Programma najaarsvergadering 2 en 3 oktober 2008

NEDERLANDSE VERENIGING VOOR GASTROENTEROLOGIE

Sectie Gastrointestinale Endoscopie
Netherlands Society for Parenteral and Enteral Nutrition
Sectie Neurogastroenterologie en Motiliteit
Sectie Experimentele Gastroenterologie
Sectie Kindergastroenterologie
Sectie Endoscopie Verpleegkundigen en Assistenten
Vereniging Maag Darm Lever Verpleegkundigen

NEDERLANDSE VERENIGING VOOR HEPATOLOGIE

NVGIC GastroIntestinale Chirurgie

NEDERLANDSE VERENIGING VOOR GASTROINTESTINALE CHIRURGIE

MDL

NEDERLANDSE VERENIGING VAN MAAG-DARM-LEVERARTSEN

Locatie:

NH KONINGSHOF VELDHOVEN

INHOUDSOPGAVE pag.

N.B. De met een asterisk gemerkte abstracts in het programma zijn ingezonden door leden van de Sectie Kindergastroenterologie.

Tijdstippen diverse ledenvergaderingen tijdens najaarsvergadering:
Nederlandse Vereniging voor Hepatologie 2 oktober, 15.30 uur – Parkzaal

INHOUDSOPGAVE pag.

VRIJDAG 3 OKTOBER 2008

N.B. De met een asterisk gemerkte abstracts in het programma zijn ingezonden door leden van de Sectie Kindergastroenterologie.

Aandachtspunt voor de sprekers:
u dient zich strikt te houden aan de beschikbare spreektijd! U vindt dit aangegeven bij de betreffende sessie. Indien u een eigen laptop gebruikt, dan dient u deze aan te sluiten tijdens de discussietijd van de spreker voor u.
In **zaal 25** kunt u uw PowerPoint presentatie tevoren controleren.

Tijdstippen diverse ledenvergaderingen tijdens najaarsvergadering:

Nederlandse Vereniging voor Gastroenterologie	3 oktober, 07.30 uur - Genderzaal
Nederlandse Vereniging van MDL-artsen	3 oktober, 13.00 uur - Genderzaal
Sectie Endoscopie Verpleegk. en Assistenten	3 oktober, 13.30 uur – Diezezaal

VOORWOORD

Hierbij treft u het volledige programma aan van de najaarsvergadering op 2 en 3 oktober in Congrescentrum NH Koningshof te Veldhoven. Zoals gebruikelijk worden deze dagen vooraf gegaan door het cursorisch onderwijs in maag-, darm- en leverziekten, waarvan u het programma aantreft op bladzijde 5. Aanvang cursus: 15.00 uur.

Het programma zal donderdag 2 oktober om 10.30 uur van start gaan met abstract-presentaties van de Nederlandse Vereniging voor Gastrointestinale Chirurgie en de Nederlandse Vereniging voor Hepatologie. In de Baroniezaal vindt een symposium rond de CBO-richtlijn Coeliakie plaats. In de middag verzorgt de NVGIC de gebruikelijke 'minibattle' van de NVGIC, dit keer rond de verschillende benaderingen van cholecystectomie. De Sectie Neurogastroenterologie en Motiliteit heeft een programma samengesteld rond NERD en de klinische sectie van de Nederlandse Vereniging voor Hepatologie organiseert voorts een symposium waarin de nieuwe ontwikkelingen in de detectie en behandeling van colorectale levermetastasen worden besproken.
Om 17.00 volgt – plenair - de President Select in de Diezezaal. Om 18.00 uur zal aansluitend de AstraZeneca Gastrointestinale Research Award 2008 worden uitgereikt, waarna de eerste prijswinnaar een erevoordracht zal houden. Met deze lezing wordt het programma van de donderdag afgesloten. In de Brabantzaal zal om 19.30 uur voor de leden van de vereniging vanwege de viering van het 95-jarig bestaan een feestelijk diner plaatsvinden. De organisatie van deze avond is in handen van collega André Smout. Na het diner, vanaf omstreeks 22.30 uur, is er muziek in de Baroniezaal en de gebruikelijke borrel in de Limburgfoyer.

Op vrijdagochtend is er na de ledenvergadering van de NVGE om 07.30 uur in de Genderzaal (met ontbijtbuffet), vanaf 08.30 casuïstiek in de Brabantzaal, gevolgd door een symposium rond Barrett surveillance. Het programma in de Brabantzaal wordt afgesloten met de Frieda den Hartog Jager lecture, verzorgd wordt door Dr. B.G. Taal uit het Antoni van Leeuwenhoekhuis. In de Baroniezaal is een programma gepland rond de IBD richtlijn. Verder deze ochtend diverse sessies met vrije voordrachten. In de Diezezaal en het Auditorium worden door de Sectie Endoscopie Assistenten en Verpleegkundigen en de Vereniging van Maag Darm Lever Verpleegkundigen eigen programma's met lezingen verzorgd. Na de lunch is er – dit najaar op proef - in de meeste zalen geen programma meer, voortgekomen uit de wens het congres zoveel mogelijk 'filevrij' te organiseren.

Dr. R.J.F. Felt-Bersma, secretaris

Belangrijk: *indien u gebruik maakt van overnachting in Koningshof dan dient u op de dag van vertrek de kamer vóór 10.00 uur te verlaten en de keycard in te leveren bij de receptie. Na dit tijdstip zullen er door Koningshof extra kosten in rekening worden gebracht. Uw bagage kunt u desgewenst in een locker deponeren. Deze vindt u nabij de hoofdingang.*

Belangrijke mededeling

over de aanwezigheid van farmaceutische industrieën

Aan alle deelnemers aan de najaarsvergadering

De Nederlandse Vereniging voor Gastroenterologie kent een jarenlange samenwerking met de farmaceutische industrie. De vereniging stelt de farmaceutische industrie in de gelegenheid aanwezig te zijn bij de wetenschappelijke vergaderingen met een stand. Mede hierdoor kan de vereniging haar wetenschappelijke bijeenkomsten organiseren.
In het “besluit van 31 oktober 1994, Stb. 787, houdende regels voor reclame voor geneesmiddelen (Reclamebesluit Geneesmiddelen)” is onder andere geregeld wat wel en wat niet is toegestaan ten aanzien van gunstbetoning voor artsen door de farmaceutische industrie. De wet zegt dat - onder strikte voorwaarden - de farmaceutische industrie alleen reclame mag maken voor receptgeneesmiddelen voor personen die bevoegd zijn om dergelijke geneesmiddelen voor te schrijven. Alle andere personen (inclusief bijvoorbeeld verpleegkundigen, endoscopie assistenten en biochemici) worden beschouwd als “publiek”. De farmaceutische industrie mag geen reclame maken voor receptgeneesmiddelen voor publiek.
De Nederlandse Vereniging voor Gastroenterologie is een wetenschappelijke vereniging voor personen die beroepsmatig betrokken zijn bij zorg, onderwijs en onderzoek ten behoeve van patiënten met maag-, darm- en leveraandoeningen. Dat betekent dat ook personen die geen arts zijn, lid van de NVGE kunnen zijn.
De aanwezigheid van artsen, niet-artsen en farmaceutische industrieën tijdens de najaarsvergadering kan de NVGE ongewild in aanraking brengen met de inspectie voor de gezondheidszorg, sectie reclametoezicht en daarmee in diskrediet worden gebracht.
Dat willen wij te allen tijde voorkomen.

Wij delen u dan ook het volgende mede:
Reclame-uitingen en merkproductinformatie van farmaceutische industrieën in het voorliggende programmaboekje zijn alleen gericht op personen die bevoegd zijn om de betreffende geneesmiddelen voor te schrijven.
Al het aanwezige reclamemateriaal, reclame-uitingen en merkproductinformatie van farmaceutische industrieën die aanwezig zijn op het najaarscongres, zijn alleen bedoeld en alleen gericht op personen die bevoegd zijn om de betreffende geneesmiddelen voor te schrijven. Wij maken u erop attent dat het voor niet-artsen dan ook niet is toegestaan de stands van de aanwezige farmaceutische industrieën te bezoeken.

De NVGE en farmaceutische industrie (sponsoren) meent u allen, en met name de niet BIG geregistreerde personen, voldoende te hebben ingelicht en kunnen niet verantwoordelijk worden gehouden indien u geen acht slaat op deze mededeling.

Het bestuur van de NVGE

Cursuscommissie: Dr. R.A. de Man (voorzitter) (MDL-arts, Erasmus MC)
Dr. R. van Hillegersberg (chirurg UMCU)
Dr. D.J. de Jong, (MDL-arts UMCN)
Prof. dr. J.H. Kleibeuker (MDL-arts, UMCG)
Drs. A.D. Koch (aios MDL, Erasmus MC)
Dr. A.M.P. de Schryver (aios MDL, UMCU)
Dr. R. Timmer (MDL-arts, Antonius Nieuwegein)

Onderwerp: IBD

Voorzitters middagprogramma:
Dr. D.J. de Jong (UMCN) en Dr. N.G. Venneman (St. Antonius Ziekenhuis)

15.00 – 15.30	Het natuurlijk beloop van IBD, en zijn voorspellers *Dr. M. Pierik, aZM Maastricht*
15.30 – 16.00	IBD genetica en de dagelijkse praktijk *Dr. R.K. Weersma, UMC Groningen*
16.00 – 16.30	Toepassing van beeldvormende technieken bij IBD *Prof. dr. J. Stoker , AMC, Amsterdam*
16.30 – 17.00	pauze
17.00 – 17.30	Endoscopie bij IBD als gouden standaard *Dr. P. Mensink, Erasmus MC, Rotterdam*
17.30 – 18.00	Maligne potentie van IBD en mogelijke surveillance *Dr. B. Oldenburg, UMC Utrecht*
18.00 – 19.00	Diner buffet

Voorzitters avondprogramma:
Dr. R. Timmer, Sint Antonius Ziekenhuis en Drs. A.G.L. Bodelier, azM Maastricht

19.00 – 19.30	Voedingsinterventies bij IBD *Dr. A.A. van Bodegraven, VU medisch centrum, Amsterdam*
19.30 – 20.00	Is conventionele therapie achterhaald? *Dr. D.J. de Jong, UMC St. Radboud, Nijmegen*
20.00 – 20.30	IBD Chirurgie *Prof. dr. W.A. Bemelman, AMC, Amsterdam*
20.30 – 21.00	Extra-intestinale zaken *Dr. G. Dijkstra, UMC Groningen*
21.00 - 21.30	Biologisch logisch? Bij wie, wanneer en hoe *Dr. C.J. van der Woude, Erasmus MC, Rotterdam*
21.30 – 22.00	Panel discussie betreffende therapie bij IBD *Moderator: Dr. R. Timmer, Sint Antonius Ziekenhuis, Nieuwegein*

De cursuscommissie verwacht van de MDL-artsen i.o. dat ze de Cursus Klinische Hepatologie (NVH) éénmaal bezoeken in het tweede deel van de MDL-opleiding (jaar vier tot zes).

Programma donderdag 2 oktober 2008

DONDERDAG	DIEZEZAAL	BARONIEZAAL	PARKZAAL	AUDITORIUM	BRABANTZAAL
10.30 – 12.00	Vrije voordrachten Nederlandse Vereniging voor Gastrointestinale Chirurgie p. 10	**CBO-richtlijn:** Coeliakie in de praktijk p. 12	Vrije voordrachten Nederandse Vereniging voor Hepatologie, klinisch p. 13	Geen programma in deze zaal donderdag	Geen programma in deze zaal donderdag
12.00 – 13.00	Lunchbuffet expositiehal	Lunchbuffet expositiehal	Lunchbuffet expositiehal		
13.00 – 15.30	Vrije voordrachten Nederlandse Vereniging voor Gastrointestinale Chirurgie p. 16 14.00 **Minibattle NVGIC** "De verschillende benaderingen van cholecystectomie" p. 17	Vrije voordrachten Nederlandse Vereniging voor Gastroenterologie 13.30 **Symposium** "Non-erosive reflux disease" p.21	Vrije voordrachten Nederandse Vereniging voor Hepatologie, p. 24 14.00 **Symposium NVH** "Nieuwe ontwikkelingen in de detectie en behandeling van colorectale levermetastasen" p. 25		
15.30 – 16.00	Theepauze	Theepauze	Theepauze **Ledenvergadering NVH**		
16.00 – 17.00	Vrije voordrachten Nederlandse Vereniging voor Gastroenterologie p. 18	Vrije voordrachten Netherlands Society of Parenteral and Enteral Nutrition p. 22	Vrije voordrachten Nederandse Vereniging voor Hepatologie Klinisch p. 27		
17.00 - 18.00	**President Select** p. 19	Geen programma in deze zaal	Geen programma in deze zaal		
18.00 – 18.30	**Uitreiking AZ-prijs** p. 20	Geen programma in deze zaal	Geen programma in deze zaal		
18.30 – 19.30	Congresborrel expositiehal	Congresborrel expositiehal	Congresborrel expositiehal		
19.30 – 22.00	Diner in Brabantzaal	Diner in Brabantzaal	Diner in Brabantzaal		
22.00 – 01.00	Borrel / Muziek in de foyer	Borrel / Muziek in de foyer	Borrel / Muziek in de foyer		

Programma vrijdag 3 oktober 2008

VRIJDAG	BRABANTZAAL	BARONIEZAAL	PARKZAAL	AUDITORIUM	DIEZEZAAL
07.30 – 08.30	**Ledenvergadering NVGE** in Genderzaal – met ontbijtbuffet				
08.30 – 09.00	**Casuïstiek voor de clinicus** p. 29	Vrije voordrachten Nederlandse Vereniging voor Gastroenterologie p. 33	Vrije voordrachten Nederlandse Vereniging voor Gastroenterologie p. 37		
09.00 – 10.30	**Barrett Surveillance** "De zin en onzin van Barrett endoscopieën in Nederland: een interactief symposium" p.29	Vrije voordrachten Nederlandse Vereniging voor Gastroenterologie p. 34	Vrije voordrachten Nederlandse Vereniging voor Gastroenterologie p. 38	Programma Vereniging voor Maag-Darm-Lever Verpleegkundigen p. 44	Programma Sectie Endoscopie Verpleeg-kundigen en Assistenten p. 43
10.30 – 11.00	Koffiepauze	Koffiepauze	Koffiepauze	Koffiepauze	Koffiepauze
11.00 – 13.00	Vrije voordrachten Sectie Gastrointestinale Endoscopie 12.30 **Frieda den Hartog Jager lecture:** Dr. B.G. Taal "Carcinoid anno 2008" p. 32	**IBD-richtlijn** p. 36	Vrije voordrachten Nederlandse Vereniging voor Gastroenterologie p. 40	Programma Vereniging voor Maag-Darm-Lever Verpleegkundigen p. 44	Programma Sectie Endoscopie Verpleeg-kundigen en Assistenten p. 43
13.00 – 14.30	Lunchbuffet expositiehal **Ledenvergadering NVMDL**	Lunchbuffet expositiehal	Lunchbuffet expositiehal	Lunchbuffet expositiehal	Lunchbuffet expositiehal
14.30	Einde programma	Einde programma, thee	Einde programma, thee	Einde programma, thee	Einde programma, thee

Nederlandse Vereniging voor Gastrointestinale Chirurgie **Diezezaal**

10.00 Inschrijving, koffie

Voorzitters: J.W. Dekker en L. Stassen

Voordrachten in het Nederlands, spreektijd 7 minuten, discussietijd 3 minuten.

10.30 Clinical outcome of patients with infection of extrapancreatic collections without pancreatic parenchymal necrosis (p. 45)
O.J. Bakker[1], U. Ahmed Ali[1], H.C. van Santvoort[2], M.G. Besselink[2], H.G. Gooszen[1] and T.L. Bollen[2] for the Dutch Pancreatitis Study Group, [1]Division of Surgery, University Medical Center Utrecht, Utrecht, [2]Dept of Radiology, St. Antonius Hospital, Nieuwegein, The Netherlands

10.40 Transcolonic Peritoneoscopy for the Detection of Peritoneal Metastases (p. 46) *R.P. Voermans[1,2], D.O. Faigel[3], M.I. van Berge Henegouwen[2], B. Sheppard[4], P. Fockens[1], [1]Dept. of Gastroenterology and Hepatology, [2]Dept of Surgery, Academic Medical Center, Amsterdam, The Netherlands, [3]Dept of Gastroenterology and Hepatology, [4]Dept of Surgery, Oregon Health & Science University, Portland, OR, USA*

10.50 Number of lymph nodes examined among patients with gastric cancer: variation between departments of pathology and clear prognostic impact in node-negative disease (p. 47)
A.E. Dassen[1], V.E.P.P. Lemmens[2], A.A.M. van der Wurff[3], S.J. Brennink-meijer[4], D.J. Lips[1], K. Bosscha[1],[1]Jeroen Bosch Hospital, Dept of Surgery, 's-Hertogenbosch, [2]Eindhoven Cancer Registry, Comprehensive Cancer Centre South (IKZ), Eindhoven, [3]St Elisabeth Hospital, Dept of Pathology, Tilburg, [4]Twee Steden Hospital, Dept of Surgery, Tilburg, The Netherlands

11.00 Concurrent chemoradiation with cisplatin and 5FU followed by surgery or as definitive treatment for localized oesophageal cancer (p. 48)
E.F.W. Courrech Staal[1], A. Cats[2], B.M.P. Aleman[3], M.L.F. van Velthuysen[4], H. Boot[2], F. van Coevorden[1], J.W. van Sandick[1], [1]Department of Surgery, [2]Department of Gastroenterology, [3]Department of Radiotherapy, [4]Depart-ment of Pathology, Cancer Institute-Antoni van Leeuwenhoek Hospital, Amsterdam, The Netherlands

11.10 Robot-assisted thoracoscopic esophagectomy for esophageal cancer: short- and mid-term results (p. 49)
J. Boone[1], M.E.I. Schipper[2], W.A. Moojen[1], I.H.M. Borel Rinkes[1],G.J.E. Cromheecke MD[3], R. van Hillegersberg[1], Department of [1]Surgery, [2]Pathology and [3]Anaesthesiology, University Medical Center Utrecht, Utrecht, The Netherlands

11.20 Influence of circumferential resection margin on prognosis in distal esophageal and gastro-esophageal cancer approached through the transhiatal route (p. 50)
J.J.G. Scheepers, D.L. van der Peet, A.A.F.A. Veenhof, and M.A. Cuesta, Department of Surgery, Vrije Universiteit Medical Center (VUmc), Amsterdam, The Netherlands

11.30 Boerhaave Syndrome:
20 years of experience in the Erasmus Medical Centre, Rotterdam (p. 51)
M.P. de Jong[1], W.M.U. van Grevenstein[2], J.J.B. Van Lanschot[2], H.W. Tilanus[2], [1]Medisch Centrum Rijnmond Zuid, Rotterdam, [2]Erasmus Medisch Centrum, Rotterdam, The Netherlands

11.40 Feasibility of laparoscopic Nissen as a day-case procedure (p. 52)
M.S. Vlug[1], J. Wind[1], J.H. Eshuis[2], M.I. van Berge Henegouwen[1], D.J. Gouma[1], W.A. Bemelman[1], [1]Department of Surgery, Academic Medical Centre at the University of Amsterdam, Amsterdam, [2]Department of Anaesthesiology, Academic Medical Centre at the University of Amsterdam, Amsterdam, The Netherlands

11.50 Preoperative biliary drainage in patients with proximal bile duct obstruction: Endoscopic or percutaneous approach? (p. 53)
J.J. Kloek[1], N.A. van der Gaag[1], Y. Aziz[1], O.M van Delden[2], E.A.J. Rauws[3], O.R.C. Busch[1], D.J. Gouma[1], T.M. van Gulik[1], [1]Dept of Surgery, Academic Medical Center, University of Amsterdam, [2]Dept of Radiology, Academic Medical Center, University of Amsterdam, [3]Dept of Gastroenterology, Academic Medical Center, University of Amsterdam, The Netherlands

12.00 Lunchbuffet in expositiehal

Donderdag 2 oktober 2008

Symposium Nederlandse Vereniging voor Gastroenterologie **Baroniezaal**

10.00 Inschrijving, koffie

Voorzitter: C.J.J. Mulder

CBO-richtlijn Coeliakie in de praktijk

10.30 Opening en inleiding
Prof. dr. C.J.J. Mulder, maag-darm-leverarts,
VU medisch centrum, Amsterdam

10.45 Lymfocytaire enteritis
Dr. P.J. Wahab, maag-darm-leverarts,
Alysis Ziekenhuis, Arnhem

11.00 Serologie
Dr. B.M.E. Blomberg, immunoloog,
VU medisch centrum, Amsterdam

11.15 Histologie M IIIABC
Dr. J. Meijer, patholoog,
Alysis Ziekenhuis, Arnhem

11.30 Kinder diagnostiek en therapie
Dr. L. Mearin, kinderarts,
Leids Universitair Medisch Centrum, Leiden

11.45 Gecompliceerde Coeliakie
Prof. dr. C.J.J. Mulder, maag-darm-leverarts,
VU medisch centrum, Amsterdam

12.00 Lunchbuffet Kempenhal

Nederlandse Vereniging voor Hepatologie (klinisch) **Parkzaal**

10.00 Inschrijving, koffie

Voorzitters: J.P.H. Drenth en R.J. de Knegt

Voordrachten in het Nederlands, spreektijd 7 minuten, discussietijd 3 minuten

10.30 Improved prognosis for patients with Primary Biliary Cirrhosis showing relevant biochemical response to UDCA. Results of a multicenter long-term cohort study involving 375 patients (combinatievoordracht, p. 54 + 55)
E.M.M. Kuiper[1], B.E. Hansen[2], R.A. de Vries[3], J.W. den Ouden-Muller[4], Th.J.M van Ditzhuijsen[5], E.B. Haagsma[6], M.H.M.G. Houben[7], B.J.M. Witteman[8], K.J van Erpecum[9], H.R. van Buuren[1] for the Dutch PBC study group., [1]Dept of Gastroenterology and Hepatology and [2]Dept of Epidemiology and Biostatistics, Erasmus University Medical Center, Rotterdam, [3]Dept of Gastroenterology and Hepatology, Rijnstate Hospital, Arnhem, [4]Dept of Internal medicine, Sint Franciscus Gasthuis, Rotterdam, [5]Dept of Internal medicine, Jeroen Bosch Hospital, Den Bosch, [6]Dept of Gastroenterology and Hepatology, University Medical Center Groningen, [7]Dept of Gastroenterology and Hepatology, Haga Hospital, Den Haag, [8]Dept of Gastroenterology and Hepatology, Hospital Gelderse Vallei, Ede, [9]Dept of Gastroenterology and Hepatology, University Medical Center Utrecht, The Netherlands

10.40 Antiviral effect of entecavir: Results from 153 chronic hepatitis B patients in an international multicenter cohort study (p. 56)
J.G.P. Reijnders[1], K. Deterding[2], J. Petersen[3], F. Zoulim[4], T. Santantonio[5], M. Buti[6], F. van Bömmel[7], B.E. Hansen[1], H. Wedemeyer[2], H.L.A. Janssen[1], [1]Dept of Gastroenterology and Hepatology, Erasmus MC University Medical Center Rotterdam, Rotterdam, the Netherlands, [2]Dept of Gastroenterology, Hepatology, and Endocrinology, Medical School Hannover, Hannover, Germany, [3]Dept of Medicine, University of Hamburg, Hamburg, Germany[4], Dept of Hepatology, Hotel Dieu Hospital Lyon, Lyon, France[5], Clinic of Infectious Diseases, University of Bari, Bari, Italy[6], Dept of Hepatology, Hospital Vall de Hebron, Barcelona, Spain[7], Dept of Gastroenterology and Hepatology, Charité University Medical Center Berlin, Berlin, Germany

10.50 No beneficial effects of adding amantadine to standard PEG-interferon alfa-2b and ribavirin therapy in naïve chronic hepatitis C patients (p. 57)

H. van Soest[1], P.J. van der Schaar[2], G.H. Koek[3], R.A. de Vries[4], N.A.M. van Ooteghem[5], B. van Hoek[6], J.P.H. Drenth[7], J.M. Vrolijk[8], R.J. Lieverse[9], G.M.P. Houben[10], A. van der Sluys Veer[11], P.D. Siersema[1], A.M. van Loon[12], M.E.I. Schipper[13], K.J. van Erpecum[1], G. Boland[1,12], Depts. of Gastroenterology and Hepatology of [1]University Medical Center Utrecht, [2]Atrium Medical Center Heerlen, [3]University Hospital Maastricht, [4]Rijnstate Hospital Arnhem, [5]St Lucas Andreas Hospital Amsterdam, [6]Leiden University Medical Center, 7University Hospital Nijmegen, [8]Erasmus Medical Center Rotterdam, [9]Gelre Ziekenhuizen Apeldoorn, [10]Ziekenhuis Zeeuws Vlaanderen, [11]Onze Lieve Vrouwe Gasthuis Amsterdam, and Depts of Virology[12] and Pathology[13], University Hospital Utrecht, The Netherlands

11.00 Liver cirrhosis at baseline is an important predictor of resistance to adefovir (p. 58)

J.G.P. Reijnders[1], B.E. Hansen[1,2], S.D. Pas[3], R.A. de Man[1], M. Schutten[3], H.L.A. Janssen[1], [1]Dept of Gastroenterology and Hepatology, Erasmus MC, University Medical Center Rotterdam, [2]Dept of Epidemiology and Biostatistics, Erasmus MC, University Medical Center Rotterdam, [3]Dept of Virology, Erasmus MC, University Medical Center Rotterdam.

