSCs gain the ability to accumulate glycogen and express G6P. Best results could be generated by differentiation of Ad-MSCs, after demethylation, with a supplement combination of FGF4, ITS and Nicotinamid. Glucose production expression reached 50% of non-differentiated cells. Compared to human hepatocytes differentiated cells generated 60% urea production and reached up to 100% of Phase I and II enzyme activities. Pluripotency of isolated Ad-MSCs were tested via Oct3/4, KLF4, Sox2 and c-Myc. Injected cells could be detected in the liver of mice.

Discussion/Conclusion: Our work identified Ad-MSCs as a reliable cell source which might be used in drug screening and toxicity studies as well as a future source for cell transplantation.
Predictors of development hepatocellular carcinoma in chronic hepatitis C

Sladjana Pavic, Gordana Lucic
General Hospital Uzice, Serbia

Introduction: The most common risk factors for the development of hepatocellular carcinoma (HCC) are hepatitis C virus and hepatitis B virus. Of importance are biological and genetic factors, stage of disease and social factors, too. Aim of the study is to investigate predictors of development HCC in patients with chronic hepatitis C (HH-C).

Methods: A retrospective study was performed patients with HH-C and HCC who were followed in General Hospital Uzice, between of June 1999 to December 2009. We reviewed the following aspects regarding HH-C: demographic, genotype, biochemical and histological parameters. Patients were not treated with antiviral therapy or do not achieve a stable virological response.

Results: Of the total 184 (60.8% male, 27% older then 50 years, 48.5% were married), patients with HH-C, 42 (22.8%) had HCC (71.1% male, all older then 50 years, 73.5% married), (P 0.04, P 0.00, P 0.02). The most common genotype HCV was 1b (63.6% in HH-C, 86.1% in HCC). Noncirrhotic liver was in 123 (66.8%) patients with HH-C, 13 (30.1%) with HCC (P 0.02). Gender, age, marital status and stage of disease are still evaluated as predictors of development of HCC. Multivariate linear regression analysis revealed age older 50 as the most important positive variable for development of HCC (B 0.408; S.E. 0.104; P < 0.01).

Discussion/Conclusion: Patients with HCC are older then 50 years, more often male and married in then other patients with chronic hepatitis C. Older age is the most predictable group for the development of HCC in patients with HH-C.
Quality of life in patients with chronic hepatitis C after antiviral therapy

Sladjana Pavic¹, Neda Svirtlih², Dragan Delic², Jasmina Simonovic²
¹Department for Infectious Disease, General Hospital, Uzice, Serbia
²Clinic for Infectious and Tropical Diseases, Clinical Centre of Serbia, Belgrade, Serbia

Introduction: Hepatitis C virus is the leading cause of chronic liver disease development of cirrhosis and hepatocellular carcinoma reducing physical, mental and social functions in these patients. Aim of the study is to investigate quality of life in patients with chronic hepatitis C after antiviral treatment.

Methods: The generic Short form-36 (SF-36) questionnaire and Chronic Liver Diseases Questionnaire (CLDQ) were used in this prospective study for investigation of quality of life in patients with chronic hepatitis C. Quality of life was determined before and after treatment with peginterferon-α2b plus ribavirin (24 weeks treatment for HCV genotype 2 and 3, 48 weeks for genotype 1,4) in total of 58 patients (25 patients with cirrhosis hepatitis) who achieved sustained virologic response. Patients were treated at the Clinic for Infectious Disease in Belgrade, between June 2004 and June 2007.

Results: There was significantly higher total score of SF 36, mental and physical components of CLDQ in all of patients after treatment (ANOVA, P < 0.05). Significant difference was especially for body pain, physical function, vitality, systemic function, abdominal symptoms and role emotion (ANOVA, P 0.00). Activity was particularly better in patients without cirrhosis (ANOVA, P 0.00). Patients with cirrhosis had significantly improvement in almost all domains of both questionnaires.

Discussion/Conclusion: Achievement of response to antiviral therapy of chronic hepatitis C can be associated with significant improvements in quality of life, especially in an advanced liver disease.
Treatment of severe hepatitis with transplantation of autologous bone-marrow stem cells in human

Department of Infectious Disease, the Second Affiliated Hospital of Xi’an Jiaotong University, Xi’an, China

Objective: To discuss the effect of transplantation of self-bone marrow derived stem cells (BMSC) for patients with liver disease and to find a new way to treatment severe hepatitis in human.

Methods: 120 patients with severe hepatitis from our department, age from 20 to 60. 80 patients received the treatment with transplantation of BMSC, 40 patients act as control. Bone marrow was harvested (100 ml) from patients in the transplant group, then, the bone marrow was processed by density gradient sedimentation use Percoll to get the BMSC, the final preparation of BMSC were infused into liver of patients via liver artery. At different time (1 week, 4 weeks, 8 weeks, 12 weeks, 24 weeks) after transplantation, ALT, TBIL, ALB, PTA were detected, and the survival rate and improve of symptom were investigated.

Results: Our results show that the liver function of patients was improved after transplantation of bone marrow stem cells. After 24 weeks of transplantation, the ALT reduced from 183.2 IU/L to 98.3 IU/L; TBIL from 151.3 µmol/L to 81.3 µmol/L; ALB were rise from 26.1 g/L to 32.5 g/L; the PTA rise from 43.8% to 60.2%; the survival rate of transplant group little higher than control group; the symptoms (include appetite, physical strength, sleep and so on) of patients with transplantation of BMSC were improved after treatment. No correlative serious events were found in patients with bone marrow stem cells transplantation.

Discussion/Conclusion: The liver function of patients with serious liver disease were improved after bone marrow stem cells transplantation, the treatment of bone marrow stem cells transplantation is safe and effective.
MMP-9 and TNF-α as factors implicated in pathogenesis of autoimmune hepatitis type 1

C.A. Silosi, Isabela Silosi, V. Biciusca
University of Medicine Craiova, Craiova, Dolj, Romania

Introduction: The goal of our studies was to identity immunomarkers that fluctuate with autoimmune hepatitis type 1 (AIH1) development and severity. Matrix metalloproteinase 9 (MMP-9) play an essential role in tissue degradation and can influence the progression of various inflammatory conditions. TNF-α is produced and secreted by infiltrating mononuclear cells in focal inflammatory areas of the liver, and may have a role in the inflammatory activity of chronic liver disease. To assess serum MMP-9 and TNF-α as markers of inflammation in patients with AIH type 1 and the relationships of these biomarkers.

Methods: Thirty patients (43.07 ± 3.14 years) with type 1 AIH and 10 non-hepatitis persons (40.81 ± 9.69 years) with normal liver enzymes were investigated. Serum concentrations MMP-9 and TNF-α were measured using Quantikine and DRG Diagnostics Germany sandwich ELISA kits.

Results: Serum MMP-9 activity was found increased in patients compared to controls (365 ± 158 ng/ml versus 130.45 ± 80 ng/ml, p < 0.05). The highest rising in serum MMP-9 levels was superior to the rising in serum transaminase levels, indicating its advantage in assessing the progression of disease activity. Serum MMP-9 values correlated with liver histologic inflammatory grade. TNF-α serum levels were significantly higher in patients with MMP-9 serum-elevated concentrations compared to patients with low serum levels (p < 0.001). Our results suggest that in chronic inflammation associated with liver injury there is upregulation of MMP-9 either by TNF-α.

Discussion/Conclusion: MMP-9, implicated in the pathogenesis of AIH patients, can influence the outcome of inflammation and can serve as marker of disease activity. Inhibition of MMP-9 can be a promising treatment target in patients with AIH.
Clinical utility of autoantibodies in liver disease patients

Isabela Silosi, C.A. Silosi, V. Biciusca, F.I. Petrescu
University of Medicine Craiova, Craiova, Dolj, Romania

Introduction: Autoimmune hepatitis, an inflammation of the liver of unknown cause, has a global occurrence, diverse clinical phenotype and is characterized by interface hepatitis on histological examination, hypergammaglobulinemia, and autoantibodies. Our paper evaluate the diagnostic significance of autoantibodies: antinuclear (ANA), anti-smooth muscle, anti-actin (SMA), anti-mitochondrial anti-M2 (AMA), perinuclear anti-neutrophil cytoplasmic antibodies (pANCA) and liver kidney microsomal antibody (LKM1) in autoimmune liver disease.

Methods: We studied 54 untreated patients with autoimmune liver diseases: 16 with type 1 autoimmune hepatitis (AIH-1), 18 with primary biliary cirrhosis (PBC), 10 with primary sclerosing cholangitis (PSC), 10 with overlap syndromes (OS) AIH/PBC, and 20 controls. Sera of patients with autoimmune liver diseases were investigated for the presence of autoantibodies. ANA, SMA, AMA were evaluated by indirect immunofluorescence (IIF) technique on frozen sections of rodent multi-organ (kidney, liver and stomach) tissue substrates and by ELISA. The immunomarkers pANCA and LKM1 were evaluated only by ELISA, using Quanta Lite™-INOVA Diagnostics-USA kit.

Results: The highest frequency (62.4) of ANA was found in AIH. 18.7% of AIH1 patients had low titers of ANA (1:40 or 1:80) and 43% had titers > 1:160. SMA was detected in 12 (75%) of AIH-1 patients, 3 (30%) in PSC and missed in PBC and controls. The concomitant positivity for ANA and SMA was detected in 5 (31%) of AIH1 patients. pANCA were found in 70% of AIH-1 patients but only 31% of AIH patients with pANCA-positive sera presented SMA. All patients and healthy controls were negative for anti-LKM1. AMA levels were higher in PBC than in overlap syndrome (p < 0.0001) and negative in PSC and in controls. OS was associated with ANA-20%, pANCA-10% and AMA-30%.