11.10 Early HBeAg Loss during Peginterferon Alpha-2b Therapy Predicts HBsAg Loss – Results of a Long-Term Follow-Up Study in Chronic Hepatitis B (p. 59)

E.H.C.J. Buster[1], H.J. Flink[1], H. Simsek[2], E.J. Heathcote[3], S. Sharmila[4], G.E. Kitis[5], G. Gerken[6], M. Buti[7], R.A. de Vries[8], E. Verhey[1], B.E. Hansen[1,9], H.L.A. Janssen[1], [1]Dept of Gastroenterology and Hepatology, Erasmus MC University Medical Center Rotterdam, Rotterdam, The Netherlands, [2]Hacettepe University Faculty of Medicine, Ankara, Turkey, [3]Dept of Medicine, Toronto Western Hospital University Health Network, Toronto, Canada; [4]Hepatology Unit, Hospital Selayang, Selangor, Malaysia, [5]Dept of Gastroenterology, George Papanikolaou General Regional Hospital, Thessaloniki, Greece, [6]Dept of Gastroenterology and Hepatology, University Hospital, Essen, Germany, [7]Liver Unit, Hospital General Universitari Vall d'Hebron & CIBEREHD, Barcelona, Spain, [8]Dept of Gastroenterology and Hepatology, Rijnstate Hospital, Arnhem, The Netherlands, [9]Dept of Epidemiology and Biostatistics, Erasmus MC University Medical Center Rotterdam, Rotterdam, The Netherlands

11.20 Diabetes Mellitus after Liver Transplantation for Chronic Hepatitis C – Impact of Calcineurin Inhibition (p. 60)

B.J. Veldt [1,3], J.J. Poterucha[1], K.D.S. Watt[1], C.B. Rosen[2], J.K. Heimbach[2], M.R. Charlton[1],Mayo Clinic, Division of Gastroenterology and Hepatology[1] and Division of Transplantation Surgery[2], Rochester MN, USA, [3]Erasmus MC University Medical Center, Dept of Gastroenterology and Hepatology, Rotterdam, The Netherlands

11.30 Clinical and basal aspects of anemia during antiviral therapy for hepatitis C (p. 61)

C.H. van Soest[1], W. Renooij[2], K.J. van Erpecum[1], Depts of Gastro-enterology[1] and Surgery[2] University Medical Center Utrecht, Utrecht, The Netherlands

11.40 Identifying transmission pairs in hepatitis B source and contact tracing: agreement of epidemiological and phylogenetic analysis in the multi-ethnic community of Rotterdam (2002-2005) (p. 62)

I.K. Veldhuijzen[1, 2], T.H. Mes[3], M.C. Mostert[1], Niesters[3], S.D. Pas[3]; J.J. Voermans[3], R.A.de Man[2], H.M. Götz[1], G.J. van Doornum[3], J.H. Richardus[1, 4], [1]GGD Rotterdam-Rijnmond, Cluster Infectieziektebestrijding, [2]Erasmus MC, Universitair Medisch Centrum, Afdeling Maag-, Darm- en Leverziekten, Rotterdam, [3]Erasmus MC, Universitair Medisch Centrum, Afdeling Virologie, Rotterdam, [4]Erasmus MC, Universitair Medisch Centrum, Afd. Maatschappelijke Gezondheidszorg, Rotterdam, The Netherlands

11.50 Etiology of Budd-Chiari Syndrome – The Role of Multiple Underlying Risk Factors (p. 63)

J. Hoekstra[1], S.D. Murad[1], A. Plessier[2], M. Hernandez-Guerra[3], E. Elias4, M. Primignani[5], M. Bahr[6], J. Heller[7], A. Hadengue[8], P. Langlet[9], H. Miranda[10], J.C. Garcia-Pagan[3], D.C. Valla[2], H.L.A. Janssen[1] for the European Network for Vascular Disorders of the Liver (EN-Vie), [1]Dept of Gastroenterology and Hepatology, Erasmus University Medical Center, Rotterdam, The Netherlands, [2]Dept of Hepatology, Hopital Beaujon, AP-HP, INSERM-U773 & University Paris-7, Clichy, France, [3]Hepatic Hemodynamic Laboratory, Liver Unit, Hospital Clinic, IDIBAPS and Ciberehd, Barcelona, Spain, [4]Liver Unit, Queen Elisabeth Hospital Birmingham, Birmingham, United Kingdom, Gastroenterology and Gastrointestinal Endoscopy Unit, Ospedale Policlinico, Mangiagalli and Regina Elena Foundation, Milan, Italy, [6]Dept of Gastroenterology, Hepatology, and Endocrinology, Hannover Medical School, Hannover, Germany, [7]Dept of Internal Medicine I, University Hospital of Bonn, Bonn, Germany, [8]Div.of

Gastroenterology and Hepatology, Geneva University Hospitals, Geneva, Switzerland, [9]Dept of Hepatogastroenterology, Centre Hospitalier Univ. Brugmann, Bruxelles, Belgium, [10]Liver Transplantation Unit, Hospital General Santo Antonio, Porto, Portugal.

12.00 Lunchbuffet in expositiehal

Nederlandse Vereniging voor Gastrointestinale Chirurgie **Diezezaal**

Voorzitters: B.A. Bonsing, J. Ruurda

13.00 Piecemeal endoscopic mucosal resection appears equally effective as, but associated with less morbidity than transanal endoscopic microsurgery for the treatment of large rectal adenomas (p. 64)
F.J.C. van den Broek[1], E. Dekker[1], E.J.R. de Graaf[2], W.A. Bemelman[3], P. Fockens[1], J.B. Reitsma[4], [1]Dept of Gastroenterology and Hepatology, [3]Dept. of Surgery, [4]Dept. of Clinical Epidemiology, Academic Medical Centre Amsterdam; and [2]Dept of Surgery, IJsselland Hospital, Cappelle a/d IJssel, The Netherlands

13.10 Transanal Endoscopic Microsurgery for local resection of rectal tumours: Initial results in a university affiliated teaching hospital (p. 65)
B. Koebrugge, K. Bosscha, M.F. Ernst, Dept of Surgery, Jeroen Bosch Hospital, `s Hertogenbosch, The Netherlands

13.20 The gut releases taurine under post-absorptive circumstances (p. 66)
M.F.M. van Stijn[1,2], G.C. Ligthart-Melis[2], M.A.R. Vermeulen[1], L.N. Wong[2], M.P.C. Siroen[2], M.P. van den Tol[2], A.P.J. Houdijk[1], P.A.M. van Leeuwen[2], [1]Medical Center Alkmaar, Alkmaar, the Netherlands; surgical Dept [2]VU University Medical Center, Amsterdam, The Netherlands; surgical Dept

13.30 What is the value of a CT-scan in diagnosing a clinically relevant anastomotic leakage after a colon resection with a primary anastomosis? (p. 67)
M.N.G.J.A. Braat[1], R.M.P.H. Crolla[2], L. van der Laan[2],
[1]UMCU Utrecht, [2]Amphia Ziekenhuis, Breda, The Netherlands

13.40 The Dutch multicentre experience of the Endo-Sponge treatment of anastomotic leakage after colorectal surgery (p. 68)
P.J. van Koperen[1], M.I. van Berge Henegouwen[1], C. Rosman[2], C.M. Bakker[3], P. Heres[4], W.A. Bemelman[1], [1]Dept of Surgery, Academic Medical Centre, Amsterdam, [2]Dept of Surgery, Canisius Wilhelmina Hospital, Nijmegen, [3]Dept of Gastroenterology, Atrium Medical Centre, Heerlen, [4]Dept of Surgery, Waterland Hospital, Purmerend, The Netherlands

13.50 Local recurrence is no longer the main problem in rectal cancer with optimal multidisciplinary management (p. 69)
W. Truin[1], J.G. Bloemen[1], S.M.E. Engelen[1], R.G. Jansen[2], G. Lammering[4], R.G.H. Beets-Tan[3], G.L. Beets[1], [1]Dept of Surgery, [2]Dept of Internal Medicine, [3]Dept of Radiology, Maastricht University Medical Centre, Maastricht, [4]Maastro Clinic, Maastricht, The Netherlands

14.00 Einde abstractprogramma

Minibattle Nederlandse Vereniging voor Gastrointestinale Chirurgie **Diezezaal**

Voorzitters: R.J. Porte en P.D. Siersema

"De verschillende benaderingen van cholecystectomie"

14.00 Minilaparotomie.
Prof. dr. C.J.H.M. van Laarhoven, chirurg, UMCN, Nijmegen

14.30 Laparoscopie.
Prof. dr. J.F. Lange, chirurg, Erasmus MC, Rotterdam

15.00 Natural Orifice Transluminal Endoscopic Surgery (NOTES).
Dr. F.J. Berends, chirurg, Rijnstate Ziekenhuis, Arnhem

15.30 Discussie

16.00 Einde programma, theepauze

Nederlandse Vereniging voor Gastroenterologie **Diezezaal**

Voorzitters: J.B.M.J. Jansen en P.D. Siersema

Voordrachten in het Nederlands, spreektijd 7 minuten, discussietijd 3 minuten

16.30 Factors associated with success and complication rate of colonic stenting (p. 70)
J.J. Driest, M. Ledeboer, M. Eeftinck Schattenkerk[1], E.J. Kuipers[2], F. ter Borg , Dept of Gastroenterology and [1]Gastrointestinal surgery, Deventer ziekenhuis and [2]Eramus Medical Center Rotterdam, The Netherlands

16.40 Foreign body ingestion: Management in childhood * (p. 71)
T.E. Matthews, J.A. Taminiau, M.A. Benninga, M.M. Tabbers, B.G. Koot, A. Kindermann , Dept of Pediatric Gastroenterology, Emma Children's Hospital, Academic Medical Center Amsterdam, The Netherlands

16.50 Gastrointestinal Bleeding in Patients with Budd-Chiari Syndrome: a Prospective Evaluation (p. 72)
J. Hoekstra[1], S.D. Murad[1], A. Plessier[2], M. Hernandez-Guerra[3], E. Elias[4], M. Primignani[5], Matthias J. Bahr[6], J. Heller[7], A. Hadengue[8], P. Langlet[9], H. Miranda[10], J.C. Garcia-Pagan[3], D.C. Valla[2], H.L.A. Janssen[1] for the European Network for Vascular Disorders of the Liver (EN-Vie),[1]Dept of Gastroenterology and Hepatology, Erasmus University Medical Center, Rotterdam, The Netherlands, [2]Dept of Hepatology, Hopital Beaujon, AP-HP, INSERM-U773 & University Paris-7, Clichy, France, [3]Hepatic Hemodynamic Laboratory, Liver Unit, Hospital Clinic, IDIBAPS and Ciberehd, Barcelona, Spain, [4]Liver Unit, Queen Elisabeth Hospital Birmingham, Birmingham, United Kingdom, [5]Gastroenterology and Gastrointestinal Endoscopy Unit, Ospedale Policlinico, Mangiagalli and Regina Elena Foundation, Milan, Italy, [6]Dept of Gastroenterology, Hepatology, and Endocrinology, Hannover Medical School, Hannover, Germany, [7]Dept of Internal Medicine I, University Hospital of Bonn, Bonn, Germany, [8]Division of Gastroenterology and Hepatology, Geneva University Hospitals, Geneva, Switzerland, [9]Dept of Hepatogastroenterology, Centre Hospitalier Universitaire Brugmann, Bruxelles, Belgium, [10]Liver Transplantation Unit, Hospital General Santo Antonio, Porto, Portugal

President Select (plenaire sessie) **Diezezaal**

Voorzitter: J.B.M.J. Jansen

Voordrachten in het Nederlands, spreektijd 10 minuten, discussietijd 5 minuten

17.00 Randomised double-blind controlled trial evaluating elective laparoscopic appendectomy for chronic right lower abdominal quadrant pain (p. 73)
R.M.H. Roumen[1], R.P.R. Groenendijk[2], C.E.J. Sloots[1],K.E.S. Duthoi[3], M.R.M. Scheltinga[1], C.M.A. Bruijninckx[1], Depts. of Surgery[1] and Pathology, Stichting [3]PAMM Máxima Medisch Centrum, Veldhoven, The Netherlands

17.15 Prognosis of 375 Ursodeoxycholic Acid-Treated Patients With Primary Biliary Cirrhosis. A Follow-up to 17-Yrs (p. 74)
E.M.M. Kuiper[1], B.E. Hansen[2], R.A. de Vries[3], J.W. den Ouden-Muller[4], Th.J.M van Ditzhuijsen[5], E.B. Haagsma[6], M.H.M.G. Houben[7], B.J.M. Witteman[8], K.J van Erpecum[9], H.R. van Buuren[1] for the Dutch PBC study group,[1]Department of Gastroenterology and Hepatology and [2]Department of Epidemiology and Biostatistics, Erasmus Univ. Medical Center, Rotterdam, [3]Department of Gastroenterology and Hepatology, Rijnstate Hospital, Arnhem, [4]Department of Internal medicine, Sint Franciscus Gasthuis, Rotterdam, [5]Department of Internal medicine, Jeroen Bosch Hospital, Den Bosch, [6]Department of Gastroenterology and Hepatology, Univ. Medical Center Groningen, [7]Department of Gastroenterology and Hepatology, Haga Hospital, Den Haag, [8]Department of Gastroenterology and Hepatology, Hospital Gelderse Vallei, Ede, [9]Department of Gastroenterology and Hepatology, University Medical Center Utrecht, The Netherlands

17.30 Non-polypoid colorectal neoplasms: clinico-pathological features in a Dutch population (p. 75)
M. van der Valk[1], E. Rondagh[1], A. de Bruïne[2], A.A.M. Masclee[1], S. Sanduleanu[1], [1]Department of Gastroenterology and Hepatology, [2]Department of Pathology, Maastricht University Medical Center, The Netherlands

17.45 Stepwise circumferential and focal radiofrequency ablation of Barrett esophagus with early neoplasia: first European multi-centre trial (p. 76)
R.E. Pouw[1], K. Wirths[2], P. Eisendrath[3], C.M. Sondermeijer[1], F.J. Ten Kate[4], P. Fockens[1], J. Devière[3], H. Neuhaus[2], J.J. Bergman[1], [1]Gastroenterology, Academic Medical Center, Amsterdam, The Netherlands, [2]Internal Medicine, Evangelisches Krankenhaus, Düsseldorf, Germany, [3]Gastroenterology, Erasme University Hospital, Brussels, Belgium, [4]Pathology, Academic Medical Center, Amsterdam, The Netherlands

18.00 Einde abstractsessie

Prijsuitreiking **Diezezaal**

18.00 Uitreiking van de **AstraZeneca Gastrointestinale Research Award 2008** door de voorzitter van de jury, prof. dr. D.W. Hommes.

Aansluitend aan de uitreiking volgt een erevoordracht door de eerste prijs winnaar.

18.30 Congresborrel in expositiehal

19.30 Lustrumdiner in Brabantzaal

Nederlandse Vereniging voor Gastroenterologie **Baroniezaal**

Voorzitters: A. J. Bredenoord en J.W.A. Straathof

Voordrachten in het Nederlands, spreektijd 7 minuten, discussietijd 3 minuten

13.00 HLA-DQ typing of extra-intestinal T-cell lymphomas: evidence for an association with undiagnosed coeliac disease? (p. 77)
J.M.W. van de Water[1], S.A.G.M. Cillessen[2], W.H.M. Verbeek[1], L.R. de Baaij[2], J.J. Oudejans[2], C.J.L.M. Meijer[2], C.J.J. Mulder[1], M.W.J. Schreurs[2], [1]Dept of Gastroenterology and Hepatology and [2]Dept of Pathology, VU University Medical Centre, Amsterdam, The Netherlands

13.10 The prognostic value of alarm symptoms for developing chronic abdominal pain in children presenting with abdominal pain in general practice * (p. 78)
R.E. Bax, Y. van Leeuwen, M.Y. Berger, Dept of General Practice, Erasmus MC – University Medical Center, Rotterdam, The Netherlands

13.20 Patients With Early PBC Predominantly Die From Non-Liver Related Causes (p. 79)
E.M.M. Kuiper[1], B.E. Hansen[2], R.A. de Vries[3], J.W. den Ouden-Muller[4], Th.J.M van Ditzhuijsen[5], E.B. Haagsma[6], M.H.M.G. Houben[7], B.J.M. Witteman[8], K.J van Erpecum[9], H.R. van Buuren[1] for the Dutch PBC study group, [1]Dept of Gastroenterology and Hepatology and [2]Dept of Epidemiology and Biostatistics, Erasmus University Medical Center, Rotterdam, [3]Dept of Gastroenterology and Hepatology, Rijnstate Hospital, Arnhem, [4]Dept of Internal medicine, Sint Franciscus Gasthuis, Rotterdam, [5]Dept of Internal medicine, Jeroen Bosch Hospital, Den Bosch, [6]Dept of Gastroenterology and Hepatology, University Medical Center Groningen, [7]Dept of Gastroenterology and Hepatology, Haga Hospital, Den Haag, [8]Dept of Gastroenterology and Hepatology, Hospital Gelderse Vallei, Ede, [9]Dept of Gastroenterology and Hepatology, University Medical Center Utrecht, The Netherlands

13.30 Einde abstractsessie

Symposium Sectie Neurogastroenterologie en Motiliteit **Baroniezaal**

Voorzitters: A. J. Bredenoord en J.W.A. Straathof

"Non-erosive reflux disease"

13.30 Definition, clinical features and impact on quality of life
Prof. M. Simrén, Gothenborg, Germany

14.00 Minimal macroscopic and microscopic changes
(magnification endoscopy, chromoendoscopy, light microscopy, electron microscopy)
Prof. M. Cicala, Rome, Italy

Symposium Sectie Neurogastroenterologie en Motiliteit *(vervolg)* **Baroniezaal**

14.30 Diagnostic tests
(pH/impedance monitoring, PPI-test)
Prof. A.J.P.M. Smout, Utrecht, The Netherlands

15.00 Therapeutic options
(acid inhibition, endoscopic and surgical options, perception modulation, TLOSR inhibitors)
Prof. J. Tack, Leuven, Belgium

15.30 Theepauze

Netherlands Society of Parenteral and Enteral Nutrition **Baroniezaal**

Voorzitters: G. Wanten en W.G. van Gemert

Voordrachten in het Nederlands, spreektijd 7 minuten, discussietijd 3 minuten

16.00 Is gluten challenge really necessary for the diagnosis of coeliac disease in children under the age of two years? * (p. 80)
V.M. Wolters[1], C.M.F. Kneepkens[2,4], C.F.M. Gijsbers[3], J.J. Schweizer[2,4], M.A. Benninga[7], R.H.J. Houwen[1], Depts of Paediatric Gastroenterology, University Medical Centre, Utrecht[1], VU Medical Centre, Amsterdam[2], Paediatric Gastroenterology, Juliana Children's Hospital/ Haga Teaching Hospital, The Hague[3], Paediatric Gastroenterology, Leiden University Medical Centre, Leiden[4], Paediatric Gastroenterology, Academic Medical Centre, Amsterdam[5], The Netherlands

16.10 Taurolidine versus heparin lock to prevent catheter-related bloodstream infections (CRBSI) in patients on home parenteral nutrition: a prospective randomized trial (p. 81)
G. Wanten[1], M. Willems[2], T. Bisseling[1], R. Vissers[1], Depts of [1]Gastro-enterology and Hepatology and [2]Vascular Surgery, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands

16.20 Medium-chain triglyceride-induced neutrophil activation is not mediated by the Pertussis Toxin sensitive G-protein coupled receptor GPR84 (p. 82)
M.W. Versleijen[1], J. van Esterik[1], H. Roelofs[1], S.E. van Emst-de Vries[2], P.H. Willems[2], G.J. Wanten[1], Depts of Gastroenterology and Hepatology[1] and Biochemistry[2], Radboud University Nijmegen Medical Centre, The Netherlands

16.30 The citrulline generation test in stable ICU patients: optimizing a new enterocyte function test (p. 83)
J.H.C. Peters[1], L.C. Dobrowolski[1], N.J. Wierdsma[2], T. Teerlink[3], A.R.J. Girbes[4], C.J.J. Mulder[1], B. Beishuizen[4], A.A. van Bodegraven[1] , [1]Dept of Gastroenterology, Small Bowel Disease Unit, [2]Dept of Nutrition and Dietetics, [3]Dept of Clinical Chemistry, Metabolic Laboratory, [4]Intensive Care Unit, VU medical center, Amsterdam, The Netherlands

16.40 Is removal of the fat component from the PN mixture efficient in preventing long-term PN patients from chronic hepatic dysfunction? (p. 84)
L. van der Aa[1], K.S. Vedder[1], C.F. Jonkers-Schuitema[2], H.P. Sauerwein[3], [1]Student Hogeschool van Amsterdam, Nutrition & dietetics, [2]Dietetic Dept/Home parenteral utrition support team, Academic Medical Center, Amsterdam, [3]Dept of Internal Medicine and Endocrinology, Academic Medical Center, Amsterdam, The Netherlands

16.50 Nutritional status of patients with de novo coeliac disease (p. 85)
N.J. Wierdsma[1], J.H.C. Peters[2], M.A.E. van Bokhorst-de van der Schueren[1], C.J.J. Mulder[2], A.A. van Bodegraven[2], [1]Nutrition and Dietetics, [2]Gastroenterology, VU University Medical Center, Amsterdam, The Netherlands

17.00 Einde programma in deze zaal.

Voor de plenaire sessie (President Select) en de uitreiking van de AstraZeneca Gastrointestinale Research Award 2008 kunt u zich begeven naar de Diezezaal.