Discussion/Conclusion: The detection of unconventional pANCA autoantibodies is useful for the diagnosis of AIH 1, especially in the absence of the typical autoantibodies. New autoantibodies can be considered as diagnostic and prognostic tools in liver diseases.
Influential factors of prognosis in lamivudine treatment for patients with acute-on-chronic hepatitis B liver failure

Li-Jie Sun, Jian-Wu Yu, Yong-Hua Zhao, Peng Kang, Shu-Chen Li
Department of Infectious Diseases, Second Affiliated Hospital, Harbin Medical University, Harbin 150086, China

Background and aims: Chronic hepatitis B virus (HBV) infection is a major global health issue, and the prognosis of patients with HBV-associated acute-on-chronic hepatic failure (ACLF) is extremely poor. In this study, the efficacy of lamivudine was investigated in patients with ACLF. The effects of HBV DNA load and its related factors on the prognosis were also further explored.

Methods: A matched retrospective cohort study using data on ACLF patients derived from our hospital database was conducted. 130 patients receiving lamivudine were selected into the lamivudine treatment group with another 130 without lamivudine treatment studied as control. They were matched for sex, age and imaging finding with lamivudine treatment group. All the patients were followed up for 3 months and the survival rates were compared. The influential factors on the mortality were studied by Cox proportional hazards model.

Results: The cumulative survival rates of patients in lamivudine group were higher than those of the control group ($\chi^2 = 9.50, P = 0.0021$). The mortality of patients with high virus load group (71/95, 74.7%) was higher than that of those with low virus load group (15/29, 51.7%) ($\chi^2 = 5.536, P = 0.019$). For patients with MELD score 20–30, by week 4, the mortality of those with HBV DNA undetectable or declined for more than $2 \log_{10}$ (2/12, 16.7%; 18/40, 45.0%) was lower than that of those with a less than $2 \log_{10}$ decline (18/23, 78.3%) ($\chi^2 = 10.106, P = 0.001$). In Cox proportional hazards model, for patients with MELD score 20–30, treatment method ($P = 0.002$), pretreatment HBV DNA load ($P = 0.007$) and decline of HBV DNA load during therapy ($P = 0.003$) were independent predictors; for those with MELD score above 30, MELD score ($P = 0.008$) was the only independent predictor.

Conclusions: Lamivudine can significantly decrease the 3-month mortality of patients with MELD score 20–30, and a low pre-treatment viral load and rapid decline of HBV DNA load are good predictors for the outcome of the treatment.

Key words: acute-on-chronic liver failure (ACLF); hepatitis B; model for end-stage liver disease (MELD); lamivudine
Active state of T lymphocytes and expression of CD45RA, CD45RO and CXCR3 of liver infiltrating lymphocytes and peripheral blood mononuclear cells in primary biliary cirrhosis

Ying-mei Tang1, Wei-min Bao2, Xianghua Xia3, Li-ying You1, Senlin Zhu4, Jin-hui Yang1

1Center of Hepatology, the Second Affiliated Hospital of Kunming Medical College, Kunming 650101, China
2General Surgery, Yunnan Provincial First People’s Hospital, Kunming 650032, China
3Internal Medicine, Queen Mary Hospital, Hong Kong University, Hong Kong, China
4Department of Gastroenterology, the First Affiliated Hospital of Sun Yat-sen University, Guangzhou 510080, China

Introduction: Liver is the target organ of primary biliary cirrhosis (PBC) and the immune state of liver is of importance to the development and prognosis of disease. However, the immune state of liver is still not known clearly. To explore the state of activation lymphocyte and influential factor in PBC we conduct this investigation.

Methods: CD3, CD4, CD8, CD4/CD8, HLADR+CD3+, HLADR+CD8+, CD45RA, CD45RO, CCR5 and CXCR3 of intrahepatic and PBL in PBC patients and NASH patients were detected with flow cytometric analysis.

Results: CD4+ T cells are the most abundant lymphocytes in the blood in PBC, while CD8+ and CD4+ T lymphocytes are the most abundant subsets in the liver. In PBC patients, frequency of CD4+ T cells in the liver was lower than those in the blood and the ratio of CD4 and CD8 was decreased, too. However, the frequency of CD4+ T cells and CD4/CD8 in PBC were higher than that of NASH. Furthermore, HLADR+CD3+, HLDR+CD8+ T cells, CXCR3 were expressed at significantly higher frequencies on IHL than on PBL. The frequency of CD45RA in blood was higher than that in the liver. While no significant difference of CD45RO was investigated between blood and liver.

Discussion/Conclusion: We concluded that the activation and proliferation of CD4+ T cells in the liver may be the critical element of PBC. CXCR3 may play an important role in trafficking T lymphocyte to liver. The number of memory T lymphocyte may contribute to the autoimmune response in PBC.

Supported by the Technology Program of Yunnan Province, No. 2006GH14
Expression of pituitary homeobox 1 gene in human hepatocellular carcinoma and its clinic pathological significance

Wang Baoyong, Ye Jin, Li Liang, Zhou Wen, Yang Ling, Hou Xiaohua
Department of Gastroenterology, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, Hubei 430022, China
Correspondence should be addressed to: yejin8688@sina.com

Introduction: PITX1, first identified as a bicoid-related transcription factor involved in proopiomelanocortin (POMC) gene expression, takes part in differentiation and formation of pituitary cells as well as in the development of oral epithelium, hindlimbs, first branchial arch, and their derivatives. Recently, PITX1 has been regarded as a tumor suppressor due to its suppression of tumorigenicity. Little is known about possible tumor-inhibitory function of PITX1 in HCC. The purpose of this study was to investigate the expression of pituitary homeobox 1 gene (PITX1) in human hepatocellular carcinoma (HCC) and its clinicopathological significance.

Methods: PITX1 mRNA and protein in cancerous tissues and their adjacent non-cancerous tissues were evaluated through semi-quantitative RT-PCR and Western blot.

Results: The PITX1 expression at both mRNA and protein level in para-carcinoma tissues was higher than that in the cancerous tissues from 30 HCC patients (both p < 0.01); the PITX1 expression decreased in the well differentiated cancerous tissues compared with 30 para-cancerous tissues, and was further reduced in poorly differentiated tissues, compared with either para-carcinoma tissues or well differentiated tissues; Expression of PITX1 in high AFP group (serum AFP ≥ 400 µg/L) was significantly lower than that in low AFP group (serum AFP < 400 µg/L) (both p < 0.05).

Discussion/Conclusion: PITX1 was a new candidate of tumor suppressor gene in HCC, PITX1 down-regulation may be a key molecular event during oncogenesis and play a key role in differentiation of HCC.
The clinical features of parenteral nutrition-associated cholestasis (PNAC) in preterm infants

Chenhong Wang, Liping Shi, Zheng Chen
Children's Hospital Zhejiang University, Hangzhou, China

Introduction: To analyze the clinical features and influential factors of parenteral nutrition-associated cholestasis (PNAC) in preterm infants.

Methods: 359 less than 2000 g or/and smaller than 34 weeks preterm infants were given longer than 7 days parenteral nutrition during 2007.7–2009.6. Of these infants, 42 cases who had PNAC were the PNAC group, 130 cases without PNAC choosed from the other 317 infants randomly were the non-PNAC group. Both groups' PNAC occurring time, duration, the degree of PNAC and hepatic injury were obversed. Besides, to analyze the correlative factors of PNAC.

Results: PNAC happened about 22.8 ± 11.8 days after beginning PN, usually lasted for 91.5 ± 38.4 days. The maximum of directed bilirubin was 131.1 ± 68.1 µmol/L. Of the PNAC patients, there were 74.4% suffering hepatic injury. Hepatic injury usually happened 46.7 ± 21.8 days after beginning PN, and lasted for 65.6 ± 38.0 days. The maximum of alanine aminotransferase (ALT) was 120.2 ± 48.0 U/L. The logistic regression of the possible correlative factors showed that gestational age, time to start enteric feeding, persistence time of PN, intolerance of enteric feeding, asphyxia, necrosis enterocolitis (NEC), intraventricular haemorrhage (IVH), transient hypothyroidism were related to the happening of PNAC.

Discussion/Conclusion: The prognosis of PNAC was good. Early enteral feeding, shortens the time of PN, avoidance of the complications such as asphyxia, NEC, were the important measure to lower PNAC.
Prognostic factors and outcome of 438 Chinese patients with hepatocellular carcinoma underwent partial hepatectomy in a single centre

Jie WANG, M.D., Ph.D.; Lei-bo XU, M.D.; Chao LIU*, M.D., Ph.D.; Hao-wei PANG, M.D.; Ya-jin CHEN, M.D., Ph.D.; Ji-sheng CHEN, M.D.; Qing-jia OU, M.D.
Department of General Surgery, Memorial Hospital, Sun Yat-Sen University, Guangzhou 510120, China
*Correspondence to: Dr. Chao LIU, E-Mail: mdlchiuchao@hotmail.com

Introduction: To evaluate the prognostic factors and outcome of 438 Chinese patients with hepatocellular carcinoma who underwent partial hepatectomy in a single centre.