Nederlandse Vereniging voor Hepatologie Klinisch **Parkzaal**

Voorzitters: S.W.M. Olde Damink en R.A. de Man

Voordrachten in het Nederlands, spreektijd 7 minuten, discussietijd 3 minuten

13.00 A double blind, placebo-controlled trial with escitalopram to prevent psychiatric adverse events during treatment with pegylated interferon-alpha and ribavirin for chronic hepatitis C: The "Prevention Of Psychiatric Side effects (POPS)-study" (p. 86)
G. Bezemer, A.R. van Gool, J.P.H. Drenth, B.E. Hansen, H.A. Droogleever Fortuyn, C.J. Weegink, M.W. Hengeveld, H.L.A. Janssen, R.J. de Knegt, Erasmus MC University Medical Center, Rotterdam, the Netherlands, Depts. Gastroenterology & Hepatology, and Psychiatry. Radboud University Nijmegen Medical Center, Nijmegen, The Netherlands, Dept of Gastroenterology and Hepatology and Psychiatry, Academic Medical Center Amsterdam, The Netherlands, Depts of Gastroenterology and Hepatology and Psychiatry

13.10 Diagnostic accuracy of Transient Elastography: a comparison between chronic hepatitis B and C correlated with optimal-length liver biopsies (p. 87)
C. Verveer[1], B. E. Hansen[2], P.E. Zondervan[3], H.L.A. Janssen[1], R.J. de Knegt , [1]Dept. of Gastroenterology and Hepatology, [2]Dept of Biostatistics [3]Dept of Pathology, Erasmus MC Rotterdam, The Netherlands

13.20 Hepatitis C viral kinetics during PEG-interferon alfa-2b and ribavirin therapy in naïve chronic hepatitis C patients (p. 88)
G. Boland[1,10], H. van Soest[1], R.A. de Vries[2], N.A.M. van Ooteghem[3], B. van Hoek[4], J.P.H. Drenth5, R.J. de Knegt[6], R.J. Lieverse[7,] P. Houben[8], A. van der Sluys Veer[9], P.D. Siersema[1], A.M. van Loon[10], K.J. van Erpecum[1] , Depts. of Gastroenterology and Hepatology[1] University Medical Center Utrecht, [2]Rijnstate Hospital Arnhem, [3]St Lucas Andreas Hospital Amsterdam, [4]Leiden University Medical Center, [5]University Hospital Nijmegen, [6]Erasmus Medical Center Rotterdam, [7]Gelre Ziekenhuizen Apeldoorn, [8]Ziekenhuis Zeeuws Vlaanderen, [9]Onze Lieve Vrouwe Gasthuis Amsterdam and [10]Dept of Medical Microbiology, University Hospital Utrecht, The Netherlands.

13.30 48 Weeks of Peginterferon Alfa-2a alone or in Combination with Ribavirin for HBeAg-negative Chronic Hepatitis B: Addition of Ribavirin does not increase Response Rates (combinatievoordracht, p. 89 + p 90)

H.L.A. Janssen[1], V. Rijckborst[1], Y. Cakaloglu[2], P. Ferenci[3], F. Tabak[4], M. Akdogan[5], K. Simon[6], M. Raptopoulou-Gigi[7], N. Örmeci[8] ,P.E. Zondervan[9], G.J.J. van Doornum[10], E. Verhey[1], A.J. van Vuuren[1], M.J. ter Borg[1], B.E. Hansen[1,10] for the PARC Study, [1]Dept of Gastroenterology and Hepatology, Erasmus MC, University Medical Center Rotterdam, Rotterdam, The Netherlands, [2]Dept of Gastroenterohepatology, Istanbul University Medical School, Istanbul, Turkey, [3]Dept of Internal Medicine [3], Gastroenterology and Hepatology, Medical University of Vienna, Vienna, Austria, [4]Dept of Infectious Diseases, Istanbul University Cerrahpasa Medical School, Istanbul, Turkey, [5]Dept of Gastroenterology, Turkiye Yuksek Ihtisas Hospital, Ankara, Turkey, [6]Dept and Clinic of Infectious Diseases, Hepatology and Acquired Immune Deficiences, Medical University Wroclaw, Wroclaw, Poland, [7]Second Medical Dept, Aristototle University of Thessaloniki, Thessaloniki, Greece, [8]Dept of Gastroenterology, Ankara University School of Medicine, Ankara, Turkey, [9]Dept of Pathology, Erasmus MC, University Medical Center Rotterdam, Rotterdam, The Netherlands, [10]Dept of Epidemiology and Biostatistics, Erasmus MC, University Medical Center Rotterdam, Rotterdam, The Netherlands

13.40 Impaired Fibrinolysis as a Risk Factor for Budd-Chiari Syndrome (p. 91)

J. Hoekstra[1], F.W. Leebeek[2], A.H.C. Guimarães[2], S. Darwish Murad[1], J.J.M.C. Malfliet[2], A. Plessier[3], P. Langlet4, E. Elias[5], J. Heller[6], M. Primignani[7], J.C. Garcia-Pagan[8], D.C. Valla[3], D.C. Rijken[2], H.L.A. Janssen[1] for the European Network for Vascular Disorders of the Liver (EN-Vie), [1]Dept of Gastroenterology and Hepatology, Erasmus University Medical Center, Rotterdam, The Netherlands, [2]Dept of Hematology, Erasmus University Medical Center, Rotterdam, The Netherlands, [3]Dept of Hepatogastroenterology, Centre Hospitalier Universitaire Brugmann, Bruxelles, Belgium, [4]Liver Unit, Queen Elisabeth Hospital Birmingham, Birmingham, United Kingdom, [5]Dept of Internal Medicine I, University Hospital of Bonn, Bonn, Germany, [6]Gastroenterology and Gastrointestinal Endoscopy Unit, Ospedale Policlinico, Mangiagalli and Regina Elena Foundation, Milan, Italy, [7]Hepatic Hemodynamic Laboratory, Liver Unit, Hospital Clinic, IDIBAPS and Ciberehd, Barcelona, Spain, [8]Dept of Hepatology, Hopital Beaujon, AP-HP, INSERM-U773 & University Paris-7, Clichy, France

13.50 High incidence of histological hepatitis and portal fibrosis at 1 year after pediatric liver transplantation using a tacrolimus-based immunosuppressive regimen (p. 92)
R. Scheenstra[1,4], A.S.H. Gouw[2,4], P.M.J. Peeters[3,4], H.J. Verkade[1,4], [1]Dept of Pediatric Gastroenterology, Beatrix Children's Hospital, [2]Deptartment of Pathology, [3]Dept. of Hepatobiliary Surgery, [4]Liver transplantation Team, University Medical Center Groningen, Groningen, The Netherlands

14.00 Einde abstractsessie

Symposium Nederlandse Vereniging voor Hepatologie **Parkzaal**

Voorzitters: S.W.M. Olde Damink en R.A. de Man

"Nieuwe ontwikkelingen in de detectie en behandeling van colorectale levermetastasen"

14.00 Rol beeldvorming bij levertumoren
Dr. M.S. van Leeuwen, UMC Utrecht, The Netherlands

14.20 Chemotherapie geinduceerde leverschade bij colorectale levermetastasen
Prof. dr. L. Rubbia-Brandt, Head Division of Clinical Pathology, University Hospital, Geneva, Switzerland

14.40 Mogelijkheden en besprekingen van RFA bij de behandeling van levertumoren
Prof. dr. J.N.M. IJzermans, Erasmus MC, Rotterdam, The Netherlands

15.00 Rol van radiotherapie bij de behandeling van colorectale levermetastasen. Heden en toekomst
Prof. dr. W. Sauerwein, Dept of Radiation Oncology, University of Duisberg-Essen, Germany

15.20 Discussietijd

15.30 Einde symposium

Nederlandse Vereniging voor Hepatologie **Parkzaal**

15.30 Ledenvergadering Nederlandse Vereniging voor Hepatologie
(koffie / thee in de zaal)

Nederlandse Vereniging voor Hepatologie (klinisch) **Parkzaal**

Voorzitters: J.P.H Drenth en R.J. de Knegt

16.00 Efficacy of Nasobiliary Drainage for Refractory Cholestatic Pruritus (p. 93)
E.M.M. Kuiper[1], R.A. de Man[1], H.R. van Buuren[1], [1]Dept of Gastro-enterology and Hepatology, Erasmus University Medical Center, Rotterdam, The Netherlands

16.10 Detection of Hepatitis B covalently closed circular DNA in paraffin--embedded liver biopsy specimens of chronic hepatitis B patients (p. 94)
R.B. Takkenberg[1], H.L. Zaaijer[2], S. Menting[2], C.J. Weegink[1], V. Terpstra3, M.G.W. Dijkgraaf[4], M. Cornelissen[5], P.L.M. Jansen[1], H.W. Reesink[1] and M.G.H.M.Beld[2],1AMC Liver Center, Dept of Gastroenterology and Hepatology, Academic Medical Center, University of Amsterdam, Amsterdam, [2]Section of Clinical Virology, Dept of Medical Microbiology, Academic Medical Center, University of Amsterdam, The Netherlands, [3]Dept of Pathology, Academic Medical Center, University of Amsterdam, Amsterdam, [4]Dept of Clinical Epidemiology and Biostatistics, Academic Medical Center, University of Amsterdam, [5]Laboratory of Experimental Virology, Dept of Medical Microbiology, Academic Medical Center, University of Amsterdam, The Netherlands

16.20 HBV Genotype is an Important Predictor of Sustained Off-Treatment Response to both Peginterferon Alpha-2b and Entecavir in HBeAg Positive Chronic Hepatitis B (p. 95)
E.H.C.J. Buster[1], B.E. Hansen[1,2], E. Verhey[1], R.A. de Man[1], H.L.A. Janssen[1], Depts of [1]Gastroenterology and Hepatology, [2]Epidemiology and Biostatistics, Erasmus MC University Medical Center Rotterdam, Rotterdam, The Netherlands

16.30 Prediction of response to peginterferon-alfa in HBeAg positive chronic hepatitis B: A model based on 721 patients (p. 96)
E.H.C.J. Buster[1], B.E. Hansen[1,2], G.K.K. Lau[3], T. Piratvisuth[4], P. McCloud[5], P. Button[5], E.W. Steyerberg[6], S. Zeuzem[7], H.L.A. Janssen[1], Depts of [1]Gastroenterology and Hepatology, [2]Epidemiology and Biostatistics, and [6]Public Health, Erasmus MC University Medical Center Rotterdam, The Netherlands, [3]Dept of Medicine, Queen Mary Hospital, University of Hong Kong, Hong Kong SAR, China, [4]Dept of Medicine, Songklanakarin Hospital, Songkla, Thailand, [5]Roche, Dee Why, Australia, [7]Medizinische Klinik I, Klinikum der Johann Wolfgang Goethe-Universität, Frankfurt am Main, Germany

16.40 HBeAg seroconversion induced by nucleos(t)ide analogues in chronic hepatitis B is not durable in a majority of cases (p. 97)
M.J. Perquin[1], J.G.P. Reijnders[1], N. Zhang[1,2], H.L.A. Janssen[1], [1]Dept of Gastroenterology and Hepatology, Erasmus MC University Medical Center Rotterdam, Rotterdam, The Netherlands, [2]Dept of Gastroenterology and Hepatology, Zong Shan Hospital, Fudan University, Shanghai, China

16.50 Interferon- rather than ribavirin-related side effects are associated with non-response to peginterferon alfa-2b and ribavirin in naïve chronic hepatitis C patients (p. 98)
L.G. van Vlerken[1], E.J. Huisman[1], H. van Soest[1], G. Boland[1,12], P.J. van der Schaar[2], G.H. Koek[3], R.A. de Vries[4], N.A.M. van Ooteghem[5], B. van Hoek[6], J.P.H. Drenth[7], R.J. de Knegt[8], R.J. Lieverse[9], P. Houben[10], A. van der Sluys Veer[11], P.D. Siersema[1], A.M. van Loon[12], K.J. van Erpecum[1], Depts. of Gastroenterology and Hepatology[1] University Medical Center Utrecht, [2]Atrium Medical Center Heerlen, [3]University Hospital Maastricht, [4]Rijnstate Hospital Arnhem, [5]St Lucas Andreas Hospital Amsterdam, [6]Leiden University Medical Center, [7]University Hospital Nijmegen, [8]Erasmus Medical Center Rotterdam, [9]Gelre Ziekenhuizen Apeldoorn, [10]Ziekenhuis Zeeuws Vlaanderen, [11]Onze Lieve Vrouwe Gasthuis Amsterdam and [12]Dept of Virology University Hospital Utrecht, The Netherlands

17.00 Einde programma in deze zaal.

Voor de plenaire sessie (President Select) en de uitreiking van de AstraZeneca Gastrointestinale Research Award 2008 kunt u zich begeven naar de Diezezaal.

Nederlandse Vereniging voor Gastroenterologie **Genderzaal**

07.30 -08.30 **Ledenvergadering NVGE**
Onbijtbuffet in de zaal

Casuïstiek voor de clinicus **Brabantzaal**

Voorzitter: W. Hameeteman

08.30 Casuïstische Patiëntenbespreking

Symposium Sectie Gastrointestinale Endoscopie **Brabantzaal**

Voorzitters: W. Hameeteman en B.L.A.M. Weusten

"De zin en onzin van Barrett endoscopieën in Nederland: een interactief symposium"

09.00 Interactieve inleiding met stemkastjes.
Dr. W. Hameeteman, maag-darm-leverarts, academisch ziekenhuis Maastricht

09.10 Barrett surveillance: een absolute noodzaak.
Prof. dr. P.D. Siersema, maag-darm-leverarts, Universitair Medisch Centrum Utrecht

09.20 Barrett surveillance: kostbaar en zinloos.
Dr. M.E. Craanen, maag-darm-leverarts, Flevoziekenhuis, Almere

Symposium Sectie Gastrointestinale Endoscopie *(vervolg)* **Brabantzaal**

09.30 Interactieve discussie met behulp van stemkastjes

09.45 Endoscopische therapie voor Barrett neoplasie
Dr. E.J. Schoon, maag-darm-leverarts
Catharina Ziekenhuis, Eindhoven

10.00 Interactieve casuïstiek met stemkastjes

10.30 Koffiepauze

Dit symposium wordt mogelijk gemaakt dankzij de ondersteuning van AstraZeneca

Sectie Gastrointestinale Endoscopie **Brabantzaal**

Voorzitter: W. Hameeteman en B.L.A.M. Weusten

11.00 Early ERCP is only beneficial in predicted severe acute biliary pancreatitis in case of concurrent cholestasis: a prospective multicenter study (p. 99)
H.C. van Santvoort[1], M.G. Besselink[1], A.C. de Vries[2], M.A. Boermeester[3], K. Fischer[4], T.L. Bollen[5], G.A. Cirkel[1], A.F. Schaapherder[6], V.B. Nieuwenhuijs[7], H. van Goor[8], C.H.C. Dejong[9], C.H. van Eijck[10], B.J. Witteman[11], B.L. Weusten[12], C.J. van Laarhoven[13], P.J. Wahab[14], A.C. Tan[15], M.P. Schwartz[16], E. van der Harst[17], M.A Cuesta[18], P.D. Siersema[19], H.G. Gooszen[1], K.J. van Erpecum[19] and the members of the Dutch Acute Pancreatitis Study Group, [1]Dept of Surgery, University Medical Center Utrecht, [2]Dept of Gastroenterology, Erasmus University Medical Center, Rotterdam, [3]Dept of Surgery, Amsterdam Medical Center, [4]Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, [5]Dept of Radiology, St. .Antonius Hospital, Nieuwegein, [6]Dept of Surgery, Leiden University Medical Center, [7]Dept of Surgery, University Medical Center Groningen, [8]Dept of Surgery, Radboud University Nijmegen Medical Centre, [9]Dept of Surgery and NUTRIM, Maastricht University Medical Center, [10]Dept of Surgery, Erasmus Medical Center, Rotterdam, [11]Dept of Gastroenterology, Gelderse Vallei Hospital, Ede,

[12]Dept of Gastroenterology, St. Antonius Hospital, Nieuwegein, [13]Dept of Surgery, St. Elisabeth Hospital, Tilburg, [14]Dept of Gastroenterology, Rijnstate Hospital, Arnhem, [15]Dept of Gastroenterology, Canisius Wilhelmina Hospital, Nijmegen, [16]Dept of Gastroenterology, Meander Medical Center, Amersfoort, [17]Dept of Surgery, Medical Center Rijnmond Zuid, Rotterdam, [18]Dept of Surgery, VU medical center, Amsterdam, [19]Dept of Gastroenterology, University Medical Center Utrecht, The Netherlands

11.10 Endoscopic treatment of ampullary adenomas as an alternative to surgical resection (p. 100)
G.J. de Bruin, J-W. Poley, E.J. Kuipers, Erasmus Medisch Centrum Rotterdam, The Netherlands

11.20 Temporary esophageal stenting in the management of benign disease (combinatievoordracht, p. 101 + p. 102)
N.C.M. van Heel, V.M.C.W. Spaander, J. Haringsma, E.J. Kuipers, Dept of Gastroenterology and Hepatology, Erasmus MC University Medical Center, Rotterdam, The Netherlands

11.30 Gastrojejunostomy versus duodenal stent placement for the palliation of malignnant gastric outlet obstruction: multicenter randomized trial (p. 103)
S.M. Jeurnink[1], E.W. Steyerberg[2], C.H.J. van Eijck[3], E.J. Kuipers[1,4], P.D. Siersema[1,5]. ,*
Dept. of Gastroenterology and Hepatology[1], Public Health[2], Surgery[3] and Internal Medicine[4], Erasmus MC-University Medical Center Rotterdam and Dept. of Gastroenterology and Hepatology[5], University Medical Center Utrecht, The Netherlands

11.40 Feasibility of percutaneous endoscopic jejunostomy (PEJ) and colostomy (PEC) katheters: first results in a Dutch academic centre (p. 104)
T.E.H. Römkens[1], D.J. de Jong[1], J.O. Kristinsson[2], G.J. Wanten[1], [1]Dept of Gastroenterology and Hepatology, University Medical Centre St. Radboud, Nijmegen, [2]Dept of Gastroenterology and Hepatology, Landspitali University Hospital Reykjavik, Iceland

11.50 Endoscopic treatment of pancreatico-cutaneous fistulas after intervention for infected necrotizing pancreatitis (p. 105)
M.C. van Baal[1], O.J. Bakker[1], H.C. van Santvoort[2], M.G. Besselink[2], J.W. Poley[3], J. Heisterkamp[4], H.G. Gooszen[1] and C.H. van Eijck[5] for the Dutch Pancreatitis Study Group.,

[1]Dept of Surgery, University Medical Center Utrecht, Utrecht, [2]Dept of Surgery, St. Antonius Hospital, Nieuwegein, [3]Dept of Gastroenterology & Hepatology, Erasmus Medical Center, Rotterdam, [4]Dept of Surgery, St. Elisabeth hospital, Tilburg, [5]Dept of Surgery, Erasmus Medical Center, Rotterdam, The Netherlands

12.00 Accuracy and interobserver agreement of international experts on a new classification scheme for probe-based confocal fluorescence microscopy (p.106)
F.J.C. van den Broek[1], A. Meining[2], M.B. Wallace[3], A.M. Buchner[3], J.A. van Es[1], P. Fockens[1], E. Dekker[1], Dept of Gastroenterology and Hepatology, [1]Academic Medical Centre Amsterdam; [2]Klinikum rechts der Isar, Munich; [3]Mayo Clinic, Jacksonville

12.10 Miniprobe-based confocal fluorescence microscopy is feasible for in-vivo histological differentiation of neoplasia and non-neoplastic tissue in patients (p. 107) with Ulcerative Colitis.
J.A. van Es1, F.J.C. van den Broek[1], P.C.F. Stokkers[1], C.Y. Ponsioen[1], S. van Eeden[2], P. Fockens[1], E. Dekker[1], Depts of [1]Gastroenterology and Hepatology and [2]Pathology, Academic Medical Centre, Amsterdam, The Netherlands