Methods: Clinicopathological data of 438 patients with hepatocellular carcinoma who underwent partial hepatectomy at author’s hospital between 1991 and 2004 were reviewed retrospectively. The Kaplan-Meier method was adopted for evaluating the survival. Prognostic factors were assessed by Cox proportional hazard model and logistic regression model.

Results: The perioperative (30 days) mortality and morbidity were 7.5% (33/438) and 21.7% (95/438), respectively. The operative mortality decreased significantly from 10.6% (23/218) in 1991–2001 to 4.5% (10/220) in 2002–2004 (P = 0.019). Postoperative overall survival rates at 1-year, 3-year and 5-year were 72.2%, 53.5% and 43.3%, respectively. Cox multivariate analysis indicated that Child-Pugh score, tumour size, capsular invasion, tumour stage, vascular invasion and resection margin were independent prognostic factors for overall survival (P < 0.05). Besides, 254 cases had tumour recurrence after operation and 87 cases of them were re-operated. Logistic multivariate analysis showed that tumour size, capsular invasion, vascular invasion, lymph node metastasis, extra-hepatic metastasis and resection margin were independent risk factors of tumour recurrence (P < 0.05).

Discussion/Conclusion: Tumour size, capsular invasion, vascular invasion and resection margin were the main factors that may impact the overall survival and tumour recurrence. As resection margin is the only factor that relates to the surgery, enough resection margin (> 2 cm) should be obtained whenever possible.

Supported by: The Special Research Foundation of the National Nature Science Foundation of China (30872487)
Management experiences for portal vein thrombosis in liver transplantation

Zheng-xin WANG**, MD, Hao YIN*, MD, Guo-Shan DING, MD, Zhi-ren FU, MD
Organ Transplantation Centre of Shanghai Changzheng Hospital, China

**Introduction:** To investigate the surgical options for portal vein thrombosis (PVT) during liver transplantation and their impact on the outcomes of the patients.

**Methods:** From October 2001 to November 2008, 773 liver transplantations were performed and PV occurred in 107 patients (grade I, n = 59; grade II, n = 33; grade III, n = 12; grade IV, n = 3). Thrombectomy or thrombus-extraction was performed in patients with grades I and II PVT. In the 12 patients who had grade III PVT, thrombus-extraction was performed or an interposition vein graft from the donor iliac vein was used to bridge the recipient superior mesenteric vein to the donor portal vein. Two cases of grade IV PVT received modified cavo-portal hemi-transposition and one case received an anastomosis between the donor portal vein and recipient varicose left gastric vein.

**Results:** All patients with grades I and II PVT had liver function restored and the perioperative mortality rate was 4.3%. Five patients with grade III PVT who received thrombus extraction had normal liver function. The other 7 cases of grade III PVT underwent portal vein reconstruction. Two of them died from liver dysfunction. There was no death in the grade IV group.

**Discussion/Conclusion:** Our results showed that PVT is no longer a contraindication of liver transplantation. Satisfactory results can be obtained by applying the appropriate operative techniques to individual patients.
Altered gene profile of placenta from women with intrahepatic cholestasis of pregnancy

Jing Wei*, Huimin Wang*, Xiaofu Yang, Minyue Dong, Zhengping Wang
Women's Hospital, School of Medicine, Zhejiang University, China
*These authors contributed equally

Introduction: Intrahepatic cholestasis of pregnancy (ICP) is a pregnancy-specific complication in the second and third trimester and is characterized by pruritus, jaundice and the disturbances of liver tests, especially the elevation of bile acid. The etiology of ICP remains unclear. Recently, the causes of elevated bile acid and the alteration of bile acid transporter in liver and placenta were the focus of investigation. The aim was to investigate the alterations in gene profile of placenta from ICP and to enhance the insight of etiology and pathogenesis of ICP.

Methods: Ten pregnant women diagnosed ICP were recruited and 10 healthy pregnant women served as control. Four samples were taken from each placenta and RNA was isolated. Gene expression was analyzed with microarray and real time PCR was used to validate the differentially expressed genes.

Results: 392 genes were found differentially expressed. Among these differentially expressed genes, 280 were up-regulated and 112 were down-regulated. These differentially expressed genes involved 20 categories including genes involved in transportation, cell growth, apoptosis and immune response that were putatively participated the pathogenesis of ICP.

Discussion/Conclusion: 392 differentially expressed genes of 20 categories were found in ICP placenta, suggesting the diversity of gene expression alteration and the complexity of etiology and pathogenesis of ICP.
Case report of 5 patients with hepatic veno-occlusive disease induced by herbs and literature review

Xun Yun-hao, Shi Jun-ping, Guo Jian-chun, Shi Wei-zhen
Hangzhou 6th Hospital, Hangzhou 310014, Zhejiang, China

Introduction: To investigate the clinical features of hepatic veno-occlusive disease (HVOD) induced by herbs contained pyrrolizidine alkaloid (PA).

Method: To analyse the clinical features, diagnosis and treatment of 5 patients with HVOD induced by herbs (4 by gynura root and 1 by other) in our hospital retrospectively, meanwhile to review the progress about HVOD in recent years.

Results: In this study, male (4/5) was predominant, mean age was 38.3 and the lowest was six, which was below the historical reports in China. All patients presented with weight gain rapidly, abdominal distension, oliguria, hepatomegaly and ascites. The ultrasound features included hepatomegaly, discrepancy echo within liver, ascites, slower flow rate of portal vein and more or less stenosis of hepatic vein but different to manifestations of Budd-Chiari syndrome. Two patients accepted dynamic enhanced CT scan, and demonstrated imaging feature of venous hepatic congestion, which was in concord with the results of similar studies. All of the patients received symptomatic and supportive treatment, one received anticoagulant therapy with defibrotide but died eventually, the others recovered.

Conclusion: Individuals of any age who ate herbs contained PA like as gynura root could have HVOD. Ultrasound echo of HVOD had some features, but would be interfered with judgement of operator heavenly. Dynamic enhanced CT had significant characteristics in early period, and definite diagnosis can be made if combined with reliable history and typical symptoms and signs. The treatment of HVOD is still relyed on symptomatic and supportive therapy.

Key words: hepatic veno-occlusive disease; gynura root; pyrrolizidine alkaloid; diagnosis; treatment
Fuzheng Huayu formula inhibits activation of primary hepatic stellate cells through inhibiting apoptosis of primary hepatocytes

Xiuchuan Yan¹, Qinglan Wang¹, Yun Ran¹, Chenghai Liu¹,²
¹Institute of Liver Diseases, Shuguang Hospital Affiliated to Shanghai University of Traditional Chinese Medicine, Shanghai 201203, China
²E-institute of TCM Internal Medicine, Shanghai Municipal Education Commission, Shanghai 201203, China

Introduction: Fuzheng Huayu formula is an effective Traditional Chinese Medicine (TCM) preparation against liver fibrosis in China. Previous research has already unveiled many mechanisms how it takes effect. Recent studies found it attenuates hepatocyte apoptosis and then fibrosis in CCl₄-induced fibrotic mice. However, the specific mechanism by which Fuzheng Huayu formula regress liver fibrosis through inhibiting hepatocyte apoptosis is still unknown.

Methods: Primary hepatocyte and HSC were isolated from rats. Hepatocyte apoptosis was induced by Act D plus TNF-α. DNA in all groups of hepatocytes were extracted with Kit and apoptosis was assessed by DNA electrophoresis. Expression of α-SMA and collagen I in rHSCs were determined by immunofluorescence and western blot.

Results: Fuzheng Huayu formula effectively inhibited TNF-α-induced hepatocyte apoptosis. Apoptotic DNA extracted from apoptotic hepatocytes stimulated expression of α-SMA in rHSCs in a dose-dependent manner. DNA extracted from Fuzheng Huayu formula-treated apoptotic hepatocytes less stimulated the expression of α-SMA and collagen I in rHSCs in comparison with that in apoptotic DNA group.

Discussion/Conclusion: Fuzheng Huayu formula inhibits the initiative activation of hepatic stellate cells partially through its effects on ameliorating apoptosis of primary hepatocytes.
Figure 1

A

<table>
<thead>
<tr>
<th>DNA Condition</th>
<th>Nuclear</th>
<th>α-SMA</th>
<th>Merge</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy DNA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Apoptotic DNA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fuzheng Huayu formula-treated DNA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Z-VAD-FMK treated DNA</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Figure 1: DNA extracted from Fuzheng Huayu formula-treated apoptotic hepatocytes inhibits the expression of α-SMA in rHSCs. A. Immunofluorescence, x400. B. Western blot. 1, health DNA. 2, apoptotic DNA. 3, Fuzheng Huayu formula-treated DNA. 4, Z-VAD-FMK (caspase-inhibitor)-treated DNA. 5, marker.
Biliary decompression strategies in relation to acute suppurative cholangitis with intestinal dysfunction

Fu-chun Yang, Wei-lin Wang, Ting-bo Liang, Min Zhang, Yan Shen, Tian-an Jiang, Yun-shen Qing, Qi-yong Li, Fen Chen, Qi-yu Zhao, Shu-sen Zheng
Zhejiang University, 310003 Hangzhou, China
Corresponding author: Shu-sen Zheng

Background: Endoscopic drainage and percutaneous transhepatic cholangial drainage (PTCD) have replaced emergent surgery for biliary decompression in patients with acute suppurative cholangitis (ASC). The aim of this study was to prospectively compare the efficacy of endoscopic nasobiliary or plastic stent drainage and PTCD as temporary measures for biliary decompression in ASC with intestinal dysfunction.

Methods: In a 5 years period, 117 patients with ASC accompanied by intestinal dysfunction who required emergent biliary drainage were recruited. All patients had fever, jaundice, abdominal pain and abdominal distention. Parts of them had acute pancreatitis. Most of them had hemodynamic instability. According to pre-therapeutic strategies, patients were randomized to receive either a nasobiliary catheter or plastic stent without/with sphincterotomy or PTCD for biliary decompression. Outcome measures included complications, patient morbidity and mortality, and total hospital stay time.

Results: Of the 117 patients, 93 were randomized to receive a nasobiliary catheter (ENBD group), 13 to receive plastic stent (ERBD group), ERCP group total 106 patients, and 11 to PTCD group. Demographic data were similar between the groups. All procedures were successful in the ERBD group; there was one failure in the ENBD group for fear of endoscopic therapy and alter to PTCD group. There were 5 ERCP-related complications in the ENBD and ERBD groups, and 3 patients PTCD-related complications. One patient developed severe intestinal distention and inflammatory intestinal obstruction after ERBD, two patients developed gastrointestinal bleeding after ENBD. One patient developed abdominal hemorrhage post PTCD. Two patients respectively in ENBD and PTCD group catheter occluded. The overall mortality rate was 6.8% (4.3% ENBD group, 7.8% ERBD group, and 27% PTCD group).

Conclusions: Minimal intervention therapy is the option choice for the treatment of ASC offering definite treatment with low morbidity, mortality and short hospitalization. Urgent biliary decompression with ERCP or PTCD is crucial for the outcome of patients having ASC with intestinal dysfunction according to suitable strategies.
Logistic regression analysis of risk factors on hepatitis B-related liver cirrhosis complicated by hepatorenal syndrome

YANG Jin-sun, WANG Chang-sheng, YANG Shan-bing, YANG Jiang-hua, YU Yan-lin
Department of Infectious Diseases, Affiliated Yijishan Hospital of Wannan Medical College, Wuhu 241001, China
E-Mail: yangjinsun999@yahoo.com.cn; Telephone: 013866358440

Introduction: Hepatorenal syndrome (HRS) appears mostly acute renal failure in patients with cirrhosis as well as the major cause of death for the patients with advanced cirrhosis of the liver. For the high incidence of hepatitis B in China, the study aimed to explore the risk factors on hepatitis B-related liver cirrhosis complicated by HRS.

Methods: 642 cases of hepatitis B-related liver cirrhosis inpatient patients from January 2004 to January 2010, in which 46 cases of HRS occurred, were analyzed retrospectively. The patients’ clinical data including sex, age, history of hepatitis B schedule, Child-Pugh score, ALT, AST, AKP, GGT, ALB, pre-ALB, TBIL, PT, APTT, cholinesterase, serum sodium values, degree of ascites, the existence of infection, gastrointestinal bleeding, strong diuretic and large number of releasing ascites, were collected. The data were statistically analyzed by unconditional logistic regression.

Results: It was revealed in univariate and multivariate unconditional logistic regression analysis that Child-Pugh score, infection, gastrointestinal bleeding and HRS put a large number of statistically significant correlation ($P < 0.05$), OR values were 6.21, 3.57, 4.56, respectively.

Discussion/Conclusion: Child-Pugh score, infection and gastrointestinal bleeding are the risk factors of the presence of HRS for the patients with hepatitis B-related liver cirrhosis. The patients with these risk factors need to be raised vigilance and need to be taken appropriate preventive control measures.
Clinical analysis of 94 cases with Budd-Chiari syndrome

Yang Ling, Tang Shunyu, Ye Jin, Hou Xiaohua
Department of Gastroenterology, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology. Wuhan, Hubei 430022, China
Correspondence should be addressed to: Yang Ling: yang_lng@yahoo.com.cn

Introduction: To study the clinical features of different kinds of Budd-Chiari syndrome, in order to improve the diagnostic level of this disease.

Methods: Ninety-four patients diagnosed as B-CS by DSA, B ultrasonic, CT from 2002 to 2009 were retrospectively included into this study and according to the parts, all the patients were divided into inferior vena cava obstruction (type I), hepatic vein obstruction (type II), mixed type (type III), and compare the clinical features and blood biochemistry features of the three groups.

Results: Among them, type I, type II, type III were 53 cases (56.4%), 24 cases (25.5%), 17 cases (18.1%), and male is 55 cases (58.5%), female is 39 cases (42.5%). The incidence of the disease of male is higher. 23 cases of the 55 male cases (41.8%) had a history of smoke and drinking; 6 cases (10.9%) had a history of HBV, while the 39 female had none of them. Type I is mainly lower leg edema, abdominal wall veins revealed; type II is mostly splenomegaly, bloating; type III is nearly ascites, lower leg edema. In biochemistry inspection, the incidence of bilirubin metabolism, three-line decrease, coagulation abnormalities is higher than liver impairment. Thrombocytopenia and elevated total bilirubin of type III are more common than others (p = 0.005, p = 0.019).

Discussion/Conclusion: The three types have differences in clinical features and biochemistry features, which will help the clinician realize and diagnose the Budd-Chiari syndrome.
Analysis of clinical features and prognostic factors in inpatients with nonalcoholic fatty liver disease

Yao Yuan-Tao, Sha Wei-Hong, Wang Qi-Yi, Cen Rong-Ying, Zheng Yue
Department of Gastroenterology and Hepatology, Guangdong General Hospital, Guangdong Academy of Medical Sciences, Guangzhou, 510080, China
Corresponding author: Sha Wei-Hong, E-Mail: wh-sha@163.com

Objective: The aims of this study were to evaluate the clinical features and prognostic factors of inpatients with nonalcoholic fatty liver disease (NAFLD).

Methods: Clinical data of 4437 inpatients with NAFLD in Guangdong Provincial hospital were collected. The distributions of concomitant diseases, causes of admission and risk factors of NAFLD-related liver injury and death were analyzed.

Results: Major admission causes of NAFLD were non-diabetic-related angiopathy (34.1%), diabetes-related complications (24.0%), liver injury (7.8%), biliary-pancreatic diseases (4.8%). Common concomitant diseases of NAFLD were hypertension (42.0%), diabetes mellitus (32.4%), cerebrovascular disease (26.3%), coronary heart disease (16.6%), cholelithiasis (11.2%) and acute pancreatitis (6.3%). The distributions of NAFLD-concomitant diseases were different in different age groups. The peak age of diabetes mellitus, hypertension and coronary heart disease in patients with NAFLD were from 60 to 70 years old. Whereas the cerebrovascular disease, cholelithiasis and pancreatitis were from 70 to 80 years old and less than 40 years old, respectively. The risk factors of liver damage were pancreatitis (OR = 3.0), biliary infection (OR = 2.6), diabetic peripheral vascular complication (OR = 1.7) and age (OR = 0.8), all p < 0.01. The risk factors of death were diabetic peripheral vascular complication (OR = 29.5), cardiovascular events (OR = 24.6), tumor (OR = 9.8), diabetes-related infection (OR = 4.7) and age (OR = 1.7), all p < 0.01.

Conclusion: The clinical manifestations and prognosis of NAFLD are closely related to age and its concomitant diseases. Age should be paid more attention when interventions are made.

Key words: nonalcoholic fatty liver disease, prognosis; liver damage; diabetes mellitus; cardiovascular diseases; cerebral
Anti-inflammatory effects of Traditional Chinese Medicine on nonalcoholic steatohepatitis

Li Ying, Bing-Dong Lu, Liu-Qin Guo, Chun-Meng Jiang
Department of Gastroenterology, Second Affiliated Hospital, Dalian Medical University, Daliana, Liaoning, China

Introduction: Nonalcoholic steatohepatitis (NASH) can progress to advanced fibrosis and may account for most cases of cryptogenic cirrhosis. There is no widely accepted method to treat NASH except behavioral treatment such as weight loss and physical activity. Traditional Chinese herbs have been found to improve hepatic steatosis and inflammation in alcoholic liver disease. This study aimed to investigate the therapeutic effects of a traditional herb formula, Gan Zheng Fu Fang, on experimental NASH and to explore its possible mechanisms.

Methods: Thirty Wistar rats were randomly divided into three groups (n = 10): normal control group fed a standard diet; high-fat diet (HFD) group fed a high fat diet and GZFF group, fed a high fat diet for 12 weeks followed by 4-week gavage of GZFF liquid extract. Serum aspartate aminotransferase and alanine aminotransferase were detected. TNF-α and adiponectin were determined using ELISA. Hepatic histological change was observed by HE stain. Protein and mRNA expression of peroxisome proliferator-activated receptor γ was measured by Western blot and semi-quantitative RT-PCR.

Results: In comparison to normal group, ALT, AST and TNF-α were elevated whereas adiponectin were decreased (P < 0.05, respectively); significant steatosis and inflammation of hepatic lobule were found in HFD group accompanied by decreased expression of PPARγ protein and mRNA. GZFF group were noted to reveal lowered ALT, AST, and TNF-α and elevated adiponectin compared with HFD group (P < 0.05, respectively). Steatosis and inflammation of liver showed a significant improvement and both protein and mRNA expression of PPARγ were increased in GZFF group compared with HFD group (both P < 0.05).