12.20 Nurse-administered Propofol (NAP) sedation for endoscopy: first experience in the Netherlands (p. 108)
G. Geerders, J. Haringsma, M. Klimek, E.J. Kuipers, Dept. Gastroenterology & Hepatology and Dept. Anaesthesiology, Erasmus MC Rotterdam, The Netherlands

Frieda den Hartog Jager Lecture **Brabantzaal**

12.30 **'Carcinoid anno 2008'**
Mevr. Dr. B.G. Taal, internist
Antoni van Leeuwenhoekhuis NKI, Amsterdam

13.00 Lunchbuffet in expositiehal

Nederlandse Vereniging voor Gastroenterologie **Baroniezaal**

Voorzitters: C.J.J. Mulder en H.J. Verkade

08.30 Incidence of Inflammatory Bowel Disease in the Netherlands 1991-2002: Results of a population based study; the IBD-South Limburg cohort
(p. 109)
M.J.L. Romberg-Camps[1,4], M.A.M. Hesselink-van de Kruijs[1], L.J. Schouten[2], P.C. Dagnelie[2], A.D.M. Kester[3], L.P. Bos[4] , J. Goedhard[5], W.. Hameeteman[1], F. Wolters[6], M.G.V.M. Russel[7], R.W. Stockbrügger[1], [1]Dept of Gastroenterology and Hepatology, Maastricht University Medical Center, [2]Dept of Epidemiology, University of Maastricht, The Netherlands, [3]Dept of Methodology and Statistics, University of Maastricht, [4]Dept of Internal Medicine and Gastroenterology, Maasland Hosp. Sittard, [5]Dept of Internal Medicine and Gastroenterology, Atrium Medical Center Heerlen, [6]Dept of Gastroenterology, Vie-Curi Medical Center Venlo, [7]Dept of Gastroenterology, Medisch Spectrum Twente, Enschede, The Netherlands

08.40 Influence of phenotype at diagnosis and of other potential prognostic factors on the course of Inflammatory Bowel Disease. A long-term follow-up study of the IBD-South Limburg cohort
(combinatievoordracht, p. 110 + p 111)
M.J.L. Romberg-Camps[1,4], P.C. Dagnelie[2], A.D.M. Kester[3], M.A.M. Hesselink-van de Kruijs[1], M. Cilissen[1], L.G.J.B. Engels[4], C. van Deursen[5], W. Hameeteman[1], F.L. Wolters[6], M.G.V.M. Russel[7], R.W. Stockbrügger[1], [1]Dept of Gastroenterology and Hepatology, Maastricht University Medical Center, [2]Dept of Epidemiology, University of Maastricht, [3]Dept of Methodology and Statistics, University of Maastricht, [4]Dept of Internal Medicine and Gastroenterology, Maasland Hospital Sittard, [5]Dept of Internal Medicine and Gastroenterology, Atrium Medical Center Heerlen, [6]Dept of Gastroenterology, Vie-Curi Medical Center Venlo, [7]Dept of Gastroenterology, Medisch Spectrum Twente Enschede, The Netherlands

08.50 Quality of health information on the internet in inflammatory bowel disease (p. 112)
S. van der Marel, D.W. Hommes, H.H. Fidder, Leiden University Center, Leiden, The Netherlands

Vrijdag 3 oktober 2008

09.00 Pediatric crohn's disease: the activity at diagnosis, its influence on pediatrician's prescription behavior and clinical outcome five years later * (p.113)
[1]Tamara Mesker, [1]Patrick F. van Rheenen, [2]Obbe F. Norbruis, [3]Jan Uitentuis, [4]Herman J. Waalkens, 5Gieneke Gonera, [6]Lidy A.T. van Overbeek, [7]Joke Butler, [1]Edmond H.H.M. Rings , [1]Dept of Pediatrics, Beatrix Children's Hospital, University Medical Center Groningen, University of Groningen, Groningen, [2]Dept of Pediatrics, Isala Clinics, Location Sophia, Zwolle, [3]Dept of Pediatrics, Medical Center Leeuwarden, Leeuwarden, [4]Dept of Pediatrics, Martini Hospital, Groningen, [5]Dept of Pediatrics, Wilhelmina Hospital, Assen, [6]Dept of Pediatrics, Scheper Hospital, Emmen,[7]Dept of Pediatrics, Deventer Hospital Location Geertruida, Deventer, The Netherlands

09.10 Infliximab treatment in pediatric IBD: survey of treatment decisions* (p.114)
J.C. Escher, on behalf of the pediatric IBD working group of ESPGHAN, Erasmus MC-Sophia, Rotterdam, The Netherlands

09.20 Early occurrence of colorectal carcinoma in IBD patients in non-tertiary cohorts: follow-up on a nation wide long-term survey (p.115)
J.E. Baars[1], E.J. Kuipers[1], R. Beukers[2], G.W. Erkelens[3], A.C.I.T.L. Tan[4] B.L.A.M. Weusten[5], C.J. van der Woude[1], Depts of Gastroenterology and Hepatology, Erasmus MC, Rotterdam[1], Albert Schweitzer ziekenhuis, Dordrecht[2], Reinier de Graaf Gasthuis, Delft[3], Canisius Wilhelmina ziekenhuis, Nijmegen[4], Sint Antonius ziekenhuis, Nieuwegein[5], The Netherlands

09.30 The role of TNF(-receptor) family members in inflammatory bowel disease (p.116) *B.J. Olivier[1], M. Greuter [1]and R.E. Mebius[1], [1]Deptartment Mol. Cell Biology and Immunology, Free University Medical Centre, Amsterdam, The Netherlands*

09.40 Serious infections, neoplasms and mortality in association with therapies for Crohn's disease: preliminary results from the ENCORE registry. (p.117)
D.W. Hommes[1], J. Panés[2], J.F. Colombel[3], G. D'Haens[4], P. Rutgeerts[5], A. Ekbom[6], U. Barai[7], H. van Hoogstraten[7], M. Wiekowski[7], C. Antoni[7], [1]Leids Universitair Medisch Centrum, Leiden, The Netherlands; [2]Hospital Clinic Provincial, Barcelona, Spain; [3]CHRU Lille, Service d'Hépato- Gastroentérologie, Cedex, Lille, France; [4]Imeldaziekenhuis, Gastroenterologie, Bonheiden, Belgium; [5]University of Leuven, Division of Gastroenterology, Leuven, Belgium; [6]Karolinska Institutet, Dept of Medical Epidemiology and Biostatistics, Stockholm, Sweden; [7]Schering-Plough Research Institute, Kenilworth, NJ, United States

09.50 Breast Cancer Resistance Protein (BCRP/ABCG2) expression is reduced during active colitis and translocated in IBD-related neoplasia (p. 118)
C.L.. Koelewijn[1], K..N. Faber[2], M.M. Gerrits[1], H.J. Verhoog[1], H. van Dekken[3], E..J. Kuipers[1], R. Smits[1], C.J. van der Woude[1], Erasmus MC - University Medical Centre Rotterdam, Depts [1] Gastroenterology and Hepatology, [3]Pathology, Rotterdam, The Netherlands[2], University Medical Center Groningen, Dept of Gastroenterology and Hepatology, Groningen, The Netherlands

10.00 Progression rate of flat low-grade dysplasia to advanced neoplasia in IBD (p.119)
F.D.M. van Schaik[1], F.P. Vleggaar[1], G.J.A. Offerhaus[2], M.E.I. Schipper[2], P.C.F. Stokkers[3], C.J. van der Woude[4], D.W. Hommes[5], A.A. van Bodegraven[6], P.D. Siersema[1], B. Oldenburg[1] ,[1]University Medical Center Utrecht, Dept of Gastroenterology and Hepatology, [2]University Medical Center Utrecht, Dept of Pathology, [3]Academic Medical Center Amsterdam, Dept of Gastroenterology and Hepatology, [4]Erasmus Medical Center Rotterdam, Dept of Gastroenterology and Hepatology, [5]Leiden University Medical Center, Dept of Gastroenterology and Hepatology, [6]VU University Medical Center Amsterdam, Dept of Gastroenterology and Hepatology, The Netherlands

10.10 Active transcellular Ca2+ transport in the intestine during health and disease (p. 120)
S. Huybers, R. Bindels, J. Hoenderop. , Dept. of Physiology, Radboud University Nijmegen Medical Centre, The Netherlands

10.20 Severe malnutrition in Dutch patients with liver cirrhosis (p.121)
E.J. Huisman[1], B. van Hoek[2], P.D. Siersema[1], K.J. van Erpecum[1], Depts. of Gastroenterology and Hepatology[1], University Medical Center Utrecht, [2]Leiden University Medical Center, The Netherlands

10.30 Koffiepauze

Vrijdag 3 oktober 2008

Symposium rond de IBD-richtlijn **Baroniezaal**

Voorzitters: A.A. van Bodegraven en B. Oldenburg

IBD-richtlijn

11.00 Opening / Inleiding

11.10 Highlights diagnostiek IBD
Dr. D.J. de Jong, maag-darm-leverarts,
UMC St. Radboud Nijmegen

11.35 Discussie diagnostiek

11.45 Highlights inductietherapie
Dr. G. Dijkstra, maag-darm-leverarts,
UMC Groningen

12.10 Discussie inductietherapie

12.20 Highlights onderhoudsbehandeling
Dr. L.J.J. Derijks, ziekenhuisapotheker,
Máxima Medisch Centrum, Veldhoven

12.45 Discussie onderhoudstherapie

12.55 Conclusies / Implementatie

13.00 Lunchbuffet in expositiehal

Nederlandse Vereniging voor Gastroenterologie **Parkzaal**

Voorzitter: R.J.F. Felt-Bersma en A.J.P. van Tilburg

Voordrachten in het Nederlands, spreektijd 7 minuten, discussietijd 3 minuten

08.30 Increased predicted colorectal cancer survival in asymptomatic patients detected by population-based screening with FOBT (p. 122)
L.G. van Rossum[1], A.F. van Rijn[2], I.P. van Munster[3], J.B. Jansen[1], R.J. Laheij[1], P. Fockens[2], E. Dekker[2], [1]Dept of Gastroenterology and Hepatology, Radboud University Nijmegen Medical Center, Nijmegen, The Netherlands, [2]Dept of Gastroenterology & Hepatology, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands, [3]Dept of Gastroenterology & Hepatology, Jeroen Bosch Hospital, 's-Hertogenbosch, The Netherlands

08.40 Immunochemical faecal occult blood testing is more cost-effective than guaiac faecal occult blood testing and no screening in colorectal cancer screening when implementing randomised controlled data according to intention to screen (p. 123)
L.G. van Rossum[1], A.F. van Rijn[2], E.M. Adang[3], M.G. van Oijen[1], R.J. Laheij[1], P. Fockens[2], J.B. Jansen[1], E. Dekker[2], [1]Dept of Gastroenterology and Hepatology, Radboud University Nijmegen Medical Center, Nijmegen, The Netherlands, [2]Dept of Gastroenterology & Hepatology, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands, [3]Dept of Epidemiology, Biostatistics and MTA, Radboud University Nijmegen Medical Center, Nijmegen, The Netherlands

08.50 Optimisation of the performance of colorectal cancer screening with a semi-quantitative immunochemical faecal occult blood test (combinatie-voordracht p. 124 + 125)
L.G. van Rossum[1], A.F. van Rijn[2], R.J. Laheij[1], M.G. van Oijen[1], P. Fockens[2], A.L. Verbeek[3], J.B. Jansen[1], E. Dekker[2], [1]Dept of Gastroenterology and Hepatology, Radboud University Nijmegen Medical Center, Nijmegen, [2]Dept of Gastroenterology & Hepatology, Academic Medical Center, University of Amsterdam, Amsterdam, [3]Dept of Epidemiology, Biostatistics and MTA, Radboud University Nijmegen Medical Center, Nijmegen, The Netherlands

Nederlandse Vereniging voor Gastroenterologie **Parkzaal**

Voorzitters: R.J.F. Felt-Bersma en A.J.P. van Tilburg

09.00 In vivo differentiation between neoplastic and non-neoplastic colorectal polyps by chromoendoscopy-guided confocal laser endomicroscopy: an ongoing prospective study (p. 126)
S. Sanduleanu[1], A. Driessen[2], W. Hameeteman[1], A. de Bruïne[2], A. Masclee[1], Dept of Gastroenterology and Hepatology[1], Dept of Pathology[2], University Hospital Maastricht, The Netherlands

09.10 Population preferences for different screening strategies for colorectal cancer in the Netherlands; a discrete choice experiment (p. 127)
L. Hol[1], E. de Bekker-Grob[2], L. van Dam1, B. Donkers[3], E. J. Kuipers[1], D.J.F. Habbema[2], E.W. Steyerberg[2], M.E. van Leerdam[1], M. Essink-Bot[4], [1]Gastroenterology and Hepatology, [2]Public Health, Erasmus MC, [3]Marketing and Organisation, Faculty of Economics, Erasmus University, Rotterdam, [4]Public Health, Academic Medical Center, Amsterdam, The Netherlands

09.20 Colorectal cancers within 3 years after colonoscopy or sigmoidoscopy: frequency and causes (p. 128)
N.D.H. Esveldt[1], H. Geldof[2], W.A. Bode[2], D.R. de Vries[1], P.D. Siersema[1] , [1]Dept of Gastroenterology and Hepatology, University Medical Center Utrecht; [2]Dept of Gastroenterology, IJsselland Hospital, Capelle aan den IJssel, The Netherlands

09.30 Effect of a fish intervention on markers of colorectal carcinogenesis: the FISHGASTRO study (p. 129)
G. Pot [1], G. Majsak-Newman, A. Geelen[1], L. Harvey, FISHGASTRO Study team gastroenterologists, P. van 't Veer[1], G. Schaafsma[1], E. Kampman[1], E. Lund[2] FISHGASTRO Study team gastroenterologistsF. Nagengast[3], B. Witteman[4], J. Uil[4], J. van Bergeijk[4], P. van de Meeberg[5], R. Timmer[6], A. Tan[7], E. Witteman[7], P. Wahab[8], A. Hart[9], Williams[10], [1]Dept of Human Nutrition, Wageningen University, Wageningen, The Netherlands; [2]Dept of Nutrition, Institute of Food Research, Norwich, United Kingdom, [3]UMC St Radboud, Nijmegen, The Netherlands; [4]Gelderse Vallei Hospital, Ede, The Netherlands;

[5]Slingeland Hospital, Doetinchem, The Netherlands, [6]St Antonius Hospital, Nieuwegein, The Netherlands, [7]Canisius Wilhelmina Hospital, Nijmegen, The Netherlands, [8]Rijnstate Hospital, Arnhem, The Netherlands [9] Norfolk & Norwich University Hospital, United Kingdom [10]James Paget University Hospital, United Kingdom

09.40 Cumulative risk of developing colorectal adenomas during colonoscopic surveillance in MLH1, MSH2 or MSH6 mutation carriers (p. 130)
M.J.M. Broes[1,2], V. Duif[1,2], N.T.M.Saksens[1,2], N.C.M. Visser[1,2], Y. Woliner[1,2], I.D. Nagtegaal², M.C.V van Kouwen¹, F.M. Nagengast[1], Depts of Gastroenterology¹ and Pathology², Radboud University Nijmegen Medical Centre, The Netherlands

09.50 Bone morphogenetic protein signaling activity as a predictive marker for survival of patients with colorectal cancer (p. 131)
R.J. Jacobs¹, L. Kodach¹, N. de Miranda, D.W. Hommes¹, G.R. van den Brink¹, H. Morreau², J.C. Hardwick[1], [1]Dept of Gastroenterology & Hepatology, [2]Dept of Pathology, Leiden University Medical Center, Leiden, The Netherlands

10.00 Hyperplastic polyps and sessile serrated adenomas as a phenotypic expression of MYH-associated polyposis (MAP) (p.132)
K.S. Boparai[1, 2], E. Dekker¹, S. van Eeden², M.M. Polak², J.F.W.M. Bartelsman¹, E.M.H. Mathus-Vliegen¹, J.J. Keller¹, C.J.M. van Noesel², [1]Dept of Gastroenterology & Hepatology, Academic Medical Center, Amsterdam, The Netherlands, [2]Dept of Pathology, Academic Medical Center, Amsterdam, The Netherlands

10.10 A complete in vitro assay to diagnose Variants of Uncertain Significance in presumed Lynch syndrome patients
(Final report MLDS projectno. MWO 05-16) (p. 133)
M. Drost¹, J.B.M. Zonneveld¹, L. van Dijk¹ and N. de Wind¹, [1]Dept. of Toxicogenetics, Leiden University Medical Centre, Leiden, The Netherlands

10.20 Additional value of jejunal measurements during 24 hours tonometry in patients suspected of chronic gastrointestinal ischemia (p. 134)
D. van Noord¹, P.B.F. Mensink¹, P.M.T. Pattynama², H.J.M. Verhagen³, E.J. Kuipers¹, Depts. of Gastroenterology and Hepatology¹, Intervention Radiology², Vascular Surgery³, Erasmus MC University Medical Center, Rotterdam, The Netherlands

10.30 Koffiepauze

Nederlandse Vereniging voor Gastroenterologie **Parkzaal**

Voorzitters: A. Cats en J.H. Kleibeuker

Voordrachten in het Nederlands, spreektijd 7 minuten, discussietijd 3 minuten

11.00 Properties of the neosquamous epithelium after radiofrequency ablation of Barrett esophagus with early neoplasia (p.135)
R.E. Pouw[*1], J.J. Gondrie[1], A.M. Rygiel[1], W.D. Rosmolen[1], C.M. Sondermeijer[1], P. Fockens[1], F.J. Ten Kate[2], M. Vieth[3], K.K. Krishnadath[1], J.J. Bergman[1], [1]Gastroenterology, Academic Medical Center, Amsterdam, The Netherlands, [2]Pathology, Academic Medical Center, Amsterdam, The Netherlands, [3]Pathology, Klinikum Bayreuth, Bayreuth, Germany*

11.10 Optimising patient's flow undergoing esophagectomy for carcinoma with reconstruction by predicting the durations of surgical procedure and length of stay at the intensive care unit (p. 136)
D.T. Nguyen[1,2], M. Van Houdenhoven[1], M.J. Eijkemans[2], E.W. Steyerberg[2], G. Wullink[1], H.W. Tilanus[3], G. Kazemier[1,3], Dept of Operating Rooms[1], Center for Clinical Decision Sciences, Dept of Public Health[2], Dept of Surgery[3], Erasmus MC - University Medical Centre, Rotterdam, The Netherlands

11.20 Morbidity in immigrants of Turkish descent undergoing upper gastrointestinal endoscopy (p. 137)
A.I. Wegman, R.J.L.F. Loffeld, Dept of Internal Medicine, Zaans Medisch Centrum Zaandam, The Netherlands

11.30 The influence of socioeconomic status on proton pump inhibitor (PPI) use in a large population in the Netherlands. (p. 138)
O.S. van Boxel[1], M.P. Hagenaars[2], A.J.P.M. Smout[1], P.D. Siersema[1], [1]Dept of Gastroenterology and Hepatology, University Medical Center Utrecht, The Netherlands [2]Achmea Health Insurance, Leiden, The Netherlands

11.40 Does extended proton pump inhibitor therapy after H. pylori eradication increase cure rates of H. pylori positive peptic ulcers? a systematic review (p. 139)

M.J.R. Janssen[1,2], D. Huis in 't Veld[1], L. Stikkelbroeck[1], W.A. de Boer[3], [1]Dept of Internal Medicine, Slingeland Hospital, Doetinchem, The Netherlands, [2]Dept of Nuclear Medicine, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands, [3]Dept of Gastroenterology, Bernhoven Hospital, Oss, The Netherlands

11.50 Serum level of leptin: a potential marker for patients at high risk of gastric cancer? (p. 140)

L.G. Capelle[1], A.C. de Vries[1], J. Haringsma[1] , C.W.N. Looman[2], N.M.A. Nagtzaam[1], H. van Dekken[3], F. ter Borg[4], R.A. de Vries[5], E.J. Kuipers[1], [1]Depts of Gastroenterology and Hepatology, [2]Public Health, and [3]Pathology, Erasmus MC University Medical Center, Rotterdam, [4]Dept of Hepato-gastroenterology, Deventer Hospital, Deventer, [5]Dept of Hepato-gastroenterology, Rijnstate Hospital, Arnhemm The Netherlands

12.00 Exploring the causative role of MYCN in esophageal atresias (p. 141)

(Final report Maag Lever Darm Stichting projectno. MWO 05-71)

A.P.M. de Brouwer[1], C. Marcelis[1], E. van Beusekom[1], P. Rieu[2], H. Brunner[1], H. van Bokhoven[1], [1]Dept of Human Genetics and [2]Pediatric Surgery, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands

12.10 Distribution of small intestinal fat delivery influences satiety and food intake (p. 142)

P.W.J. Maljaars[1], E.H. Haddeman[2], H.P.F. Peters[2], A.A.M. Masclee[1], [1]Division of Gastroenterology-Hepatology, Dept of Internal Medicine, University Hospital Maastricht, Maastricht, The Netherlands, [2]Unilever Food and Health Research Institute, Unilever Research & Development Vlaardingen, Vlaardingen, The Netherlands

12.20 Magnetic resonance enteroclysis in the diagnosis of small bowel neoplasms. Diagnostic accuracy and interobserver variance (p. 143)

S.J.B. Van Weyenberg[1], M.R. Meijerink,[2], M.A.J.M. Jacobs,[1], D.L. Van der Peet[3], C. Van Kuijk,[2], C.J.J. Mulder[1], J.H.T.M. Van Waesberghe[2], [1]Dept of Gastroenterology and Hepatology, [2]Dept of Radiology, [3]Dept of Surgery, The Netherlands

12.30 Regional and temporal stability of the intestinal microbiome (p. 144)
M.E. Grasman[1], A.E. Budding[2], C.J. Mulder[1], C.M.J.E. Vandenbroucke-Grauls[2], P.H.M. Savelkoul[2], A.A. van Bodegraven[1], Dept of Gastroenterology and Hepatology[1], Dept of Medical Microbiology and Infection Control[2], VU University Medical Centre, Amsterdam, The Netherlands

12.40 Genetic and morphological characteristics in Dutch hereditary pancreatitis patients (p. 145)
M.H. Derikx[1], R.H.M. te Morsche[1], J.B.M.J. Jansen[1], J.P.H. Drenth[1], [1]Dept of Gastroenterology and Hepatology, Radboud University Medical Center Nijmegen, The Netherlands

12.50 Chymotrypsinogen C (CTRC) variants as a genetic susceptibility factors in tropical calcific pancreatitis (p. 146)
M.H.M. Derikx[1], M. Sahin-Tóth[2], R.H.M. te Morsche[1], R. Szmola[2], S. Santhosh[3], A. Chacko[3], J.P.H. Drenth[1], [1]Dept of Gastroenterology and Hepatology, Radboud University Medical Center Nijmegen, The Netherlands, [2]Dept of Molecular and Cell Biology, Boston University Goldman School of Dental Medicine, 715 Albany Street, Evans-433, Boston, MA 02118, USA, [3]Dept of Gastrointestinal Sciences, Christian Medical College and Hospital, Vellore, India.

13.00 Lunchbuffet in expositiehal

Nederlandse Vereniging van Maag-Darm-Leverartsen **Genderzaal**

13.00- 14.30 **Ledenvergadering**
lunchbuffet in de zaal

Sectie Endoscopie Verpleegkundigen en Assistenten **Diezezaal**

Ochtendprogramma

10.30 Opening

10.35 Visitatiecommissie
Dr. R.A. de Man, mdl-arts, Erasmus MC, Rotterdam

11.00 Portale hypertensie, varices bloeding en behandeling
Dr. R. Slangen, mdl-arts, St. Lucas Andreas Ziekenhuis, Amsterdam

11.25 *Bacteriele 'Fingerprint' van de dikke darm*
T. Grasman, arts-onderzoeker, VU medisch centrum Amsterdam

11.45 Voorlichting over de V & VN, Nellie Kolk, Utrecht

12.15 Lunchbuffet in Kempenhal

Middagprogramma

13.30 Ledenvergadering

14.20 Begeleidingsbehoefte van vrouwen met IBD tijdens zwangerschap
D. Kanis, nurse practitioner, VU medisch centrum, Amsterdam

14.45 Zenkersdivertikel
Dr. B.J.M. Witteman, mdl-arts, Ziekenhuis Gelderse Vallei, Ede

15.05 Einde programma, thee in expositiehal

Vrijdag 3 oktober 2008

Vereniging Maag Darm Leververpleegkundigen **Auditorium**

09.30	Ontvangst met koffie en thee
09.45	Welkomstwoord *Dhr. W. Goverde, voorzitter VMDLV, UMC St. Radboud*
10.00	Pathofysiologie; hoe kort is short? *Dr. A. van Bodegraven, maag-, darm-, leverarts, VU medisch centrum*
10.45	Management van fistels *Dr. M. van der Kolk, chirurg – intensivist, UMC St. Radboud*
11.15	Voedingsaspecten bij short bowel syndroom *Mw. N. Wierdsma, diëtist – onderzoeker, VU medisch centrum*
12.00	Lunch
13.30	Kortdurend TPV thuis *Mw. M. Klos, voedingsverpleegkundige, Gelre ziekenhuizen*
13.50	Langdurig TPV thuis *Mw. T. Tas, voedingsverpleegkundige, AMC*
14.20	Kwaliteit van leven onderzoek bij langdurig TPV thuis *Mw. J. Jenniskens, maatschappelijk werker AMC* *Aansluitend het verhaal van een ervaringsdeskundige*
15.00	Darmtransplantatie *Mw. G. Sekema, verpleegkundig consulent kinder MDL, UMCG*
15.30	Afsluiting met daarna mogelijkheid tot borrelen en netwerken *Dhr. W. Goverde, voorzitter VMDLV, UMC St. Radboud*

Clinical outcome of patients with infection of extrapancreatic collections without pancreatic parenchymal necrosis

O.J. Bakker[1], U. Ahmed Ali[1], H.C. van Santvoort[2], M.G. Besselink[2], H.G. Gooszen[1] and T.L. Bollen[2] for the Dutch Pancreatitis Study Group, [1]Division of Surgery, University Medical Center Utrecht, Utrecht, [2]Dept of Radiology, St. Antonius Hospital, Nieuwegein, The Netherlands

Introduction: Infection of pancreatic parenchymal necrosis is a major cause of morbidity and mortality in acute pancreatitis. Infection of extrapancreatic collections without pancreatic parenchymal necrosis is less known but is increasingly being recognized as a separate disease entity. Data on clinical course and outcome are lacking. Methods: From a prospective database we selected all patients with extrapancreatic collections and with normal enhancement of the pancreatic parenchyma on initial contrast-enhanced computed tomography (CECT; day 4 to 7 from onset of symptoms). A subgroup of these patients developed infection of these extrapancreatic collections. Clinical outcome parameters were (multiple) organ failure (OF or MOF), need for intensive care admission (ICU), need for radiological or operative intervention, length of hospital stay and mortality.

Results: One hundred eighty-seven patients with extrapancreatic heterogeneous acute collections and a normal enhancement of pancreas parenchyma were identified. None of these patients developed pancreatic necrosis later in the course of their disease, as evidenced by follow-up CECT. Twenty-one (11%) of these patients developed infection of extrapancreatic collections. Eleven patients (52%) developed OF during admission and 6 patients (29%) developed MOF. Fifteen patients (71%) were admitted to the ICU with a mean stay of 28 days (range; 1-89). The mean length of hospital stay was 72 days (range; 13-172). The mean time until infection of extrapancreatic collections was diagnosed was 26 days (range; 6-72). All 21 patients required an intervention, either radiological drainage or operative necrosectomy. Infection was confirmed by positive culture in all patients. Primary radiological drainage was performed in 17 patients of whom 9 patients subsequently also required operative intervention. Primary necrosectomy (without prior radiological drainage) was performed in 3 patients. The overall mortality was 6.5%. In patients with infection of extrapancreatic collections without pancreatic parenchymal necrosis the mortality was 29%.
Conclusion: In patients with acute pancreatitis, infection of extrapancreatic collections without parenchymal necrosis leads to high mortality, comparable with mortality rates reported in the literature for infected pancreatic necrosis. The subgroup of patients without parenchymal necrosis, but with extrapancreatic collections, should therefore be monitored just as carefully as patients with pancreatic necrosis.

Transcolonic Peritoneoscopy for the Detection of Peritoneal Metastases

R.P. Voermans MD[1,2], D.O. Faigel MD[3], M.I. Van Berge Henegouwen MD PhD[2], Brett Sheppard MD[4], Paul Fockens MD PhD[1], [1]Dept. of Gastroenterology and Hepatology, [2]Dept of Surgery, Academic Medical Center, Amsterdam, The Netherlands. [3]Dept. of Gastroenterology and Hepatology, [4]Dept of Surgery, Oregon Health & Science University, Portland, OR, USA

Background and aims: Natural Orifice Translumenal Endoscopic Surgery (NOTES) peritoneoscopy could replace laparoscopic peritoneoscopy (LAP) for staging of gastrointestinal malignancies. In previously performed porcine experiments we successfully created a model for peritoneal metastases and established a benchmark for LAP detection. In this model the NOTES transgastric peritoneoscopy appeared to be inferior to LAP, mainly due to limited visualization of the liver. Aim was to improve visualisation of the liver by approaching through the colon and to compare the transcolonic peritoneoscopy (TCP) with the previously set LAP standard. Methods: This protocol was performed in an anesthetized porcine model. 2.5 mm color-coded beads were stapled via LAP in the peritoneum to simulate metastases. In the same model we previously established the benchmark for LAP detection: yield 95% of beads (90% CI: 91-100%). Using a non-inferiority design with a margin of equivalence of 15%, a sample size of 31 beads was determined. Three to 7 beads were placed in each of 6 animals. Randomization was performed for number and location of beads. Locations included: abdominal peritoneum (4 beads), diaphragm (8), surface of liver and hepatoduodenal ligament (18), and miscellaneous sites (1): visceral peritoneum, omentum, anterior stomach and pelvis. TCP was then performed with a 2 channel therapeutic endoscope using either standard accessories (forceps, cap)(TCP-s) or with a specially designed toolkit (bendable overtube, articulating retractors and graspers)(TCP-t) in randomized order by one of 2 endoscopists, blinded to bead placement. Results: A total of 31 beads were placed into 6 pigs. TCP-s found 23 beads (yield 74%, 90% CI: 67-88%, non-inferior to LAP minus the margin of equivalence). TCP-t found 17 beads (yield 55%; 90% CI: 39-70%, inferior to LAP minus the margin of equivalence). TCP-s was superior for detecting beads in comparison with TCP-t (p=0.034). TCP-s was, using a transparent cap, superior in detecting beads on the inferior liver surface; Exclusion of these liver beads resulted in non significant difference between TCP-s and TCP-t (p=0.317). Conclusions: In this prospective, blinded, comparative trial, TCP was non inferior in comparison with the predetermined standard. The use of a transparent cap improved visualization of the inferior liver surface. TCP resulted in improved visualization of the liver in comparison with TGP.

Number of lymph nodes examined among patients with gastric cancer: variation between Depts of pathology and clear prognostic impact in node-negative disease

A.E. Dassen[1], V.E.P.P. Lemmens[2], A.A.M. van der Wurff[3], S.J. Brenninkmeijer[4], D.J. Lips[1], K. Bosscha[1], [1]Jeroen Bosch Hospital, Dept of Surgery, 's-Hertogen-bosch, [2]Eindhoven Cancer Registry, Comprehensive Cancer Centre South (IKZ), Eindhoven, [3]St Elisabeth Hospital, Dept of Pathology, Tilburg, The Netherlands, [4]Twee Steden Hospital, Dept of Surgery, Tilburg, The Netherlands

Gastric cancer is still one of the leading cancers in incidence and mortality throughout the world. In the Netherlands, overall 5-year survival is 18%, whereas after surgery it is 41% in stage I and II. The only curative treatment is surgery with (partial) gastric resection and lymph node dissection. According to several studies and guidelines a resection with at least 15 lymph nodes should be performed for proper staging and disease control. There is no consensus about the extent of lymph node dissection worldwide however. In the West, D2-resection coincides with high morbidity and no direct effect upon cancer-related mortality, and is therefore replaced by the D1 resection.In this perspective, we conducted a retrospective study in the Southern part of the Netherlands to evaluate the amount of lymph nodes dissected and examined its relation to survival. All patients resected for primary gastric cancer without evidence for distant metastasis, diagnosed between 1999 and 2006 in the Dutch Southern Cancer Registry area were included (N=688). The area includes 10 hospitals on 15 locations, which are served by 6 Depts of pathology. The median number of lymph nodes was described by Dept of pathology, nodal status (N0 vs N+) and period of diagnosis (1999-2002 vs 2003-2006). Follow-up of vital status was complete for patients diagnosed between 1999 and 2004. Differences in 5-year crude survival rates between node-negative patients with fewer than the total median number of nodes examined vs. patients with more nodes examined were analysed by means of a log-rank test. The median number of lymph nodes examined was 7. Among patients with N0 disease, the median number was 6, while among patients with N+ disease it was 8. Between 1999-2002 and 2003-2006, the median number of nodes examined increased from 6 to 7. The median number of nodes examined varied between the Depts of pathology from 5 to 9.Among patients with N0 disease and < 7 nodes examined, 5-year survival was 56% compared to 69% among patients with ≥7 nodes examined (p=0.012). In our region insufficient number of lymph nodes are dissected and/or examined. The difference in lymph nodes examined between the Depts of pathology could lead to differences in stage distribution and survival. Attempts to improve nodal assessment seem to be mandatory.

Concurrent chemoradiation with cisplatin and 5FU followed by surgery or as definitive treatment for localized oesophageal cancer

E.F.W. Courrech Staal[1], A. Cats[2], B.M.P. Aleman[3], M.L.F. van Velthuysen[4], H. Boot[2], F. van Coevorden[1], J.W. van Sandick[1], [1]Dept of Surgery, [2]Dept of Gastroenterology, [3]Dept of Radiotherapy, [4]Dept of Pathology, The Netherlands Cancer Institute-Antoni van Leeuwenhoek Hospital, Amsterdam, The Netherlands

The poor outcome associated with surgical resection alone for patients with localized oesophageal cancer has initiated the use of combined-modality treatment protocols that include concurrent chemoradiotherapy (CRT). Various regimens are being explored worldwide. The present study aimed to evaluate the efficacy and toxicity of cisplatin and 5-fluorouracil (5FU) with conventionally fractionated radiotherapy in patients with non-metastatic oesophageal cancer.From January 2002 to June 2007, 41 patients with T2-3N0-1M0-1a oesophageal cancer were treated with radiotherapy to a dose of 45-50 Gy in 25 fractions combined with two cycles of 75 mg/m^2 cisplatin (day 1 and 29) and 800 mg/m^2 5FU (week 1 and 5). Surgery was planned 5-6 weeks thereafter. Median follow-up was 16 (3-64) months.Median age was 63 (37-76) years. Histology included adenocarcinoma (n=28), squamous cell carcinoma (n=10) and adenosquamous carcinoma (n=3). Moderate or severe adverse events during CRT occurred in 14 and 4 patients, respectively. Dose reduction of chemotherapy was necessary in 3 patients. All patients completed the scheduled radiotherapeutic regimen. In 8 patients CRT was planned as definitive treatment. Another 7 patients were not operated because of clinical deterioration/severe toxicity (n=5) or progressive disease (n=2). Twenty-six patients were operated (transhiatal oesophagectomy n=17, transthoracic oesophagectomy n=8, exploration only n=1). A microscopic radical (R0) resection was achieved in all resected patients. Pathologic response was complete (pCR) in 8 (32%) and partial (pPR) in 8 (32%) of the 25 resected patients.Postoperative morbidity occurred in 10 resected patients (40%) and consisted mainly of cardiopulmonary complications. One patient died postoperatively due to myocardial infarction. There were no anastomotic leakages or stenoses. Median postoperative hospital stay was 18 (9-22) days. Two-year survival was 50% in all patients, 61% in the resected group and 29% in the non-operated group. Of the 18 patients who are alive, 13 (72%) had no evidence of disease at last follow-up. Seven out of 8 pCR patients and 3 out of 8 pPR patients were disease-free after a median follow-up of 22 (6-63) months.
Conclusion: The combination of cisplatin and 5FU with radiation is well tolerated by selected patients with stage II-III oesophageal cancer. Pathologic response, R0 resection rate and clinical outcome of our retrospectively collected data compare favourably with other studies.

Robot-assisted thoracoscopic esophagectomy for esophageal cancer: short- and mid-term results

J. Boone[1], M.E.I. Schipper[2], W.A. Moojen[1], I.H.M. Borel Rinkes[1]G.J.E. Cromheecke MD[3], R. van Hillegersberg[1], Dept of [1]Surgery, [2]Pathology and [3]Anaesthesiology, University Medical Center Utrecht, Heidelberglaan 100, 3584 CX Utrecht, The Netherlands

Robot-assisted thoracoscopic esophagectomy (RATE) was developed to reduce the morbidity of open transthoracic esophagectomy (TTE) for esophageal cancer without compromising oncologic outcome. Aim of the present study was to assess the short- and mid-term results. Between October 2003 and May 2007, 47 patients with resectable esophageal cancer underwent RATE with a laparotomy or conventional laparoscopy. Data regarding surgery, postoperative course and follow-up were prospectively collected. Conversion to thoracotomy occurred in 7 (15%) patients. Median operation time was 450 (360-550) minutes; median blood loss was 625 (150-5300) millilitres. Median postoperative ventilation time was 1 (0-126) day, ICU stay 3 (0-136) days and hospital stay 18 (10-182) days. Pulmonary complication rate decreased from 57% in the first 23 operated patients to 33% in the last 24 patients. In-hospital mortality was 6%. A radical resection (R0) was achieved in 77% of patients. A median of 29 (range 8-68) lymph nodes were dissected. Forty-nine percent of patients had TNM stage IVa disease. After a median follow-up of 35 (range 12-55) months, median disease-free survival was 15 (95% CI 12-18) months.Conclusions: RATE has proven to be oncologically safe with a lymphadenectomy and R0 resection rate comparable to open TTE, combined with low blood loss and a steep learning curve. It is expected that surgery time, blood loss and pulmonary complication rate will further decrease with growing experience.

Influence of circumferential resection margin on prognosis in distal esophageal and gastro-esophageal cancer approached through the transhiatal route

J.J.G. Scheepers, D.L. van der Peet, A.A.F.A. Veenhof, and M.A. Cuesta. From the Dept of Surgery, Vrije Universiteit Medical Center (VUmc), Amsterdam, The Netherlands

We studied the influence of circumferential resection margin (CRM) involvement on survival in patients with malignancies of the distal esophagus and gastro-esophageal junction.110 consecutive patients undergoing a laparoscopic or open transhiatal esophagectomy for malignancy of the distal 5 centimetres of the esophagus, or a Siewert I gastro-esophageal junction tumor were analysed retrospectively. Only patients with potentially resectable tumors were included. CRM status was defined as clear (CRM^-) or involved (CRM^+) (microscopic tumor within 1 mm of the resection margin). Statistical analysis was done by means of univariate and multivariate analysis using the Kaplan-Meier method and Cox proportional hazard model. 110 patients were analysed. 60 patients underwent open and 50 patients underwent laparoscopic transhiatal esophagectomy. There were 6 (5%) T_1, 18 (16%) T_2 and 86 (89%) T_3 tumors. CRM was clear in 68 (62%) patients and involved in 42 (38%) patients. Median survival in these groups was 50 vs. 20 months (p= 0.000). Since CRM involvement was only seen in T_3 tumors this group was analysed in detail. Median survival in the T_3CRM^- and T_3CRM^+ group was 33 vs. 19 months (p=0.004). For T_3N_0 tumors median survival in CRM^- and CRM^+ was 40 and 22 months respectively (p=0.036). Median survival for T_3N_1 tumors was 22 and 13 months respectively (p=0.049)
Conclusion: Involvement of the circumferential resection margin was found to be an independent prognostic factor on survival in our study. It predicts a poor prognosis in patients with potentially resectable malignancies of the distal 5 centimetres of the esophagus and Siewert I adenocarcinomas of the gastro esophageal junction.

Boerhaave Syndrome: 20 years of experience in the Erasmus Medical Centre, Rotterdam

M.P. de Jong[1], W.M.U. van Grevenstein[2], J.J.B. Van Lanschot[2], H.W. Tilanus[2], [1]Medisch Centrum Rijnmond Zuid, Rotterdam, [2]Erasmus Medisch Centrum, Rotterdam, The Netherlands

The Boerhaave syndrome, a spontaneous oesophagus perforation, is a rare but life-threatening condition which needs an early diagnosis and treatment. The syndrome was first described by Herman Boerhaave in 1724. Until the 1940's it was a fatal condition with mortality close to 100 percent after conservative treatment. Up till these days there is no golden standard of treating the Boerhaave syndrome. Recently new techniques have been introduced by placement of a stent at the perforation with drainage of the pleura and mediastinum.In this retrospective study we describe the results of the Boerhaave syndrome over the past 20 years at the Erasmus Medical Centre of Rotterdam.From January 1988 till December 2007 23 patients with the Boerhaave syndrome were treated at the Erasmus Medical Centre, 22 men and one female. The average age was 61 years. Ten patients were operated on within 24 hours; the mortality in this group was 30%. In eleven patients operation followed after 24 hours. In this group there was a significant higher mortality rate of 45.5 %. Six patients were treated with the placement of a stent. All stents were placed within 24 hours after the oesophagus rupture. In four of the six patients operative treatment (oesophagus resection) had to follow the stent placement because of luxation of the stent. The most important complications, mediastinitis and pleura-empyema, were seen in all patients. Conclusion: The Boerhaave syndrome is a rare disorder with a high mortality rate, in which a delay of treatment shows a serious increase of mortality. This group of 23 patients is the largest series described in The Netherlands. The mortality rate of the group of patients operated on after 24 hours is lower in comparison to the international literature, which shows a mortality rate of 50-70%. The treatment of the Boerhaave syndrome with stent placement is a less invasive option. In the literature it is so far only described in case reports. At this moment the treatment of the Boerhaave syndrome with stent placement is not the first choice of treatment because of the high risk of stent luxation.

Feasibility of laparoscopic Nissen as a day-case procedure

M.S. Vlug[1], J. Wind[1], J.H. Eshuis[2], M.I. van Berge Henegouwen[1], D.J. Gouma[1], W.A. Bemelman[1], [1]Dept of Surgery, Academic Medical Centre at the University of Amsterdam, Amsterdam, [2]Dept of Anaesthesiology, Academic Medical Centre at the University of Amsterdam, Amsterdam, The Netherlands

Aim of this study was to assess the feasibility of laparoscopic Nissen fundoplication in a day-case procedure. A consecutive series of patients with refractory gastro-esophageal reflux disease who underwent day-case laparoscopic Nissen fundoplication were prospectively evaluated (group I). Outcome parameters were Visual Analogue Scale (VAS) and the Euroqol (EQ-5D) questionnaire to assess postoperative pain and health-related quality of life. The results of laparoscopic Nissens (group I) were compared with a series of laparoscopic cholecystectomies (group II). An interim analysis of the first group of laparoscopic Nissens showed high postoperative pain scores. For this reason the postoperative pain medication was increased by adding a NSAID after the 10th patient. From October 2005 to March 2008, 22 patients had a laparoscopic Nissen fundoplication (group I) and 48 patients a laparoscopic cholecystectomy (group II). Median age was 45 years (range 17-64). In group I, 1 out of 22 (95%) patients were discharged the same day, 7 (32%) patients were seen postoperatively on the First Aid with dysphagia or pain and 2 (9%) patients were readmitted. In group II, 45 out of 48 (94%) patients were discharged the same day, 6 (12.5%) patients were seen postoperatively on the First Aid because of a wound infection or pain and 3 (6%) patients were readmitted. EQ5D and VAS scores were significantly worse after a laparoscopic Nissen in day-care, repeated measurements p=0.000 and p=0.000, respectively. In a telephone survey 14 out of 22 (66.7%) patients preferred a short hospital stay over day-case surgery compared to 13 out of 48 (30.9%) in group II.
In conclusion, day-case laparoscopic Nissen fundoplication is feasible and safe, but postoperative pain is high and most patients prefer a short hospital stay.

Preoperative biliary drainage in patients with proximal bile duct obstruction: Endoscopic or percutaneous approach?