Discussion/Conclusion: GZFF can modulate lipid metabolism and ameliorate inflammation of liver tissue in experimental NASH. The possible mechanisms are that GZFF can increase the release of adiponectin, decrease the production of TNF-α, and improve insulin sensitivity via activation of PPARγ.
Analysis of the efficacy of treatment with peginterferon α2a and ribavirin in patients coinfected with hepatitis B virus and hepatitis C virus

Jian-Wu Yu, Li-Jie Sun, Yong-Hua Zhao, Peng Kang, Shu-Chen Li
Department of Infectious Diseases, Second Affiliated Hospital, Harbin Medical University, Harbin 150086, China

Objective: To study the virological features of patients coinfected with hepatitis B virus (HBV) and hepatitis C virus (HCV) and the efficacy of combination therapy with peginterferon α2a and ribavirin in these patients.

Methods: The epidemiological and virological data of 50 patients coinfected with HBV and HCV were analysed. The virological response rates of patients treated with peginterferon α2a and ribavirin between the HBV and HCV coinfection group and the HCV monoinfection group were compared.

Results: HCV-dominant virus strains accounted for 92.0% of the 50 coinfected individuals, and HCV- and HBV-dominant virus strains accounted for the remaining 8.0%. The HBV DNA level of the patients coinfected with HBV and HCV was $4.6 \pm 0.9 \log_{10}$ copies/ml, which was significantly lower than that in the HBV monoinfection group ($5.9 \pm 1.2 \log_{10}$ copies/ml) ($t = 5.964$, $P < 0.01$). The HBeAg-positive rate (12.0%, 6/50) of the coinfection group was significantly lower than (45.3%, 19/42) that of the HBV monoinfection group ($\chi^2 = 12.743$, $P < 0.01$). The partial early virological response (pEVR) rate and the end-of-treatment virological response (ETVR) rate (50.0%, 15/30; 90.0%, 27/30) of patients with genotype 1 in the coinfection group were significantly higher than those (16.0%, 4/25; 56.0%, 14/25) in the HCV monoinfection group ($\chi^2 = 6.971$, $P = 0.008$; $\chi^2 = 8.307$, $P = 0.004$). The relapse rate (55.6%, 15/27) of patients with genotype 1 in the coinfection group was significantly higher than that (21.4%, 3/14) in the HCV monoinfection group ($\chi^2 = 4.360$, $P = 0.037$). The sustained virological response (SVR) rate (40.0%, 12/30) of patients with genotype 1 in the coinfection group was compared with that of the HCV monoinfection group (44.0%, 11/25) ($\chi^2 = 0.090$, $P = 0.765$). There was no significant difference in the on-treatment virological response, ETVR, SVR and relapse rates between two groups for patients with genotype 2. The incidence of side effects (30%, 15/50) of patients in the coinfection group was significantly higher than that (13%, 6/46) in the HCV monoinfection group ($\chi^2 = 4.031$, $P = 0.045$). The reactivation rate of HBV DNA (33.3%, 9/27) with HCV SVR was significantly higher than that of patients without SVR (8.7%, 2/23) ($\chi^2 = 4.393$, $P = 0.036$).

Conclusions: The replication of HBV was suppressed, and HCV was the dominant virus strain. Compared with HCV-monoinfected patients, pEVR, ETVR and relapse rates of patients with genotype 1 in the coinfection group were high, while they shared similar SVR rates. HBV and HCV coinfection had no impact on the rate of virological response for genotype 2.
Effects of grape extract on endoplasmic reticulum stress-induced apoptosis

Jing Yu*, Vladimir Khaoustov#, Yu-min Xu#, Boris Yoffe#
*Department of Hepatology, the First Affiliated Hospital, Guangxi Traditional Chinese Medical University, Nanning, Guangxi, 530023, P. R. China
#Department of Medicine, Michael E. DeBakey Veterans Affairs Medical Center, Baylor College of Medicine, Houston, TX 77030, USA

Introduction: To investigate the potential cytoprotective effects of grape extract on the endoplasmic reticulum (ER) stress induced apoptosis in Huh7 cells and analyze the mechanism responsible for the anti-apoptosis effects of grape extract.

Methods: The ER stress-mediated apoptosis was induced by thapsigargin (TG) in human liver-derived cell line, Huh7 cells. Cells were cultured in medium with 5 µmol/L of TG for 24 hour with or without 50 µg/ml grape extract. Cell proliferation was evaluated by MTT assay. Apoptosis was measured by flow-cytometry and caspase-3/7 activity was analyzed with EnzoLyte Homogeneous AMC kit. Reactive oxygen species (ROS) was detected with DCFH-DA assay. The levels of Bip/GRP78, caspase-12, PCNA and cytochrome c were analysis with Western blot.

Results: Grape extract pretreatment of Huh7 cells elicited cytoprotection against thapsigargin-induced apoptosis. Grape extract abolished TG-induced markers of ER stress; reduced induction of Bip/GRP78, activation of caspase-12 and caspase-3/7 and restoring levels of PCNA. Grape extract inhibit TG-induced intracellular generation of ROS, release of cytochrome c.

Conclusion: Grape extract exhibit cytoprotective effects against ER stress mediated apoptosis in Huh7 cells. The mechanisms of anti-apoptotic effects of grape extract were associated with abolishing TG-induced ER stress, and caspase-12 activation and ER stress induced ROS generation and inflammation. These findings contribute to our understanding of the mechanisms of anti-apoptotic effects of grape in liver diseases associated with ER stress.
Clinicopathological characteristics of 20 cases of hepatocellular carcinoma with bile duct tumour thrombi

Xian-huan YU, M.D.; Lei-bo XU, M.D.; Chao LIU*, M.D., Ph.D.; Rui ZHANG, M.D.; Jie WANG, M.D., Ph.D.; Qing-jia OU, M.D.
Department of General Surgery, Memorial Hospital, Sun Yat-Sen University, Guangzhou 510120, China
*Correspondence to: Dr. Chao LIU, E-Mail: mdliuchao@hotmail.com

Introduction: Hepatocellular carcinoma (HCC) with bile duct tumour thrombi (BDTT) is a rare type of primary liver cancer, and its clinical and pathological characteristics remain to be defined. In this study, the clinical and pathological characteristics of 20 patients with HCC and BDTT were investigated.

Methods: Among 676 HCC patients who underwent surgical treatment from December 2002 to December 2008 at author's hospital, HCC with BDTT was identified in 20 patients. The clinical and pathological characteristics of the 20 patients were measured or analyzed retrospectively. The integrity of involved bile duct was examined macroscopically and microscopically. Meanwhile, the expression of liver stem cell markers was investigated by immunohistochemistry, and the Kaplan-Meier method was adopted for evaluating the survival.

Results: Among the 20 patients, the diameter of primary tumour was less than 5 cm in 13 patients (range: 0.5–10 cm), with a mean of 4.47 ± 0.68 cm. Most of the primary tumour had no intact tumour capsule (15/20, 75%), with simultaneous blood vessel invasion (12/20, 60%) and were poorly differentiated (13/20, 65%). There was no evidence of bile duct wall infiltration by the tumour cells macroscopically and microscopically. The positive rate of liver stem cell markers, c-kit, CD90, CD133, and EpCAM was 90%, 90%, 85% and 85%, respectively. Besides, postoperative overall survival rates at 1-, 2- and 3-year were 73.1%, 41.1% and 20.6%, respectively. Log-rank test showed that the overall survival rates was significantly worse for HCC patients with BDTT than HCC patients without BDTT (P = 0.016).

Discussion/Conclusion: HCC with BDTT has an aggressive characteristic and the long-term prognosis was extremely dismal.

Supported by: The Special Research Foundation of the National Nature Science Foundation of China (30872487)
An experimental study on the relationship between 5-hydroxytryptamine (5-HT) and human hepatocellular carcinoma

Zhang Chong, Shi De-hong, Liang Jun-rong, Li Xiao-lin
Digestive Internal Medicine Department, No. 3 Hospital of PLA, Baoji 721004, China

Introduction: To study the relationship between 5-HT and the proliferation of human hepatocellular carcinoma.

Methods: The immunohistochemical SABC method was used to observe the expressions of 5-HT and its receptor on the hepatocellular carcinoma cells and compared it with the proliferating cell nuclear antigen (PANA) label index.

Results: Localization and distribution of 5-HT and its receptor in the tissue of hepatocellular carcinoma: 41 cases human hepatocellular specimens were stained by immunohistochemical SABC method, 20 cases were 5-HT immunoreactivity and 21 cases were 5-HTR immunoreactivity. Positive cells were brown and can be recognized easily. The distributive pattern and the staining density of 5-HT and its receptor reactive productions in the carcinoma cell are similar. Positive substance distributed in plasma and was higher in the rim of carcinoma cells with negative nuclei. The positive rate of II, III grade carcinoma is higher than that of I, IV grade, but there are no difference among them according to statistics (P > 0.05). The expression of PCNA in the tissue of human hepatocellular carcinoma was tested by immunohistochemical method and PCNA label index (PCNA LI) was collected. The PCNA LI in 5-HT positive carcinoma cells (40.35 ± 22.40) is higher than the negative (17.54 ± 13.44) (P < 0.01). In the same way, the PCNA LI in 5-HTR positive carcinoma cells (37.91 ± 24.01) is higher than the negative (21.11 ± 15.85) (P < 0.05).

Discussion/Conclusion: These suggest that the hepatocellular carcinoma which express 5-HT and its receptor have strong proliferating activity.
Antibiotics in primary prophylaxis of spontaneous bacterial peritonitis in cirrhotic patients with ascites: A meta-analysis

Yan-Dan Zhong, Yong-Feng Yang, Wei-Ming Lu, Ping Huang, Ning Zhang
Department of Liver Disease, the Second Hospital of Nanjing, affiliated with Medical School of South-East University, No. 1-1 Zhongfu Road, Nanjing 210003, Jiangsu Province, China

Introduction: Previous studies showed antibiotic prophylaxis has been successful for the prevention of spontaneous bacterial peritonitis (SBP) recurrence in patients surviving an episode of SBP. But there is no consensus as to whether patients with long-term high risk of developing the first episode of SBP, should be recommended for use of antibiotics in primary prophylaxis. Thus, we conducted this meta-analysis of these trials to assess the evidence obtained on the efficacy of antibiotic primary prophylaxis in the prevention of SBP and its effect on survival rate in cirrhotic patients with ascites.

Methods: Relevant articles were identified and selected by searching the databases, Medline (1966–March 2010) and Embase (1980–March 2010). We chose two clinically meaningful events to estimate the efficacy of antibiotic primary prophylaxis for meta-analysis: incidence of SBP and death.

Results: Three randomized controlled trials met the defined inclusion criteria and were included in the analysis. 138 patients received antibiotic prophylaxis and 137 patients received placebo prophylaxis. Each study was randomized, double-blind, and placebo-controlled, with a description of withdrawals and drop-outs. The relative risk (RR) was used to measure the magnitude of the efficacy. The combined RR on the incidence of SBP was 0.62 (95% CI: 0.40–0.95), and was statistically significant (P = 0.03). The combined RR on the incidence of survival was 0.80 (95% CI: 0.59–1.09), and was not statistically significant (P = 0.15). There was no significant heterogeneity among the studies included.

Discussion/Conclusion: Primary prophylaxis with antibiotics can significantly reduce the incidence of SBP, but had no effect on the incidence of survival in cirrhotic patients with low-protein ascites.
# Author Index to Poster Abstracts

(Name – Poster Number)