J.J. Kloek[1], N.A. van der Gaag[1], Y. Aziz[1], O.M van Delden[2], E.A.J. Rauws[3], O.R.C. Busch[1], D.J. Gouma[1], T.M. van Gulik[1], [1]Dept of Surgery, Academic Medical Center, University of Amsterdam, [2]Dept of Radiology, Academic Medical Center, University of Amsterdam, [3]Dept of Gastroenterology, Academic Medical Center, University of Amsterdam, The Netherlands

Introduction: Obstructive jaundice is a significant risk factor in the treatment of patients with hilar cholangiocarcinoma (HCCA) requiring major liver resection. Controversy exists over the preferred technique of preoperative biliary drainage (PBD), either via the endoscopic route by retrograde cholangiopancreaticography (ERCP) or using percutaneous transhepatic biliary drainage (PTBD), while no randomized studies exist. The aim of this study was to compare complications and success rate of ERCP and PTBD in patients eligible for resection of HCCA. METHODS: A total of 102 patients underwent an explorative laparotomy on the suspicion of HCCA between 2001 and 2008. Demographic features, tumor stage according to the Bismuth classification, laboratory investigations and the results of radiological and endoscopic drainage interventions were investigated. Patients who underwent either ERCP or PTBD as primary procedure were compared for technical success, procedure related complications, mean number of procedures, duration of drainage until laparotomy and the decrease in serum bilirubin level.RESULTS: Of 102 patients 88 (87%) underwent PBD; 78 patients underwent ERCP as primary procedure and 10 patients PTBD. Age, gender, tumor stage did not differ significantly between groups. The technical success rate of initial stent insertion was 78% in the ERCP versus 100% in the PTBD group (P=.20). Stent dislocation was similar in the ERCP and PTBD group (27% vs. 20%, P=.56), whereas infectious complications were significantly more common in the endoscopic group (53% vs. 10%, P=.01). Patients in the ERCP group underwent significantly more drainage procedures (2.9 vs. 1.6, P<.01), of which 25 patients required a PTBD as final procedure. The drainage period until laparotomy was 15 weeks (min-max 4-29) in the ERCP group vs. 10 (3-21) in the PTBD group (P=.09). Success rate, defined as a decrease in serum bilirubin levels, was similar in both groups. A sub analysis of the 25 patients undergoing both procedures showed most stent dislocations (48%) and infectious complications (64%), resulting in a mean number of 4.3 (range 2 – 7) procedures per patient.
Conclusions: The present study shows in patients with suspicion on HCCA, lower infectious complications after PTBD compared to ERCP, resulting in significantly less procedures. These results suggest a more favourable outcome of percutaneous drainage, and underline the importance of further (randomized) studies to be performed.

Improved prognosis for patients with Primary Biliary Cirrhosis showing relevant biochemical response to UDCA. Results of a multicenter long-term cohort study involving 375 patients

E.M.M. Kuiper[1], B.E. Hansen[2], R.A. de Vries[3], J.W. den Ouden-Muller[4], Th.J.M van Ditzhuijsen[5], E.B. Haagsma[6], M.H.M.G. Houben[7], B.J.M. Witteman[8], K.J van Erpecum[9], H.R. van Buuren[1] for the Dutch PBC study group., [1]Dept of Gastroenterology and Hepatology and [2]Dept of Epidemiology and Biostatistics, Erasmus Univ.Medical Center, Rotterdam, [3]Dept of Gastroenterology and Hepatology, Rijnstate Hospital, Arnhem, [4]Dept of Internal medicine, Sint Franciscus Gasthuis, Rotterdam, [5]Dept of Internal medicine, Jeroen Bosch Hospital, Den Bosch, [6]Dept of Gastroenterology and Hepatology, Univ. Medical Center Groningen, [7]Dept of Gastroenterology and Hepatology, Haga Hospital, Den Haag, [8]Dept of Gastroenterology and Hepatology, Hospital Gelderse Vallei, Ede, [9]Dept of Gastroenterology and Hepatology, University Medical Center Utrecht, The Netherlands

Background and Aims: Ursodeoxycholic acid (UDCA) reportedly improves prognosis of patients with Primary Biliary Cirrhosis (PBC), especially in early disease. Few studies have assessed the prognostic significance of the quantitative biochemical improvement following UDCA treatment. The aim of this study was to evaluate the prognosis of patients with (responders) and without (non-responders) clear biochemical response to UDCA, particularly in advanced disease. Methods: Prospective, multicenter cohort study of patients with established PBC treated with UDCA 15 mg/kg/day. Exclusion criteria: Child-Pugh B/C, AIH overlap syndrome or immunosuppressive drugs. PBC was classified as early (pre-treatment bilirubin and albumin normal), moderately advanced (one parameter abnormal) or advanced (both abnormal). We used quantitative criteria for response proposed by Poupon (PO; ALP<3ULN; AST<2ULN; bilirubin<1ULN) and Pares (PA; ALP decrease >40% of baseline or normalization). Analysis involved biochemical response at 1 year and occurring at any time following initiation of UDCA. Endpoint was transplantation-free survival. Results: 375 patients (89% women, mean age 54 yrs) were included. Mean follow-up was 118 ± 53 months. Overall, survival of responders (according to both PO&PA) was significantly better than that of non-responders ($p<0.001$ and 0.02 resp); the prognostic importance of PO was superior. Prognosis of early PBC was comparable for responders and non-responders. In contrast, prognosis of responders (PO) with moderately advanced and advanced PBC was significantly better than that of non-responders ($p=0.004$ and $p=0.042$ resp). The hazard ratio for death and transplantation in patients with moderately advanced disease who showed biochemical response (PO) decreased significantly from 2.6 to 1.1, a level comparable to that for patients with early PBC. Prognosis in advanced disease was also better for responders to UDCA. Conclusions: In PBC, biochemical response to UDCA provides important prognostic information. UDCA significantly improves prognosis for patients with advanced disease if a relevant biochemical response to treatment occurs. In moderately advanced PBC, survival of responders is comparable to survival of patients with early PBC.

Normalization of serum bilirubin and/or albumin levels following treatment with UDCA is associated with improved prognosis for patients with moderately advanced and advanced Primary Biliary Cirrhosis

E.M.M. Kuiper[1], B.E. Hansen[2], R.A. de Vries[3], J.W. den Ouden-Muller[4], Th.J.M van Ditzhuijsen[5], E.B. Haagsma[6], M.H.M.G. Houben[7], B.J.M. Witteman[8], K.J van Erpecum[9], H.R. van Buuren[1] for the Dutch PBC study group. [1]Dept of Gastroenterology and Hepatology and [2]Dept of Epidemiology and Biostatistics, Erasmus University Medical Center, Rotterdam, [3]Dept of Gastroenterology and Hepatology, Rijnstate Hospital, Arnhem, [4]Dept of Internal medicine, Sint Franciscus Gasthuis, Rotterdam, [5]Dept of Internal medicine, Jeroen Bosch Hospital, Den Bosch, [6]Dept of Gastroenterology and Hepatology, University Medical Center Groningen, [7]Dept of Gastroenterology and Hepatology, Haga Hospital, Den Haag, [8]Dept of Gastroenterology and Hepatology, Hospital Gelderse Vallei, Ede, [9]Dept of Gastroenterology and Hepatology, University Medical Center Utrecht, The Netherlands

Background and Aims: Ursodeoxycholic acid (UDCA) has been reported to be of benefit for patients with Primary Biliary Cirrhosis (PBC), especially for those with early disease. The aim of this study was to evaluate prognosis according to the biochemical response to UDCA, particularly in subjects with advanced disease. Methods: Prospective, multicenter study of PBC patients treated with UDCA 15 mg/kg/day. Exclusion criteria: Child-Pugh B/C, AIH overlap syndrome or immunosuppressive drugs. Based on previous findings (Am J Gastroenterol 2006;101:2044-50) PBC was classified as early (pre-treatment bilirubin and albumin normal), moderately advanced (one parameter abnormal) or advanced (both abnormal). According to these prognostic classes Hazard Ratios (HR) for LTX-free survival were calculated before treatment and after 1 year. Response to UDCA was defined as normalization of previously abnormal bilirubin and/or albumin levels. Results: 321 patients were included. Mean follow-up was 118 months ± SD 53. 15-year survival in patients with early PBC was 75% and comparable to that of a matched sample of the Dutch population (p=0.179). For moderately advanced and advanced PBC this was 42% and 19% resp; corresponding HR were 2.6 and 7.3 resp. At 1 year the prognosis of patients who responded to UDCA was better than for patients who did not. Survival of patients with moderately advanced PBC who responded became comparable to survival of early PBC (p= 0.058, 15-yr-survival 69%). Similarly, prognosis of patients with advanced PBC improved significantly when they responded to UDCA. Conclusions: Bilirubin and albumin levels are powerful prognostic factors in UDCA treated PBC. Normal levels before treatment predict excellent prognosis. Levels following 1-year treatment allow to predict prognosis more accurately. Normalization of bilirubin and/or albumin at 1 year is associated with improved survival.

Antiviral effect of entecavir: Results from 153 chronic hepatitis B patients in an international multicenter cohort study

J.G.P. Reijnders[1], K. Deterding[2], J. Petersen[3], F. Zoulim[4], T. Santantonio[5], M. Buti[6], F. van Bömmel[7], B.E. Hansen[1] , H. Wedemeyer[2], H.L.A. Janssen[1], [1]Dept of Gastroenterology and Hepatology, Erasmus MC University Medical Center Rotterdam, Rotterdam, the Netherlands, [2]Dept of Gastroenterology, Hepatology, and Endocrinology, Medical School Hannover, Hannover, Germany, [3]Dept of Medicine, University of Hamburg, Hamburg, Germany, [4]Dept of Hepatology, Hotel Dieu Hospital Lyon, Lyon, France, [5]Clinic of Infectious Diseases, University of Bari, Bari, Italy, [6]Dept of Hepatology, Hospital Vall de Hebron, Barcelona, Spain, [7]Dept of Gastroenterology and Hepatology, Charité University Medical Center Berlin, Berlin, Germany

Entecavir (ETV) is a potent and selective inhibitor of viral replication in both nucleoside-naïve and lamivudine-refractory chronic hepatitis B (CHB) patients. Our aim was to investigate the efficacy and safety of ETV in CHB patients. In this investigator-initiated project within the European network of excellence (VIRGIL) we studied HBV monoinfected patients treated with ETV monotherapy from 7 large European referral centers. HBV DNA and ALT levels were measured every 3 months. Virologic response (VR) was defined as serum HBV DNA levels < 80 IU/mL, and was assessed in patients from 5 centers using an HBV DNA assay with a lower limit of detection of at most 80 IU/mL. Screening for resistance was performed at baseline in treatment-experienced patients or in case of virologic breakthrough in available serum samples by direct sequencing. A total of 153 patients (age 43±16 years; m/f: 113/40; 64 (42%) HBeAg+) treated with ETV monotherapy were analyzed. 103 patients were treatment-naïve and 50 treatment experienced (13 LAM; 11 ADV; 17 sequential LAM and ADV, 5 LAM with ADV add-on; 3 sequential LAM, ADV, TDF; 1 LdT). For the patients treated with ETV 0.5mg (n=114), mean HBV DNA at baseline was 6.27±1.74 $\log_{10}$ IU/mL. At the end of the observation period (median 39 [12-83] weeks) mean HBV DNA decline was 4.00±1.6 $\log_{10}$ IU/mL. HBeAg loss was documented in 2 (5%) patients. HBsAg loss did not occur. Virologic breakthrough was observed in 2 (2%) patients, but no ETV-resistant mutations could be detected. Mean HBV DNA at baseline in patients treated with ETV 1mg (n=39) was 6.33±1.69$\log_{10}$ IU/mL. After a median follow-up of 53 (13-134) weeks HBV DNA decline was 3.59±1.83 $\log_{10}$ IU/mL. HBeAg loss occurred in 1 (4%) patient, HBsAg loss was not observed. 4 (11%) patients experienced a virologic breakthrough, and in 2 patients ETV-resistant mutations could be detected. VR could be assessed in 129 (84%) patients, and was achieved in 59 (46%) subjects. Multivariate analysis demonstrated that independent baseline predictors of VR were low HBV DNA levels (HR 0.78; 95%CI 0.62-0.99; p = 0.04), HBeAg negativity (HR 2.52; 95%CI 1.12-5.70; p = 0.03), and treatment-naïve patients (HR 3.87; 95%CI 0.91-16.6; p = 0.07). No important side effects associated with ETV were noted. Conclusion: ETV is effective and well tolerated, but its potency is compromised by prior treatment with nucleos(t)ide analogues. The rate of HBeAg loss was low both for naïve and treatment-experienced patients.

No beneficial effects of adding amantadine to standard PEG-interferon alfa-2b and ribavirin therapy in naïve chronic hepatitis C patients

H. van Soest[1], P.J. van der Schaar[2], G.H. Koek[3], R.A. de Vries[4], N.A.M. van Ooteghem[5], B. van Hoek[6], J.P.H. Drenth[7], J.M. Vrolijk[8], R.J. Lieverse[9], G.M.P. Houben[10], A. van der Sluys Veer[11], P.D. Siersema[1], A.M. van Loon[12], M.E.I. Schipper[13], K.J. van Erpecum[1], G. Boland[1,12], Depts. of Gastroenterology and Hepatology of [1]University Medical Center Utrecht, [2]Atrium Medical Center Heerlen, [3]University Hospital Maastricht, [4]Rijnstate Hospital Arnhem, [5]St Lucas Andreas Hospital Amsterdam, [6]Leiden University Medical Center, 7University Hospital Nijmegen, [8]Erasmus Medical Center Rotterdam, [9]Gelre Ziekenhuizen Apeldoorn, [10]Ziekenhuis Zeeuws Vlaanderen, [11]Onze Lieve Vrouwe Gast-huis Amsterdam, and Depts of Virology[12] and Pathology[13], University Hospital Utrecht, The Netherlands

Benefit of adding amantadine to standard therapy for chronic hepatitis C (HCV) viral infection is controversial. We explored whether this modification could enhance sustained viral response rates (SVR). In this multicenter, double-blind randomized controlled trial, 297 previously untreated patients were treated with amantadine hydrochloride 200 mg daily or placebo, in all cases combined with weight-based ribavirin (Schering Plough, Maarssen, The Netherlands: 1000-1200 mg/day) and high-dose induction therapy (interferon alfa-2b: Schering Plough) followed by PEG-interferon alfa-2b (Schering Plough: 1.5 µg/kg/week up to 26 weeks and 1.0 µg/kg/week from week 26 to week 52). In case of positive HCV RNA at week 24, treatment was discontinued. Amantadine and placebo groups were stratified for HCV genotype (1 vs non-1). Amantadine and placebo groups were comparable for HCV genotype (genotype 1 in 45%), viral load (above 800,000 IU/mL in 70%), fibrosis score (F3/4 in 32%) and other baseline characteristics. 90 patients discontinued treatment before reaching a primary endpoint (mainly because of grade 3 or 4 toxicity). Side effects did not differ between amantadine and placebo groups. Sustained viral response (SVR: one year after therapy discontinuation) according to intention-to-treat (ITT) analysis was achieved in 47% and 51% of amantadine and placebo groups (P=0.49), and according to per protocol analysis (i.e. only pts reaching primary endpoint) in 69% and 71% (P=0.9). Also, amantadine did not improve primary non-response rates, breakthrough or relapse rates. In genotype 1, SVR in amantadine vs placebo groups according to ITT analysis was 35% vs 44% (P=0.38) and according to per protocol analysis 51% vs 69% (P=0.42). In genotype non-1, SVR in amantadine vs placebo groups according to ITT was 55% vs 57% (P=0.88) and according to per-protocol analysis 84% vs 81% (P=0.8). In high viral load, SVR according to ITT was 43% vs 51% (P=0.33) and according to per-protocol 64% vs 68% (P=0.6). In multivariate analysis, genotype non-1 and pre-treatment GGT levels, but not amantadine therapy were independent predictors for SVR. Conclusion: There are no beneficial effects of adding amantadine to standard PEG-interferon alfa-2b and ribavirin therapy in naïve chronic hepatitis C patients. *Acknowledgements: Dr J. van Hattum was Principle Investigator of this study until September 2003. The study was financially supported by Schering Plough BV.*

Liver cirrhosis at baseline is an important predictor of resistance to adefovir

J.G.P. Reijnders[1], B.E. Hansen[1,2], S.D. Pas[3], R.A. de Man[1], M. Schutten[3], H.L.A. Janssen1, [1]Dept of Gastroenterology and Hepatology, Erasmus MC, University Medical Center Rotterdam, Rotterdam, The Netherlands, [2]Dept of Epidemiology and Biostatistics, Erasmus MC, University Medical Center Rotterdam, [3]Dept of Virology, Erasmus MC, University Medical Center Rotterdam, Rotterdam, The Netherlands

Chronic hepatitis B (CHB) patients who will not respond to adefovir (ADV) monotherapy need to be identified in an early stage in order to adjust treatment and prevent future development of antiviral drug resistance. In a single center cohort study we investigated CHB patients treated with long-term ADV monotherapy. ALT and HBV DNA levels were assessed every three months (detection limit 400 copies/mL). To detect resistance-associated mutations within the HBV polymerase gene direct sequencing was performed in case of virologic breakthrough or serum HBV DNA > $4\log_{10}$ copies/mL at the end of follow-up.A total of 76 patients (age 46±14 years; m/f: 57/19; 38 (50%) HBeAg+) treated with ADV 10 mg monotherapy were included in this analysis. Mean ALT at baseline was 3.8±4.2xULN, and mean HBV DNA was 7.5±1.6 $\log_{10}$ copies/mL. Forty-two (55%) patients were previously treated with lamivudine, of whom 25 (33%) subjects developed lamivudine resistance. Thirty (40%) subjects had a diagnosis of cirrhosis. Patients with cirrhosis were older compared to patients without cirrhosis ($p<0.001$), other baseline characteristics were comparable. During a median follow-up of 122 (24-185) weeks 42 (55%) patients achieved virologic response, defined as HBV DNA levels < 10^3 copies/mL. Eight of 38 HBeAg-positive patients (21%) lost HBeAg, and ten patients (13%) developed genotypic ADV resistance. Independent predictors of virologic response were HBeAg negativity at baseline (HR 2.98; 95%CI 1.24-7.19; $p = 0.02$), high baseline ALT levels (HR 1.11; 95% CI 1.05-1.18; $p = 0.001$), and low HBV DNA levels at baseline (HR 0.56; 95% CI 0.41-0.75; $p < 0.001$) and at week 24 of ADV treatment (HR 0.70; 95% CI 0.47-1.03; $p = 0.07$). Presence of cirrhosis was an important predictor of genotypic resistance (HR 6.54; 95% CI 1.39-30.9; $p = 0.018$), yet it was not associated with virologic response ($p = 0.33$). Absence of VR during treatment (HR 6.60; 95% CI 1.35-32.4; $p = 0.008$) was related to development of genotypic resistance as well. Patients without VR at week 24 already demonstrated a trend towards the emergence of ADV resistance ($p = 0.07$).

Conclusion: Presence of cirrhosis is an important predictor of antiviral drug resistance. As virologic breakthrough can result in severe exacerbations, decompensation, and death in patients with liver cirrhosis, potent antiviral agents with higher genetic barriers or even de novo combination therapy should be considered in this specific population.

Early HBeAg Loss during Peginterferon Alpha-2b Therapy Predicts HBsAg Loss – Results of a Long-Term Follow-Up Study in Chronic Hepatitis B

E.H.C.J. Buster[1], H.J. Flink[1], H. Simsek[2], E.J. Heathcote[3], S. Sharmila[4], G.E. Kitis[5], G. Gerken[6], M. Buti[7], R.A. de Vries[8], E. Verhey[1], B.E. Hansen[1,9], H.L.A. Janssen[1], [1]Dept of Gastroenterology and Hepatology, Erasmus MC University Medical Center Rotterdam, Rotterdam, The Netherlands, [2]Hacettepe University Faculty of Medicine, Ankara, Turkey, [3]Dept of Medicine, Toronto Western Hospital University Health Network, Toronto, Canada; [4]Hepatology Unit, Hospital Selayang, Selangor, Malaysia, [5]Dept of Gastroenterology, George Papanikolaou General Regional Hospital, Thessaloniki, Greece, [6]Dept of Gastroenterology and Hepatology, University Hospital, Essen, Germany, [7]Liver Unit, Hospital General Universitari Vall d'Hebron & CIBEREHD, Barcelona, Spain, [8]Dept of Gastroenterology and Hepatology, Rijnstate Hospital, Arnhem, The Netherlands, [9]Dept of Epidemiology and Biostatistics, Erasmus MC University Medical Center Rotterdam, Rotterdam, The Netherlands

Background Treatment with peginterferon (PEG-IFN) results in HBeAg loss in 35% of patients. We determined whether long-term response to peginterferon (PEG-IFN) is dependent on the timing of HBeAg loss. Methods 91 HBeAg positive chronic hepatitis B patients treated with PEG-IFN α-2b alone (100 µg/week) and 81 treated with PEG-IFN α-2b and lamivudine (100 mg/day) for 52 weeks were enrolled in this study. Patients were initially followed at 4 week intervals for 6 months and had one additional long-term follow-up (LTFU) visit (mean 3.54 ± 0.75 years post-treatment). Results Of 172 patients included, 47 (27%) lost HBeAg within 32 weeks and 47 patients (27%) lost HBeAg after week 32. At LTFU, serum HBeAg was still undetectable in 36 of 47 patients (77%) who were HBeAg negative within 32 weeks compared to 27 of 47 patients (57%) who lost HBeAg after week 32 (p=0.05). HBV DNA <400 copies/ml was observed more often in patients with early HBeAg loss compared to those with HBeAg loss after week 32 (47% vs. 21%, p=0.009), as well as HBsAg loss (36% vs. 4%, p<0.001). Early HBeAg loss and HBsAg loss were observed in 35% and 15% of patients treated with PEG-IFN and lamivudine, and in 21% and 8% of those receiving PEG-IFN alone, respectively (p=0.10 and p=0.14, respectively). On Cox regression analysis, older age (HR 1.63 [95%-CI 1.20-2.24] per 10 year increase), HBV genotype A (HR 15.73 [95%-CI 3.59-68.99] vs. genotype-non-A), HBeAg ≤32 weeks (HR 9.19 [95%-CI 2.09-40.36] compared to HBeAg loss >32 weeks) and low HBV DNA at week 32 (HR 0.38 [95%-CI 0.38-0.75] per 1$\log_{10}$ increase) were found to be associated with a higher likelihood of HBsAg negativity at LTFU. HBeAg negativity at week 32 was found to be the best predictor of HBsAg negativity at LTFU (area under the ROC-curve 0.85 [95%-CI 0.76-0.94]), with a sensitivity, specificity, positive predictive value and negative predictive value of 89%, 80%, 36% and 98%, respectively. Virtually all patients who were HBeAg positive at week 32 remained HBsAg positive throughout follow-up. Conclusion Early PEG-IFN induced HBeAg loss results in a high likelihood of HBsAg loss and may be associated with more profound viral suppression during the first 32 weeks of therapy in patients with added lamivudine.

Diabetes Mellitus after Liver Transplantation for Chronic Hepatitis C – Impact of Calcineurin Inhibition

B.J. Veldt [1,3], J.J. Poterucha[1], K.D.S. Watt[1], C.B. Rosen[2], J.K. Heimbach[2], M.R. Charlton[1],Mayo Clinic, Division of Gastroenterology and Hepatology[1] and Division of Transplantation Surgery[2], Rochester MN, USA, [3]Erasmus MC University Medical Center, Dept of Gastroenterology and Hepatology, Rotterdam, The Netherlands

Diabetes mellitus (DM) is a common and important complication of liver transplantation (LT). DM is particularly common among patients with hepatitis C virus (HCV) infection, in part due to the effects of HCV on insulin sensitivity. The impact of immunosuppression on DM, particularly the relative contribution of calcineurin inhibitor type and level, has been poorly defined in the setting of HCV. The aim of the study is to investigate the effect of immunosuppression type and level on the development of DM in LT recipients with HCV infection. We performed a prospective cohort study of consecutive LT recipients with HCV infection who underwent transplantation between 1995 and 2005. A total of 185 patients were studied. One hundred eighty-one patients were treated with steroids, 60 requiring steroid boluses for rejection. During a median follow-up of 4.5 years (inter quartile range 2.2-6.5), 47 (29%) patients who were treated with tacrolimus and 5 (20%) patients who were treated with cyclosporine developed diabetes mellitus (p=0.47). No correlation between tacrolimus trough levels or exposure and DM was seen. Patients who developed DM had a higher baseline BMI (31 versus 28 kg/m^2). Multivariate Cox regression analysis showed that pre-transplant glucose levels and mean steroid dose during the first month after transplantation were significantly associated with development of post-LT DM. In conclusion, no dose-dependent diabetogenic effect of tacrolimus was found at levels ranging between 5-15 ng/mL in patients transplanted for chronic HCV. Treatment of rejection with corticosteroid boluses is an important predictor of post-LT DM.

Clinical and basal aspects of anemia during antiviral therapy for hepatitis C

H. van Soest[1], W. Renooij[2], K.J. van Erpecum[1], Depts of Gastroenterology[1] and Surgery[2] University Medical Center Utrecht, Utrecht, The Netherlands

Anemia is a major side effect of therapy for chronic hepatitis C. We explored potential risk factors for and potential underlying mechanisms of anemia. 44 chronic hepatitis C patients were treated with amantadine hydrochloride 200 mg daily or placebo, in all cases combined with weight-based ribavirin (Schering Plough, Maarssen, The Netherlands: 1000-1200 mg/day) and interferon alfa-2b (Schering Plough) during 52 weeks. Anemia-related parameters including (in 17 pts) serum erythopoeietin levels were measured before and during treatment. Potential changes in membrane phospholipid composition of erythrocytes of patients on anti-viral treatment and potentially increased erythrocyte susceptibility to osmotic or bile salt induced stress were explored. Decrease of Hb after six months of therapy was 2.1±0.1 mmol/L (range -0.6-4.1) with evidence of hemolysis. In multivariate analysis, higher pre-treatment Hb, highest ribavirin dosing (15-17.5mg/kg) and lower pre-treatment platelet levels were independent risk factors for decrease of Hb. Serum erythropoietin levels increased significantly from 8 (5-48) mU/mL at baseline to 51 (13-326) mU/mL after 12 weeks and to 67 (7-1590) mU/mL after 24 weeks of treatment ($p<0.001$). Baseline levels of serum erythropoietin did not correlate with baseline levels of Hb. In contrast erythropoeietin levels at 12 and 24 weeks negatively correlated with simultaneous Hb ($r= –0.70$ and $r= –0.72$, $p=0.002$). Comparing normal human erythropoeietin response to anemia with response in our patients, no significant difference in slope of hematocrit versus logEPO was found. Erythrocyte membrane phospholipids composition did not differ between anemic patients and healthy controls. Also, resistance to osmotic or bile salt induced stress was normal in anemic patients. Phosphatidylserine exposure at the outer membrane leaflet did not change upon 24 hrs ex vivo incubation with pharmacological ribavirin concentration. Conclusions: Pre-treatment levels of thrombocytes and Hb and high ribavirin dosing are independent predictors of extent of anemia. Although we found hemolysis as contributing factor to anemia, membrane phospholipid composition is not altered by antiviral therapy. Although further studies are needed, serum erythropoeietin response to anemia induced by antiviral therapy appears normal.

Identifying transmission pairs in hepatitis B source and contact tracing: agreement of epidemiological and phylogenetic analysis in the multi-ethnic community of Rotterdam (2002-2005)

I.K. Veldhuijzen[1, 2], T.H. Mes[3], M.C. Mostert[1], Niesters[3], S.D. Pas[3]; J.J. Voermans[3], R.A. de Man[2], H.M. Götz[1], G.J. van Doornum[3], J.H. Richardus[1, 4], [1]GGD Rotterdam-Rijnmond, Cluster Infectieziektebestrijding, [2]Erasmus MC, Universitair Medisch Centrum, Afdeling Maag-, Darm- en Leverziekten, Rotterdam, [3]Erasmus MC, Universitair Medisch Centrum, Afdeling Virologie, Rotterdam, [4]Erasmus MC, Universitair Medisch Centrum, Afdeling Maatschappelijke Gezondheidszorg, Rotterdam, The Netherlands

Molecular and epidemiological data typically give different types of information on the transmission of hepatitis B virus (HBV). Because both types of information are important for public health, the congruence of HBV sequence and epidemiological data from acutely and chronically infected patients seen at a Municipal Public Health Service was assessed. Molecular clusters consisted of patients with identical sequences. Information from source and contact tracing was used to define epidemiological transmission pairs. We assessed the level of molecular support for epidemiologically defined transmission pairs using parsimony, by placing topological constraints during phylogenetic analyses in agreement with epidemiological information, and by taking the presence of polymorphic sites within patients into account.

HBV genotypes of 62 acute and 347 chronic HBV patients indicated that acute infections were predominantly with an endemic genotype (A2; 52%) and a non-endemic genotype (D; 32%). Chronic HBV infections largely involved non-endemic genotypes (A1, B, C, D and E). Interestingly, while genotype A2 was least variable, which is consistent with a frequent exchange of HBV in the homosexual community, genotype D comprised multiple divergent groups of closely related sequences. In total 15 clusters including 93 patients (2-39 patients per cluster) with identical sequences were identified. Six of these clusters included epidemiological transmission pairs. Epidemiological transmission pairs differed greatly in the level of molecular support. Of 22 epidemiological clusters, six could be refuted (three harbored multiple genotypes, three conflicted with the epidemiological data in constrained analyses), four clusters received support from the molecular analysis and the support for the remaining 12 was ambiguous. Two of the four epidemiological pairs that also received molecular support had diverged considerably (3 and 15 mutations respectively). This shows that levels of divergence cannot be simply used as an indicator of the likelihood that groups of sequences constitute transmission pairs. Instead, it is necessary to assess the likelihood of a common origin of individuals in supposed transmission groups given the variation in the local community. The combined approach of source and contact tracing and molecular epidemiology provides insight in the HBV transmission routes in a multi-ethnic community and allows a refinement of the identification of transmission pairs.

Etiology of Budd-Chiari Syndrome – The Role of Multiple Underlying Risk Factors

J. Hoekstra[1], S.D. Murad[1], A. Plessier[2], M. Hernandez-Guerra[3], E. Elias4, M. Primignani[5], M. Bahr[6], J. Heller[7], A. Hadengue[8], P. Langlet[9], H. Miranda[10], J.C. Garcia-Pagan[3], D.C. Valla[2], H.L.A. Janssen[1] for the European Network for Vascular Disorders of the Liver (EN-Vie), [1]Dept of Gastroenterology and Hepatology, Erasmus University Medical Center, Rotterdam, The Netherlands, [2]Dept of Hepatology, Hopital Beaujon, AP-HP, INSERM-U773 & University Paris-7, Clichy, France, [3]Hepatic Hemodynamic Laboratory, Liver Unit, Hospital Clinic, IDIBAPS and Ciberehd, Barcelona, Spain, [4]Liver Unit, Queen Elisabeth Hospital Birmingham, Birmingham, United Kingdom, [5]Gastroenterology and Gastrointestinal Endoscopy Unit, Ospedale Policlinico, Mangiagalli and Regina Elena Foundation, Milan, Italy, [6]Dept of Gastroenterology, Hepatology, and Endocrinology, Hannover Medical School, Hannover, Germany, [7]Dept of Internal Medicine I, University Hospital of Bonn, Bonn, Germany, [8]Division of Gastroenterology and Hepatology, Geneva University Hospitals, Geneva, Switzerland, [9]Dept of Hepatogastroenterology, Centre Hospitalier Universitaire Brugmann, Bruxelles, Belgium, [10]Liver Transplantation Unit, Hospital General Santo Antonio, Porto, Portugal

In many patients with Budd-Chiari Syndrome (BCS) an underlying risk factor for thrombosis is present. The aim of this study was to characterize the multifactorial etiology of BCS and evaluate the impact of combined thrombophilic risk factors on clinical presentation, complications and survival. From the EN-Vie Study, a prospective multi-center study of 163 patients with BCS, we obtained DNA and plasma for thrombophilia analysis, as well as data on etiologic factors, clinical characteristics, interventions and outcome. Furthermore, for 80 patients DNA samples were available from a healthy, age- and sex-matched control. In these two groups we compared the frequency of Factor V Leiden (FVL), Factor II (FII), MTHFR and JAK2 mutations. Median age at diagnosis of BCS was 38 years (range 16-83) and 43% of the cases was male. Prevalence of etiologic factors was as follows: myeloproliferative disorder 39%, antiphospholipid antibodies 25%, homozygous MTHFR mutation 15%, FVL 12%, protein C deficiency 4%, protein S deficiency 3%, antithrombin deficiency 3%, FII mutation 3%. Multifactorial etiology was present in 74 patients (46%); 2, 3 or 4 risk factors were found in 41, 30 and 3 cases, respectively. There were no significant differences in age, sex, Rotterdam prognostic score and clinical presentation between patients with and without multiple underlying risk factors. Furthermore, the presence of multifactorial etiology did not affect the severity of disease with respect to complications, need for invasive interventions and survival. Additional analysis in 80 case-control pairs showed that JAK2 mutation was present in 28% of cases whereas it was not detected in any controls. FVL was also associated with an increased risk of BCS (OR 3.7, 95%CI 1.0-13.9). FII and homozygous MTHFR mutation were less strongly related to BCS (OR 1.5, 95%CI 0.3-9.5 and OR 1.3, 95%CI 0.5-3.2, respectively). This was confirmed by the finding that in 20 of 21 patients (95%) with FII or homozygous MTHFR mutation another risk factor for BCS was present. Conclusions. In approximately half of the patients with BCS more than one etiologic factor can be identified. FII and homozygous MTHFR mutation are only minor risk factors for BCS and in most cases concurrent thrombophilic factors are present. Despite the importance of a complete screening for underlying causes, the presence of multiple risk factors does not influence clinical manifestations, treatment and short-term prognosis of BCS-patients.

Piecemeal endoscopic mucosal resection appears equally effective as, but associated with less morbidity than transanal endoscopic microsurgery for the treatment of large rectal adenomas

F.J.C. van den Broek[1], E. Dekker[1], E.J.R. de Graaf[2], W.A. Bemelman[3], P. Fockens[1], J.B. Reitsma[4], [1]Dept of Gastroenterology and Hepatology, [3]Dept. of Surgery, [4]Dept. of Clinical Epidemiology, Academic Medical Centre Amsterdam; and [2]Dept of Surgery, IJsselland Hospital, Cappelle a/d IJssel, The Netherlands

Large rectal adenomas are currently treated by either transanal endoscopic microsurgery (TEM) or piecemeal endoscopic mucosal resection (EMR). Piecemeal EMR appears to be associated with lower morbidity and costs; however, these advantages may become irrelevant if these treatments are not equally effective. The aims of this systematic review were to compare the effectiveness and safety of TEM vs. EMR for large rectal adenomas. Studies were included in this systematic review if they reported on recurrence; complications; length of hospital stay; and operating times of TEM and/or EMR for large rectal adenomas. Studies of adequate methodological quality were included. The proportion of patients with recurrence or complications was used as outcome parameter for random effects meta-regression analysis, comparing pooled proportions (±95%-CI) between EMR and TEM. Since EMR may require two attempts for complete resection, two recurrence rates were calculated: early and late recurrences (including or not including adenomas successfully re-treated with EMR within 3 months). In total, 39 studies were judged to be of adequate quality; 28 reported on TEM and 11 on EMR. No studies directly compared TEM to EMR. Only one EMR series gave transparent data on rectal adenomas only; all other EMR studies reported on colorectal adenomas without specifying colonic location. A total of 1,898 patients were included for analyzing complications and 2,657 for recurrence. The mean polyp size was 36mm (3-182) for TEM vs. 32mm (10-86) for EMR. The pooled estimates of the proportions of patients with early recurrence were 5.4% (3.7-7.7) for TEM vs. 12.7% (7.9-19.8) for EMR ($p=0.004$). Late recurrence rates were 3.4% (2.4-4.8) vs. 1.6% (0.7-3.7) respectively ($p=0.102$). The pooled estimate of complication rate after TEM was 10.3% (7.9-13.5) vs. 4.5% (2.8-7.2) after EMR ($p=0.002$). Mean number of days in hospital were 4.7 for TEM vs. 0.08 for EMR ($p=0.006$); mean operating times were 90 vs. 70 minutes, respectively ($p<0.001$).

Conclusion: This systematic review suggests that TEM and EMR are equally effective, when allowing EMR to be repeated for adenoma remnants after a first resection. Recurrence rates then were equal, while EMR was associated with significantly less complications, fewer in-hospital days, and shorter operating times. However, as large heterogeneity existed between included studies, a prospective randomized trial seems imperative to assess which treatment is more cost-effective.

Transanal Endoscopic Microsurgery for local resection of rectal tumours: Initial results in a university affiliated teaching hospital

B. Koebrugge, K. Bosscha, M.F. Ernst, Dept of Surgery, Jeroen Bosch Hospital,'s-Hertogenbosch, The Netherlands

Transanal Endoscopic Microsurgery (TEM) is a minimal invasive technique for the local resection of benign and stage T1 rectal carcinomas in high-risk patients, associated with lower morbidity and mortality rates than open surgery. It can also be used in a palliative setting with or without radiotherapy. We report our initial results using TEM in the first 105 patients. In 2002, TEM was introduced in our clinic, involving air insufflation to improve access and field of vision followed by endosurgical tumour resection. All patients undergoing TEM surgery for rectal adenoma or rectal carcinoma between May 2002 and December 2007 were included. We included 54 men and 51 women with a median age of 68 years old; 104 patients with curative intention, 1 patient in a palliative setting (stage T3 tumour; TEM combined with preoperative radiotherapy). Median distance from the tumour to the anal verge was 7 centimetres and median operating time was 90 minutes. Peroperatively, 10 perforations occurred, all in high ventral or lateral situated tumours. Because of perforation, tumoursize or tumour location, 6 operations were converted to (low) anterior resection. Median amount of tissue resected in TEM was 15 square centimetres. Postoperatively, staging revealed 77 stage T0 tumours, 22 stage T1 tumours, 5 stage T2 tumours and 1 T3 carcinoma. In 86% of patients, the margins were free of tumour, meaning tumour resection was radical. In 2 patients with a stage T1 tumour and 4 patients with a stage T2 tumour TEM was followed by a low anterior resection or abdomoperineal resection. In 1 patient with a non-radical stage T2 tumour no additional resection was performed on request of the patient. Postoperatively, 1 urinary tract infection and 1 pulmonary infection occured. Five patients suffered from urinary retention, atrial fibrillation or rectal bleeding. In 1 patient a late perforation occured on the fourteenth day after surgery leading to an abdominoperineal resection. (complication rate 7,6%) Median length of stay in our hospital was 4 days. Post-operatively, patients returned to their own specialist in referring hospitals for follow up. At this moment 7 recurrences occurred (6,7%); 1 carcinoma after radical T1 carcinoma, 1 adenoma after non-radical T0 adenoma and 5 adenomas after radical T0 adenoma.
In conclusion, TEM is a safe curative operating technique for benign T0 and stage T1 rectal tumours in selected patients, with low morbidity and recurrence rates.

The gut releases taurine under post-absorptive circumstances

M.F.M. van Stijn[1,2], G.C. Ligthart-Melis[2], M.A.R. Vermeulen[1], L.N. Wong[2], M.P.C. Siroen[2], M.P. van den Tol[2], A.P.J. Houdijk[1], P.A.M. van Leeuwen[2], [1]Medical Center Alkmaar, Alkmaar, the Netherlands; surgical Dept [2]VU University Medical Center, Amsterdam, The Netherlands; surgical Dept

Taurine (Tau), an amino acid, plays a role in numerous biological processes, such as anti-oxidation, detoxification, osmoregulation, membrane stabilization and bile acid conjugation. During pathological conditions, such as surgical injury, sepsis and cancer, the plasma level of Tau decreases immensely. When glutamine (Gln) is given to trauma patients, infectious morbidity reduces, and surprisingly the plasma level of Tau rises. Still, information about human Tau metabolism under physiological circumstances is scarce and how it relates to Gln is unknown. In order to uncover the Tau metabolism under post-absorptive circumstances, we studied organ fluxes and fractional extraction (FE; uptake/availability) rates of Tau and Gln of the portally drained viscera (PDV; representing the gut), liver and kidneys. The current study included 17 patients who underwent elective abdominal surgery. During surgery, just after entering the abdominal cavity, flow of the hepatic artery, portal vein and right renal vein was measured by Duplex and blood samples were taken from the arterial line, portal vein, hepatic vein and right renal vein. Net Tau and Gln fluxes, and net FE rates were calculated using the flow measurements and Tau or Gln concentrations of the different blood vessels. The results of the fluxes of Tau showed a net release of Tau by the PDV ($p=0.039$), represented by a negative Tau flux, while the liver ($p=0.124$) and kidneys showed neither uptake nor release. Net FE of Tau by the PDV was absent ($p=0.039$). No significant results were found with regard to the FE of Tau by the liver and kidneys. No correlation between Gln and Tau was observed with regard to the fluxes ($r=0.53$, $p=0.029$) and FE ($r=0.52$, $p=0.032$) of the kidneys.

Conclusion: It is known that the kidneys have a regulatory role in Tau metabolism, mainly by excretion/re-absorption. This was not observed in the present study. However, we observed that, under post-absorptive circumstances the gut releases Tau. Although we did not observe uptake of Tau by the liver, it can be suggested that the gut is a mediator within the entero-hepatic circle or that the gut itself releases Tau.

What is the value of a CT-scan in diagnosing a clinically relevant anastomotic leakage after a colon resection with a primary anastomosis?

M.N.G.J.A. Braat[1], R.M.P.H. Crolla[2], L. van der Laan[2], [1]UMCU Utrecht, [2]Amphia Ziekenhuis, Breda, The Netherlands

The symptoms associated with anastomotic leakage after a colon resection are often atypical. Early detection and early reintervention are crucial to improve the patient's prognosis. In the current practise CT-scan (preferably with intravenous and rectal contrast) is the most commonly used imaging study to detect a leakage, thus largely replacing barium enemas. This retrospective study was done to determine the durability of the CT-scan to detect clinically relevant leakage after a primary colon anastomosis in the present everyday clinical practise. A prospective database of 456 patients with a colon resection and primary anastomosis (January 2006 – December 2007) was replenished with the data of postoperative CT-scans. The CT-scans were requested on clinical demand, when anastomotic leakage was suspected or to exclude or confirm another diagnosis. There was no limit to the interval between the operation and CT-scan. The recorded information included the presence of free fluid, free air, abscesses and leakage of rectal contrast. The CT-scan was positive if the radiologist and/or surgeon considered the image suggestive for a relevant anastomotic leakage. An anastomotic leakage was defined as clinically relevant if reoperation was required. In 40 patients an anastomotic leakage requiring reoperation was identified (8,8%). In 20 patients the decision to reoperate was based on clinical grounds and no CT scan had been made. In 78 patients a CT-scan was performed. In 15 cases the scan was considered positive. At reoperation only 10 of these cases showed a leakage. The remaining 63 CT-scans weren't suggestive for leakage. Yet in 10 patients a leakage was identified when a reoperation was nevertheless decided upon and performed. These results correspond with the following positive and negative predicting value, respectably 67% and 84% (sensitivity 50%, specificity 91%).Furthermore a non-significant delay to reoperation was observed when the CT-scan was negative (3,2 days) compared to a positive CT-scan (0,4 days). The only sign seen significantly more in patients with a relevant leakage was free air (p=0,001). In 16 cases an abscess was diagnosed and treated with radiological intervention. In conclusion the CT scan has a low sensitivity for detection of anastomotic leakage. So the CT scan may be misleading in detection of anastomotic leakage which can lead to a delayed relaparotomy. The CT scan gives information about alternative causes like an abscess.