<table>
<thead>
<tr>
<th>Author</th>
<th>Poster Numbers</th>
<th>Author</th>
<th>Poster Numbers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdullah, M.</td>
<td>1, 35, 36, 79</td>
<td>Chen, X.</td>
<td>31</td>
</tr>
<tr>
<td>Abraldes, J.G.</td>
<td>62</td>
<td>Chen, X.-W.</td>
<td>77</td>
</tr>
<tr>
<td>Akarsu, M.</td>
<td>2</td>
<td>Chen, Y.-J.</td>
<td>98</td>
</tr>
<tr>
<td>Akpınar, H.</td>
<td>2</td>
<td>Chen, Z.</td>
<td>97</td>
</tr>
<tr>
<td>Alcázar Guijo, F.J.</td>
<td>39, 40, 41</td>
<td>Cheng, J.</td>
<td>21</td>
</tr>
<tr>
<td>Alserafy, M.</td>
<td>64</td>
<td>Cheng, Y.</td>
<td>10</td>
</tr>
<tr>
<td>Altamirano, J.</td>
<td>62</td>
<td>Cong, C.-L.</td>
<td>68</td>
</tr>
<tr>
<td>Altorjai, I.</td>
<td>14, 42</td>
<td>Cullu, N.</td>
<td>2</td>
</tr>
<tr>
<td>Andrikovics, H.</td>
<td>14</td>
<td>Culmes, M.</td>
<td>88</td>
</tr>
<tr>
<td>Andrini, F.</td>
<td>63</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antal-Szalmas, P.</td>
<td>42</td>
<td>Delic, D.</td>
<td>90</td>
</tr>
<tr>
<td>Arebi, N.</td>
<td>13</td>
<td>Demir, S.</td>
<td>2</td>
</tr>
<tr>
<td>Arfianti, A.</td>
<td>63</td>
<td>Deng, H.</td>
<td>76</td>
</tr>
<tr>
<td>Auwyang, J.A.</td>
<td>3</td>
<td>Derova, J.</td>
<td>11, 12, 32</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Derovs, A.</td>
<td>11, 12, 32</td>
</tr>
<tr>
<td>Bahnaczy, A.</td>
<td>64</td>
<td>Desatová, B.</td>
<td>4, 5</td>
</tr>
<tr>
<td>Baláková, D.</td>
<td>4, 5</td>
<td>Ding, G.-S.</td>
<td>99</td>
</tr>
<tr>
<td>Baltaziak, M.</td>
<td>50</td>
<td>Dominguez, M.</td>
<td>62</td>
</tr>
<tr>
<td>Bao, W.-M.</td>
<td>95</td>
<td>Dong, M.</td>
<td>100</td>
</tr>
<tr>
<td>Bataller, R.</td>
<td>62</td>
<td>Du, Y.</td>
<td>54</td>
</tr>
<tr>
<td>Bátovsky, M.</td>
<td>4, 5</td>
<td>Duan, W.-J.</td>
<td>69</td>
</tr>
<tr>
<td>Biciusca, V.</td>
<td>92, 93</td>
<td>Duarte-Rojo, A.</td>
<td>62</td>
</tr>
<tr>
<td>Bie, J.</td>
<td>72</td>
<td>Duricova, D.</td>
<td>14</td>
</tr>
<tr>
<td>Blum, H.E.</td>
<td>87</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bokova, T.A.</td>
<td>65, 66</td>
<td>Ehnert, S.</td>
<td>88</td>
</tr>
<tr>
<td>Bortlik, M.</td>
<td>14</td>
<td>Elliott, C.</td>
<td>13</td>
</tr>
<tr>
<td>Bullas, D.</td>
<td>13</td>
<td>Endriani, R.</td>
<td>63</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Erturk, H.</td>
<td>85</td>
</tr>
<tr>
<td>Caballeria, J.</td>
<td>62</td>
<td>Estherina, J.</td>
<td>1, 36</td>
</tr>
<tr>
<td>Cai, Z.</td>
<td>76</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Catalan Ramirez, J.M.</td>
<td>39, 40, 41</td>
<td>Famulski, W.</td>
<td>50</td>
</tr>
<tr>
<td>Celec, P.</td>
<td>4, 5</td>
<td>Farkas, K.</td>
<td>42</td>
</tr>
<tr>
<td>Cen, R.-Y.</td>
<td>106</td>
<td>Fauzi, A.</td>
<td>1, 36</td>
</tr>
<tr>
<td>Chalupa, J.</td>
<td>78</td>
<td>Fen, Q.</td>
<td>10</td>
</tr>
<tr>
<td>Chen, B.-L.</td>
<td>74</td>
<td>Fiocchi, C.</td>
<td>49</td>
</tr>
<tr>
<td>Chen, C.</td>
<td>6</td>
<td>Fu, N.</td>
<td>86</td>
</tr>
<tr>
<td>Chen, C.-X.</td>
<td>57</td>
<td>Fu, W.</td>
<td>55</td>
</tr>
<tr>
<td>Chen, F.</td>
<td>103</td>
<td>Fu, Z.-R.</td>
<td>99</td>
</tr>
<tr>
<td>Chen, G.</td>
<td>10</td>
<td>Fuszek, P.</td>
<td>14, 42</td>
</tr>
<tr>
<td>Chen, J.</td>
<td>9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chen, J.</td>
<td>47</td>
<td>Gao, Y.-F.</td>
<td>70</td>
</tr>
<tr>
<td>Chen, J.</td>
<td>77</td>
<td>Garcia Fernandez, F.J.</td>
<td>39, 40, 41</td>
</tr>
<tr>
<td>Chen, J.D.Z.</td>
<td>7, 8</td>
<td>Gerova, V.</td>
<td>15, 71</td>
</tr>
<tr>
<td>Chen, J.-H.</td>
<td>7, 8, 24, 58</td>
<td>Ghosh, S.</td>
<td>72</td>
</tr>
<tr>
<td>Chen, J.-S.</td>
<td>98</td>
<td>Ginès, P.</td>
<td>62</td>
</tr>
<tr>
<td>Chen, L.</td>
<td>67</td>
<td>Göktay, Y.</td>
<td>2</td>
</tr>
<tr>
<td>Name</td>
<td>Pages</td>
<td>Name</td>
<td>Pages</td>
</tr>
<tr>
<td>-----------------------------</td>
<td>-------</td>
<td>-----------------------------</td>
<td>-------</td>
</tr>
<tr>
<td>Gregus, M.</td>
<td>4, 5</td>
<td>Kawengian, V.</td>
<td>79</td>
</tr>
<tr>
<td>Guo, J.</td>
<td>45</td>
<td>Kayahan, H.</td>
<td>2</td>
</tr>
<tr>
<td>Guo, J.-C.</td>
<td>101</td>
<td>Kedzierawski, P.</td>
<td>19</td>
</tr>
<tr>
<td>Guo, L.-Q.</td>
<td>107</td>
<td>Kemona, A.</td>
<td>16, 33, 37, 43</td>
</tr>
<tr>
<td>Guermany, S.R.</td>
<td>13</td>
<td>Khaoustov, V.</td>
<td>109</td>
</tr>
<tr>
<td>Guzinska-Ustymowicz, K.</td>
<td>16, 33, 37, 43</td>
<td>Kiss, L.S.</td>
<td>14, 42</td>
</tr>
<tr>
<td>Hameed Hassan, K.</td>
<td>73</td>
<td>Krisnohani, E.</td>
<td>36</td>
</tr>
<tr>
<td>Handjari, D.R.</td>
<td>36</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hardi, F.</td>
<td>1, 36</td>
<td>Lakatos, L.</td>
<td>14</td>
</tr>
<tr>
<td>Hardjodisastro, D.</td>
<td>1, 36</td>
<td>Lakatos, P.L.</td>
<td>14, 42</td>
</tr>
<tr>
<td>He, Y.</td>
<td>74</td>
<td>Lenicek, M.</td>
<td>14</td>
</tr>
<tr>
<td>Herrera, L.</td>
<td>62</td>
<td>Lesmana, L.A.</td>
<td>35</td>
</tr>
<tr>
<td>Higuera, F.</td>
<td>62</td>
<td>Li, J.</td>
<td>20, 80</td>
</tr>
<tr>
<td>Hlavaty, T.</td>
<td>4, 5</td>
<td>Li, J.-B.</td>
<td>70</td>
</tr>
<tr>
<td>Hlista, M.</td>
<td>4, 5</td>
<td>Li, L.</td>
<td>81</td>
</tr>
<tr>
<td>Horáková, M.</td>
<td>4, 5</td>
<td>Li, L.</td>
<td>82, 83</td>
</tr>
<tr>
<td>Hou, X.</td>
<td>81, 96, 105</td>
<td>Li, L.</td>
<td>96</td>
</tr>
<tr>
<td>Hu, A.-R.</td>
<td>75</td>
<td>Li, Q.-Y.</td>
<td>103</td>
</tr>
<tr>
<td>Hu, D.</td>
<td>91</td>
<td>Li, R.</td>
<td>55</td>
</tr>
<tr>
<td>Hu, J.</td>
<td>17, 23</td>
<td>Li, S.-C.</td>
<td>94, 108</td>
</tr>
<tr>
<td>Hu, N.</td>
<td>67</td>
<td>Li, T.</td>
<td>83</td>
</tr>
<tr>
<td>Hu, R.</td>
<td>48, 53</td>
<td>Li, X.</td>
<td>60</td>
</tr>
<tr>
<td>Hu, Y.</td>
<td>10</td>
<td>Li, X.</td>
<td>70</td>
</tr>
<tr>
<td>Huang, P.</td>
<td>112</td>
<td>Li, X.-G.</td>
<td>83</td>
</tr>
<tr>
<td>Huang, Y.</td>
<td>60</td>
<td>Li, X.-L.</td>
<td>111</td>
</tr>
<tr>
<td>Huorka, M.</td>
<td>4, 5</td>
<td>Li, Y.-M.</td>
<td>57</td>
</tr>
<tr>
<td>Hylemon, P.B.</td>
<td>60</td>
<td>Li, Z.</td>
<td>24, 58</td>
</tr>
<tr>
<td>Infantes Hernandez, J.M.</td>
<td>39, 40, 41</td>
<td>Liang, B.-L.</td>
<td>86</td>
</tr>
<tr>
<td>Ista, N.</td>
<td>1, 36</td>
<td>Liang, J.-R.</td>
<td>111</td>
</tr>
<tr>
<td>Jain, S.</td>
<td>34</td>
<td>Liang, T.-B.</td>
<td>103</td>
</tr>
<tr>
<td>Japarova, A.G.</td>
<td>87</td>
<td>Lin, L.</td>
<td>21</td>
</tr>
<tr>
<td>Ji, F.</td>
<td>76</td>
<td>Liu, B.-M.</td>
<td>83</td>
</tr>
<tr>
<td>Jia, J.-D.</td>
<td>69</td>
<td>Liu, C.</td>
<td>98</td>
</tr>
<tr>
<td>Jiang, C.-M.</td>
<td>107</td>
<td>Liu, C.-Q.</td>
<td>46</td>
</tr>
<tr>
<td>Jiang, L.</td>
<td>77</td>
<td>Liu, P.</td>
<td>22</td>
</tr>
<tr>
<td>Jiang, R.</td>
<td>46</td>
<td>Liu, T.-H.</td>
<td>80</td>
</tr>
<tr>
<td>Jiang, T.-A.</td>
<td>103</td>
<td>Liu, X.</td>
<td>23</td>
</tr>
<tr>
<td>Jie, H.</td>
<td>18</td>
<td>Liu, X.</td>
<td>24</td>
</tr>
<tr>
<td>Jin, J.</td>
<td>23</td>
<td>Liu, X.</td>
<td>47</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Liu, X.</td>
<td>51</td>
</tr>
<tr>
<td>Kádesi, L.</td>
<td>4, 5</td>
<td>Liu, X.</td>
<td>58</td>
</tr>
<tr>
<td>Kajzrlikova, I.</td>
<td>78</td>
<td>Liu, Z.</td>
<td>25</td>
</tr>
<tr>
<td>Kaldirim, U.</td>
<td>85</td>
<td>Lu, B.-D.</td>
<td>107</td>
</tr>
<tr>
<td>Kamm, M.A.</td>
<td>13</td>
<td>Lu, C.</td>
<td>84</td>
</tr>
<tr>
<td>Kanczuga-Koda, L.</td>
<td>50</td>
<td>Lu, L.-G.</td>
<td>77</td>
</tr>
<tr>
<td>Kang, P.</td>
<td>94, 108</td>
<td>Lu, Q.-M.</td>
<td>26</td>
</tr>
<tr>
<td>Kansera, D.D.</td>
<td>1, 36</td>
<td>Lu, W.-M.</td>
<td>112</td>
</tr>
<tr>
<td>Name</td>
<td>Page Numbers</td>
<td>Name</td>
<td>Page Numbers</td>
</tr>
<tr>
<td>----------------------</td>
<td>--------------</td>
<td>----------------------</td>
<td>--------------</td>
</tr>
<tr>
<td>Lucic, G.</td>
<td>89</td>
<td>Ran, Y.</td>
<td>102</td>
</tr>
<tr>
<td>Lugito, N.P.H.</td>
<td>1, 36</td>
<td>Rani, A.A.</td>
<td>1, 36, 79</td>
</tr>
<tr>
<td>Lukas, M.</td>
<td>14</td>
<td>Ren, M.</td>
<td>74</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Rotty, L.</td>
<td>79</td>
</tr>
<tr>
<td>Ma, H.</td>
<td>69</td>
<td>Sahni, M.</td>
<td>34</td>
</tr>
<tr>
<td>Makarchuk, P.</td>
<td>27</td>
<td>Salata, A.</td>
<td>19</td>
</tr>
<tr>
<td>Martinez, M.</td>
<td>62</td>
<td>Samosir, D.</td>
<td>35</td>
</tr>
<tr>
<td>Mas, M.R.</td>
<td>85</td>
<td>Sari, I.</td>
<td>2</td>
</tr>
<tr>
<td>Mas, N.</td>
<td>85</td>
<td>Schoenberger, M.</td>
<td>88</td>
</tr>
<tr>
<td>Meggyesi, N.</td>
<td>14</td>
<td>Schyschka, L.</td>
<td>88</td>
</tr>
<tr>
<td>Mei, G.</td>
<td>17, 23</td>
<td>Seeliger, C.</td>
<td>88</td>
</tr>
<tr>
<td>MendozaOlivares, F.J.</td>
<td>39, 40, 41</td>
<td>Sha, W.-H.</td>
<td>106</td>
</tr>
<tr>
<td>Meng, J.-R.</td>
<td>77</td>
<td>Shen, Y.</td>
<td>103</td>
</tr>
<tr>
<td>Miao, G.-Y.</td>
<td>26</td>
<td>Shi, D.-H.</td>
<td>111</td>
</tr>
<tr>
<td>Miao, Y.</td>
<td>54</td>
<td>Shi, J.-P.</td>
<td>101</td>
</tr>
<tr>
<td>Miheller, P.</td>
<td>14</td>
<td>Shi, L.</td>
<td>97</td>
</tr>
<tr>
<td>Mo, Y.</td>
<td>51</td>
<td>Silosi, C.A.</td>
<td>92, 93</td>
</tr>
<tr>
<td>Molnár, T.</td>
<td>14, 42</td>
<td>Silosi, I.</td>
<td>92, 93</td>
</tr>
<tr>
<td>Nan, Y.-M.</td>
<td>86</td>
<td>Simadibrata, M.</td>
<td>1, 3, 36</td>
</tr>
<tr>
<td>Nepesova, O.B.</td>
<td>87</td>
<td>Simonovic, J.</td>
<td>90</td>
</tr>
<tr>
<td>Nikolov, P.</td>
<td>28, 29</td>
<td>Silkin, S.</td>
<td>11, 12, 32</td>
</tr>
<tr>
<td>Ning, Y.</td>
<td>21</td>
<td>Sodhi, K.S.</td>
<td>34</td>
</tr>
<tr>
<td>Nüssler, A.K.</td>
<td>88</td>
<td>Sokolowski, M.</td>
<td>16, 33, 37</td>
</tr>
<tr>
<td>Nüssler, N.</td>
<td>88</td>
<td>Stöckle, U.</td>
<td>88</td>
</tr>
<tr>
<td>Ou, Q.-J.</td>
<td>98, 110</td>
<td>Stoynov, S.</td>
<td>15, 71</td>
</tr>
<tr>
<td>Ou, X.-J.</td>
<td>69</td>
<td>Studer, E.</td>
<td>60</td>
</tr>
<tr>
<td>Ouyang, Q.</td>
<td>30, 31, 48, 49, 53</td>
<td>Su, B.-Z.</td>
<td>68</td>
</tr>
<tr>
<td>Ozturk, A.</td>
<td>85</td>
<td>Su, J.</td>
<td>25</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Su, Q.</td>
<td>70</td>
</tr>
<tr>
<td>Palatka, K.</td>
<td>42</td>
<td>Sulkowska, M.</td>
<td>50</td>
</tr>
<tr>
<td>Palyu, E.</td>
<td>42</td>
<td>Sulkowski, S.</td>
<td>50</td>
</tr>
<tr>
<td>Pan, Y.</td>
<td>31</td>
<td>Sun, L.-J.</td>
<td>94, 108</td>
</tr>
<tr>
<td>Pandak, W.M.</td>
<td>60</td>
<td>Sun, M.-Y.</td>
<td>38</td>
</tr>
<tr>
<td>Pang, H.-W.</td>
<td>98</td>
<td>Svinarov, D.</td>
<td>15</td>
</tr>
<tr>
<td>Panova, D.</td>
<td>28</td>
<td>Svirtlih, N.</td>
<td>90</td>
</tr>
<tr>
<td>Papp, J.</td>
<td>14, 42</td>
<td>Tanc, H.</td>
<td>38</td>
</tr>
<tr>
<td>Papp, M.</td>
<td>14, 42</td>
<td>Tan, J.</td>
<td>75</td>
</tr>
<tr>
<td>Pavic, S.</td>
<td>89, 90</td>
<td>Tang, S.</td>
<td>105</td>
</tr>
<tr>
<td>Pen, J.</td>
<td>10</td>
<td>Tang, Y.</td>
<td>95</td>
</tr>
<tr>
<td>Peng, Y.</td>
<td>91</td>
<td>Tarius, A.</td>
<td>3</td>
</tr>
<tr>
<td>Petrescu, F.</td>
<td>93</td>
<td>Tasci, I.</td>
<td>85</td>
</tr>
<tr>
<td>Pietrzykowski, A.</td>
<td>50</td>
<td>Tendean Wenas, N.</td>
<td>79</td>
</tr>
<tr>
<td>Ping, J.</td>
<td>10</td>
<td>Tian, C.</td>
<td>76</td>
</tr>
<tr>
<td>Pokrotniæ, J.</td>
<td>11, 12, 32</td>
<td>Topal, T.</td>
<td>85</td>
</tr>
<tr>
<td>Prylicynicz, A.</td>
<td>16, 33, 37, 43</td>
<td>Tordai, A.</td>
<td>14</td>
</tr>
<tr>
<td>Pu, P.</td>
<td>54</td>
<td>Torres Dominguez, Y.</td>
<td>39, 40, 41</td>
</tr>
<tr>
<td>Qian, J.-M.</td>
<td>20</td>
<td>Toth, T.G.</td>
<td>14, 42</td>
</tr>
<tr>
<td>Qing, Y.-S.</td>
<td>103</td>
<td>Tulassay, Z.</td>
<td>14</td>
</tr>
<tr>
<td>Name</td>
<td>Page Numbers</td>
<td>Notes</td>
<td></td>
</tr>
<tr>
<td>-----------------------</td>
<td>--------------</td>
<td>-----------</td>
<td></td>
</tr>
<tr>
<td>Udvardy, M.</td>
<td>42</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ünsal, B.</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ustymowicz, M.</td>
<td>16, 33, 37, 43</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uysal, S.</td>
<td>85</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vitek, L.</td>
<td>14</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vitek, P.</td>
<td>78</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Waleleng, B.J.</td>
<td>79</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wang, B.</td>
<td>81, 96</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wang, C.</td>
<td>97</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wang, C.-S.</td>
<td>104</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wang, F.</td>
<td>44</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wang, H.</td>
<td>9</td>
<td>81, 96, 105</td>
<td></td>
</tr>
<tr>
<td>Wang, H.</td>
<td>10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wang, H.</td>
<td>100</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wang, J.</td>
<td>98, 110</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wang, L.</td>
<td>45</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wang, L.</td>
<td>46</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wang, Q.</td>
<td>102</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wang, Q.-Y.</td>
<td>106</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wang, R.-Q.</td>
<td>86</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wang, S.</td>
<td>91</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wang, W.-L.</td>
<td>103</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wang, X.</td>
<td>25</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wang, Y.</td>
<td>47</td>
<td>81, 96, 105</td>
<td></td>
</tr>
<tr>
<td>Wang, Y.</td>
<td>48</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wang, Y.</td>
<td>67</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wang, Z.</td>
<td>100</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wang, Z.-X.</td>
<td>99</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wei, J.</td>
<td>100</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wen, Z.</td>
<td>49</td>
<td></td>
<td></td>
</tr>
<tr>
<td>West, G.</td>
<td>49</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wincewicz, A.</td>
<td>50</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wollny, T.</td>
<td>19</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wu, W.-J.</td>
<td>86</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wu, X.</td>
<td>51</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wu, Z.-X.</td>
<td>52</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Xia, Q.</td>
<td>23</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Xia, X.</td>
<td>44</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Xia, X.</td>
<td>95</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Xiang, J.</td>
<td>53</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Xiang, Y.-S.</td>
<td>46</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Xiao, Y.</td>
<td>54</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Xu, D.</td>
<td>23</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Xu, J.</td>
<td>17, 23</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Xu, J.</td>
<td>83</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Xu, J.</td>
<td>84</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Xu, L.-B.</td>
<td>98, 110</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Xu, Y.-M.</td>
<td>109</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Xue, H.</td>
<td>76</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yang, F.-C.</td>
<td>103</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yang, J.</td>
<td>38</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yang, J.-H.</td>
<td>95</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yang, J.-H.</td>
<td>104</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yang, J.-S.</td>
<td>104</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yang, J.-X.</td>
<td>83</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yang, L.</td>
<td>81</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yang, P.-C.</td>
<td>25</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yang, R.-P.</td>
<td>74</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yang, S.</td>
<td>55</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yang, S.-B.</td>
<td>104</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yang, X.</td>
<td>100</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yang, Y.</td>
<td>56</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yang, Y.-F.</td>
<td>112</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yang, Z.-G.</td>
<td>61</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yao, Y.-T.</td>
<td>106</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yaruntradhani, R.</td>
<td>1, 36</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ye, C.</td>
<td>31</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ye, J.</td>
<td>81, 96, 105</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yin, H.</td>
<td>99</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ying, L.</td>
<td>107</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yoffe, B.</td>
<td>109</td>
<td></td>
<td></td>
</tr>
<tr>
<td>You, H.</td>
<td>69, 80</td>
<td></td>
<td></td>
</tr>
<tr>
<td>You, L.</td>
<td>95</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yu, C.</td>
<td>47</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yu, J.</td>
<td>86</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yu, J.</td>
<td>109</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yu, J.-W.</td>
<td>94, 108</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yu, X.-H.</td>
<td>110</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yu, Y.-L.</td>
<td>104</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yuksel, F.</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zainal, A.</td>
<td>63</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zakuciová, M.</td>
<td>4, 5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zapata, L.</td>
<td>62</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zelinková, Z.</td>
<td>4, 5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zeng, Z.-R.</td>
<td>74</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zhang, B.-L.</td>
<td>57</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zhang, C.</td>
<td>24, 58</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zhang, C.</td>
<td>111</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zhang, F.-K.</td>
<td>69</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zhang, G.</td>
<td>45</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zhang, H.</td>
<td>21</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zhang, M.</td>
<td>103</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zainal, A.</td>
<td>63</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zakuciová, M.</td>
<td>4, 5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zapata, L.</td>
<td>62</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zelinková, Z.</td>
<td>4, 5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zeng, Z.-R.</td>
<td>74</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zhang, B.-L.</td>
<td>57</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zhang, C.</td>
<td>24, 58</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zhang, C.</td>
<td>111</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zhang, F.-K.</td>
<td>69</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zhang, G.</td>
<td>45</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zhang, H.</td>
<td>21</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zhang, M.</td>
<td>103</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Zhang, N. 112
Zhang, Q. 24, 58
Zhang, R. 110
Zhang, W. 21
Zhao, B. 72
Zhao, Q.-Y. 103
Zhao, S.-X. 86
Zhao, Y.-H. 94, 108
Zhao, Z. 47
Zheng, R.-D. 77
Zheng, S.-S. 103
Zheng, W. 20
Zheng, Y. 106
Zhong, Y.-D. 112
Zhong, Y.-Q. 59
Zhou, H. 60
Zhou, W. 81, 96
Zhu, S. 95
Zhuang, H. 61
Abstracts/Poster Abstracts Falk Symposium 174

Innovative Drugs for bowel and liver diseases
Modern formulations and specially designed delivery systems ensure targeted release of the active drug

Scientific Dialogue in the interest of therapeutic progress
Falk Symposia and Workshops nearly 250, attended by more than 100,000 participants from over 100 countries since 1967
Continuing medical education seminars over 14,000, attended by more than one million physicians and patients in Germany alone
Comprehensive literature service for healthcare professionals and patients with more than 200 publications

www.falkfoundation.org www.dr Falkpharma.com
Leinenweberstr. 5 79108 Freiburg Germany Tel +49 (0)761/1514-0 Fax +49 (0)761/1514-321 Mail zentrale@drfalkpharma.de

Gut and Liver
August 27 – 28, 2010
Shangri La’s Kerry Centre Hotel
Beijing, P. R.China

Abstracts
Poster Abstracts