The Dutch multicentre experience of the Endo-Sponge treatment of anastomotic leakage after colorectal surgery

P.J. van Koperen[1], M.I. van Berge Henegouwen[1], C. Rosman[2], C.M. Bakker[3], P. Heres[4], W.A. Bemelman[1], [1]Dept of Surgery, Academic Medical Centre, Amsterdam, [2]Dept of Surgery, Canisius Wilhelmina Hospital, Nijmegen, [3]Dept of Gastroenterology, Atrium Medical Centre, Heerlen, [4]Dept of Surgery, Waterland Hospital, Purmerend, The Netherlands

Anastomotic leakage is a feared complication following colorectal surgery, which is associated with early and long term morbidity and mortality. The negative pressure of the endo-sponge results in constant drainage and potentially infection control, reduction of the size of the cavity, increased blood flow and therefore stimulation of granulation tissue. The aim was to assess the effectiveness of endo-sponge (B-Braun Medical) treatment of the presacral sinus associated with anastomotic leakage in the Netherlands.In total 18 patients (M:F=8:10) with a median age of 62 years (range 17-82) that had undergone colorectal surgery for rectal cancer (n=14) or ulcerative colitis (n=4) and endosponge treatment of anastomotic leakage were identified. This was endoscopically managed by transanal placement and frequent replacement of the endo-sponge. Definitive resolution of the sinus was achieved in 7 out of 8 patients (88%) in the group that started within six weeks of surgery compared to 5 out of 10 patients in the group that started later. Closure was achieved in 45 days (range 14-90) with a median of 14 sponge replacements (range 3-17).The endo-sponge placement might prevent a chronic presacral sinus. Early endo-sponge treatment seems to be more effective than late treatment of the presacral sinus.

Local recurrence is no longer the main problem in rectal cancer with optimal multidisciplinary management

W. Truin[1], J.G. Bloemen[1], S.M.E. Engelen[1], R.G. Jansen[2], G. Lammering4, R.G.H. Beets-Tan[3], G.L. Beets[1], [1]Dept of Surgery, [2]Dept of Internal Medicine, [3]Dept of Radiology, Maastricht University Medical Centre, Maastricht, [4]Maastro Clinic, Maastricht, The Netherlands

The last decade major changes have been made in the treatment of rectal cancer, with the main focus on improvement of local control. Since the introduction of neoadjuvant treatment consisting of short-term radiotherapy or chemoradiotherapy together with total mesorectal excision surgery, the local recurrence (LR) rate has reduced significantly. Routine preoperative magnetic resonance imaging (MRI) and multidisciplinary management can lead to further optimization of surgical outcome. Since 2001 this multimodal treatment has become standard practice in our hospital. The aim of this study was to investigate the effect of this multidisciplinary approach upon local recurrence rate. All patients with a primary resectable adenocarcinoma of the rectum operated on in our hospital between January 1998 and December 2005 were reviewed. To obtain a group of patients that can be compared to the population seen by a general hospital, only patients from within our own catchment area were included. Data about preoperative imaging, neoadjuvant and surgical treatment and local recurrences were collected. Two groups were defined; group I served as historical control and these patients were operated on between 1998-2000; group II included patients operated on between 2001-2005. Differences were tested statistically using a Chi square test. In total 271 patients (159 men, 112 women), with a median age of 68 (35-96) years were included. Group I (n=102) and group II (n=169) did not differ significantly with respect to tumor stage. The local recurrence rate in group I was 12,7% and in group II 2,4%. According to the Cox proportional hazard analysis patients in group II developed significantly less local recurrences as compared to group I (HR 0.275, CI 0.096-0.782, p=0.016). The interval between surgery and LR was 764 (171-2180) days. Use of preoperative MRI increased from 46,1% to 82,2% in group I and II, respectively (p<0.001). In group I 5,9% received neoadjuvant treatment compared to 63,9% in group II (p<0.001).
In conclusion, the incidence of local recurrences in patients with rectal cancer operated in our center has decreased dramatically since the introduction of a multidisciplinary approach. Optimal local control is most likely achieved through a combination of preoperative MRI, neoadjuvant treatment and optimal surgical technique. The focus of rectal cancer treatment should now be directed towards early detection and treatment of distant metastases.

Factors associated with success and complication rate of colonic stenting

J.J. Driest, M. Ledeboer, M. Eeftinck Schattenkerk[1], E.J. Kuipers[2], F. ter Borg , Dept of Gastroenterology and [1]Gastrointestinal surgery, Deventer ziekenhuis and [2]Eramus Medical Center Rotterdam, The Netherlands

Self-expandable metal stents (SEMS) are used to relieve colon obstruction. Expert series report high success and low complication rates, but widespread implementation has been hampered by failures and safety considerations.Many experts believe that operator experience, localisation of the stenosis, cause and severity of the obstruction play a crucial role in success and complication rate (like perforation), but data supporting these presumptions are scarce. We investigated these associations in our database, consisting of 113 prospectively collected endoscopic SEMS procedures since 1999.Factors of potential influence that were analysed were: age; sex; the year in which SEMS placement took place (indicating collective experience in our hospital); the presence or absence of an ileus; the anatomical localisation of the obstruction and the type of obstruction (benign cause, colon carcinoma, or extrinsic malignant compression). Data were analysed using Chi-Square statistics and checked for interdependent associations using multivariate logistic regression analysis. We analysed 113 procedures. None of the above mentioned variables were significantly associated with the risk of clinical failure or complications. The chance of successful stent placement was only influenced by the type of obstruction: in benign stenoses only 3 of 6 procedures were clinically successful, ($p < 0.0005$) and none of 4 SEMS placements for obstructions caused by carcinomas from another organ had clinical success, p (< 0.0005).
Conclusions: in contrast with general belief, we could not find evidence that collective in-hospital experience, the presence of ileus, or the anatomical localisation of the tumour influenced the success or complication rate after SEMS placement. Benign obstructions and obstructions caused by extrinsic malignant compression were clearly associated with SEMS failure.

Foreign body ingestion: Management in childhood

T.E. Matthews, J.A. Taminiau, M.A. Benninga, M.M. Tabbers, B.G. Koot, A. Kindermann , Dept of Pediatric Gastroenterology, Emma Children`s Hospital, Academic Medical Center Amsterdam, The Netherlands

IntroductionIngestion of foreign bodies (FB) is a common paediatric problem. Usually ingestion is uncomplicated and does not require medical intervention. But complications as respiratory symptoms, gastro-intestinal obstruction, perforation and penetration are reported. Management of foreign body ingestion varies and is not standardized. MethodsRetrospectively, we analysed data from children presenting after ingestion of a FB at our Dept of paediatric gastroenterology between 1981 and 2008. Data extracted included age, gender, nature of FB, location, presenting symptoms, investigations and interventions, complications and mortality. ResultsIn total data from 113 patients were analysed of which 68% were boys, with ages between 6 months and 17 years (mean 5,1 years). Eighteen patients (16%) suffered from an underlying disease such as mental retardation (4), oesophageal atresia (11), eosinophilic oesophagitis (2) and peptic stenosis (1). The most common ingested FB were coins (46%) followed by sharp objects (16%), food (15%), batteries (7%), toys (7%) and others (9%).At presentation 43% were located in the stomach, 19% in the proximal oesophagus, 15% mid oesophageal and 9% in the distal oesophagus. In 14% of the cases the FB had passed the pylorus.52% of children had no symptoms at presentation depending on the location of FB (10% in the oesophagus, 73% in the stomach and 87% which had passed the stomach). Most common symptoms were retrosternal pain (16%), vomiting (13%), excessive saliva production (8%), food refusal (7%) and respiratory problems (4%).Upper endoscopy was performed in 97/113 (86%). In 83 patients the FB was found at the primary location, 25% had erosions and/or ulcerations and 71% had no abnormalities. Two patients suffered from oesophageal perforation due to coins ingested weeks ago. In one case surgical intervention was necessary to remove the FB. There was no mortality. Conclusions: Rapid endoscopic removal is indicated if the FB is located in the oesophagus. Endoscopic abnormalities were only seen in 29% of all patients and were more severe if the FB were ingested weeks ago. Our data support an “wait and observe” policy in case the FB has passed the oesophagus spontaneously.

Gastrointestinal Bleeding in Patients with Budd-Chiari Syndrome: a Prospective Evaluation

J. Hoekstra[1], S.D. Murad[1], A. Plessier[2], M. Hernandez-Guerra[3], E. Elias[4], M. Primignani[5], Matthias J. Bahr[6], J. Heller[7], A. Hadengue[8], P. Langlet[9], H. Miranda[10], J.C. Garcia-Pagan[3], D.C. Valla[2], H.L.A. Janssen[1] for the European Network for Vascular Disorders of the Liver (EN-Vie), [1]Dept of Gastroenterology and Hepatology, Erasmus University Medical Center, Rotterdam, The Netherlands, [2]Dept of Hepatology, Hopital Beaujon, AP-HP, INSERM-U773 & University Paris-7, Clichy, France, [3]Hepatic Hemodynamic Laboratory, Liver Unit, Hospital Clinic, IDIBAPS and Ciberehd, Barcelona, Spain, [4]Liver Unit, Queen Elisabeth Hospital Birmingham, Birmingham, United Kingdom, [5]Gastroenterology and Gastrointestinal Endoscopy Unit, Ospedale Policlinico, Mangiagalli and Regina Elena Foundation, Milan, Italy, [6]Dept of Gastroenterology, Hepatology, and Endocrinology, Hannover Medical School, Hannover, Germany, [7]Dept of Internal Medicine I, University Hospital of Bonn, Bonn, Germany, [8]Division of Gastroenterology and Hepatology, Geneva University Hospitals, Geneva, Switzerland, [9]Dept of Hepatogastroenterology, Centre Hospitalier Universitaire Brugmann, Bruxelles, Belgium, [10]Liver Transplantation Unit, Hospital General Santo Antonio, Porto, Portugal

Obstruction of the hepatic veins or inferior vena cava, defined as Budd-Chiari Syndrome (BCS), often leads to portal hypertension. Bleeding from gastroesophageal varices is an important complication of portal hypertension. However, little is known about the characteristics of gastrointestinal (GI) bleeding in patients with BCS. Therefore, the aim of this study was to evaluate the type, frequency and outcome of GI-bleeding in these patients. We studied 163 BCS-patients that were prospectively included in the EN-Vie Study, a multi-center European study. At baseline and during follow-up, data was collected on clinical characteristics, episodes of GI-bleeding, complications and survival. Median age at diagnosis of BCS was 38 years (range 16-83), 43% of the patients was male and median follow-up period was 17 months (range 0.1-31). During the study period, a total of 40 bleeding episodes occurred in 24 patients (15%). In 8 patients (5%), GI-bleeding was present at diagnosis. Of the other patients, a first bleeding event occurred within the first year of follow-up in 12 patients and after 1 year in 4 patients. Nine patients (38%) experienced recurrent bleeding, of which five patients had more than two events. Compared to patients without bleeding (n=139), patients that experienced an episode of bleeding were more often males (63% vs. 40%, p=0.036) and had a higher frequency of concurrent portal vein thrombosis (32% vs. 14%, p=0.042). Of all events, 50% was caused by bleeding from gastroesophageal varices or portal hypertensive gastropathy. Other causes of bleeding were ischemic enterocolitis, ulcerative colitis and gastric antral vascular ectasia. All patients that bled from esophageal varices (n=9) were treated with endoscopic band ligation or sclerotherapy. In one of these patients, failure to control bleeding was an indication for a transjugular intrahepatic portosystemic shunt (TIPS). Two patients (8%) died as a result of GI-bleeding. Baseline Rotterdam prognostic score did not differ significantly between patients with and without GI-bleeding (1.29 vs. 1.26, p=0.868). Conclusions. GI-bleeding occurs as a presenting symptom in 5% of BCS--patients and in another 10% during short-term follow-up. Patients with additional portal vein thrombosis appear to be more prone to bleeding complications. Most cases of bleeding in BCS are related to portal hypertension but other causes should also be explored, especially since many patients will use anticoagulation.

Randomised double-blind controlled trial evaluating elective laparoscopic appendectomy for chronic right lower abdominal quadrant pain

R.M.H. Roumen[1], R.P.R. Groenendijk[2], C.E.J. Sloots[1],K.E.S. Duthoi[3], M.R.M. Scheltinga[1], C.M.A. Bruijninckx[1], Depts. of Surgery[1] and Pathology, Stichting [3]PAMM Máxima Medisch Centrum, Veldhoven, The Netherlands

Background: It is questionable whether elective appendectomy can effectively reduce pain in persistent or recurrent right lower abdominal quadrant pain due to chronic or recurrent appendicitis. Methods: A single centre randomised double-blind sham surgery controlled clinical trial studied the effects of elective laparoscopic appendectomy on postoperative pain perception in selected patients with persistent or recurrent lower abdominal quadrant pain on abdominal pain level at 6 months postoperatively. Secondary outcome was the relation between clinical response and the appendix' histopathology. The analysis was performed on an intention-to-treat basis. Pain scores were compared using a Fisher's exact test. Results: Forty patients were randomised, 18 patients had a laparoscopic appendectomy and 22 patients had a laparoscopic inspection only. The postoperative pain scores were significantly different favouring appendix removal ($p < 0.01$). Relative risk calculations indicated a 2.4 fold (95% CI: 1.3 – 4.0) greater chance of improving or becoming pain free after laparoscopic appendectomy. The number needed to treat was 2.2 patients (95% CI: 1.5 – 6.5). However, there was no significant relation between postoperative pain scores and histopathology findings. Conclusions: Chronic or recurrent appendicitis is a realistic clinical entity that can be treated successfully by elective appendectomy leading to significant pain reduction in properly selected cases. Histopathology of the removed appendix does not contribute to the diagnosis.

Prognosis of 375 Ursodeoxycholic Acid-Treated Patients With Primary Biliary Cirrhosis. A Follow-up to 17-Yrs

E.M.M. Kuiper[1], B.E. Hansen[2], R.A. de Vries[3], J.W. den Ouden-Muller[4], Th.J.M van Ditzhuijsen[5], E.B. Haagsma[6], M.H.M.G. Houben[7], B.J.M. Witteman[8], K.J van Erpecum[9], H.R. van Buuren[1] for the Dutch PBC study group., [1]Dept of Gastroenterology and Hepatology and [2]Dept of Epidemiology and Biostatistics, Erasmus University Medical Center, Rotterdam, [3]Dept of Gastroenterology and Hepatology, Rijnstate Hospital, Arnhem, [4]Dept of Internal medicine, Sint Franciscus Gasthuis, Rotterdam, [5]Dept of Internal medicine, Jeroen Bosch Hospital, Den Bosch, [6]Dept of Gastroenterology and Hepatology, University Medical Center Groningen, [7]Dept of Gastroenterology and Hepatology, Haga Hospital, Den Haag, [8]Dept of Gastroenterology and Hepatology, Hospital Gelderse Vallei, Ede, [9]Dept of Gastroenterology and Hepatology, University Medical Center Utrecht, The Netherlands

Background and Aims: The only accepted medical treatment for patients with Primary Biliary Cirrhosis (PBC) is Ursodeoxycholic Acid (UDCA). However, only few data on the long-term prognosis of UDCA treated patients are available and the benefit of this treatment remains controversial. The aim of this study was to compare observed survival of UDCA treated PBC patients in our cohort to the survival predicted by the Mayo risk score (MRS) and to survival of a matched control cohort of the Dutch population. Furthermore, independent risk factors of impaired survival were determined. Methods: Prospective, multicenter cohort study. Inclusion criteria were established PBC, UDCA-therapy at doses of 13-15mg/kg/day. Exclusion criteria were Child Pugh class B or C, AIH/PBC overlap syndrome or immunosuppressive drugs. The main endpoint was survival free of orthotopic liver transplantation (OLT). Results: Three hundred seventy-five patients (89% women, mean age 54 yrs) were included. Mean follow-up was 10 yrs (118 months ± SD53). We observed 22 OLT's, 26 liver related deaths and 43 non-liver related deaths. In multivariate analysis elevated bilirubin (≥1ULN), decreased albumin (≤1LLN), age and cirrhosis before start of UDCA were independent risk factors significantly ($p<0.001$) associated with survival. OLT-free survival in patients with normal bilirubin and albumin serum levels at entry (n=244) was significantly improved compared to survival predicted by the MRS ($p<0.001$). Their prognosis was comparable to that of a matched sample of the Dutch population ($p=0.179$). Survival of patients with abnormal bilirubin and/or albumin at entry was not better than predicted by the MRS. Conclusions: Serum bilirubin and albumin levels allow easy identification of UDCA treated PBC patients with an excellent prognosis. For patients with normal bilirubin and albumin levels observed survival is significantly improved compared to survival predicted by the Mayo model. This suggests a therapeutic effect of UDCA in early PBC.

Non-polypoid colorectal neoplasms: clinico-pathological features in a Dutch population

M. van der Valk[1], E. Rondagh[1], A. de Bruïne[2], A. Masclee[1], S. Sanduleanu[1], [1]Dept of Gastroenterology and Hepatology, [2]Dept of Pathology, Maastricht University Medical Center, The Netherlands

It is widely accepted that the majority of colorectal cancers develop through polypoid growth. Emerging evidence indicates that non-polypoid colorectal neoplasms (NP-CRNs), known as flat lesions, also contribute to the development of colorectal cancer. These lesions are difficult to detect during routine colonoscopy. Moreover, it has been suggested that NP-CRNs are associated with a more aggressive behavior than polypoid colorectal neoplasms (P-CRNs). Most data originate from Japan, and so far, there are only a few studies to reflect the Western experience. Our aim was, to compare the clinico-pathological features of NP-CRNs and P-CRNs in a prospective, case-control study. All endoscopists at our center were trained to recognize NP-CRNs, by systematic sessions including video training. CRNs were classified according to the Paris classification. Selective chromoendoscopy was used to clarify the borders of NP-CRNs before endoscopic removal. According to size, lesions were categorized as diminutive (<6mm), small (6-9mm) and large (>9mm). Starting from August 2007, clinico-pathological data are prospectively collected from all NP- and P-CRNs. Here we report the first results of this ongoing study, comparing data from 90 NP-CRNs (60 patients) and 94 P-CRNs (53 patients). Both groups underwent colonoscopy for screening, surveillance or GI symptoms. Of the NP-CRNs, 95% were slightly elevated, 2% were completely flat and 3% were slightly depressed. NP-CRNs did not differ from P-CRNs with regard to: i) demographic characteristics (median age: 65.0 vs. 65.0 years; gender: 58.3% vs. 56.6% males); ii) distribution of size; and iii) prevalences of tubular, (tubulo)villous, serrated adenomas and hyperplastic polyps. Of the 124 adenomas found, 61 were NP-adenomas and 63 were P-adenomas. In contrast to P-adenomas, NP-adenomas were characterized by: i) more frequent location in the proximal colon: 41 (67.2%) vs. 28 (44.4%), p=0.011; and ii) significantly higher prevalence of high-grade dysplasia (HGD): 19 (31.1%) vs. 9 (14.3%), p=0.025. Moreover, HGD was significantly more common in diminutive NP-adenomas than diminutive P-adenomas: 7 (22.6%) vs. 1 (2.9%), p=0.014.
Conclusion: Non-polypoid colorectal neoplasms are commonly observed by trained endoscopists during routine colonoscopy. NP-adenomas harbor significantly more frequently HGD than P-adenomas. Our findings underline the importance of clinical awareness and training to recognize and adequately remove such lesions.

Stepwise circumferential and focal radiofrequency ablation of Barrett esophagus with early neoplasia: first European multi-centre trial

R.E. Pouw[1], K. Wirths[2], P. Eisendrath[3], C.M. Sondermeijer[1], F.J. Ten Kate[4], P. Fockens[1], J. Devière[3], H. Neuhaus[2], J.J. Bergman[1],[1]Gastroenterology, Academic Medical Center, Amsterdam, The Netherlands, [2]Internal Medicine, Evangelisches Krankenhaus, Düsseldorf, Germany, [3]Gastroenterology, Erasme University Hospital, Brussels, Belgium, [4]Pathology, Academic Medical Center, Amsterdam, The Netherlands

Stepwise circumferential and focal radiofrequency ablation (RFA) of Barrett esophagus (BE) with high-grade dysplasia (HGD) or early cancer (EC) +/- prior endoscopic resection (ER) of visible lesions has been proven safe and effective in single-centre studies. Study aim was to assess safety and efficacy of this new treatment modality in a European multicentre setting. Eligible patients had BE <12cm with HGD/EC; visible lesions were removed with the cap or multiband mucosectomy (MBM) technique. Excl. criteria were signs of submucosal invasion or N+ disease on EGD or EUS, and EC in the BE after ER prior to ablation. Primary balloon-based circumferential ablation (CA) was performed 6 wks after any ER, followed every 2 months by secondary focal ablation (FA). Two months after the last treatment eradication of dysplasia and intestinal metaplasia (IM) was assessed with EGD (NBI) and 4Q/1cm biopsies. 24 pts (19M, median age 65 yrs, median Prague C5M7) were included. In 22 patients 24 ERs were performed prior to CA (11 cap, 12 MBM, 1 ESD; 9 en-bloc, 15 piecemeal). Worst ER-histology/patient: 16 EC, 6 HGD. Worst residual histology prior to RFA: 11 HGD, 9 LGD, 4 IM. Complete eradication of dysplasia was achieved in 23/24 patients (96%) after 1 CA and a median of 1.5 (IQR 1-2) FA's, and additional ER in 2 patients. In one patient with very poor healing after initial CA, further RFA treatment was ceased (protocol failure). In 4 patients a non-transmural laceration occurred during CA at the level of prior ER; none required treatment or caused complaints. One patient presented with melena 2 weeks after FA, on EGD no active bleeding was seen, 2 visible vessels in the ablated area were preventively clipped. One patient with widespread prior ER and a mucosal laceration after CA developed dysphagia, resolved with endoscopic dilation. After median FU of 13 (IQR 11-15) months no dysplasia recurred. In one patient a 1 mm isle of IM was observed at the upper end of the initial C9M10 BE at 16 months FU that had probably been missed at preceding endoscopies and was therefore not treated sufficiently. None of 456 biopsies from neosquamous epithelium showed subsquamous IM.
Conclusion: Preliminary data of this first European multicentre study on stepwise CA and FA of BE with HGD/EC +/- prior ER suggest that this new treatment modality effectively removes dysplasia and IM, without serious adverse events, and therefore compares favorably to esophagectomy, radical ER or PDT.

HLA-DQ typing of extra-intestinal T-cell lymphomas: evidence for an association with undiagnosed coeliac disease?

J.M.W. van de Water[1], S.A.G.M. Cillessen[2], W.H.M. Verbeek[1], L.R. de Baaij[2], J.J. Oudejans[2], C.J.L.M. Meijer[2], C.J.J. Mulder[1], M.W.J. Schreurs[2], [1]Dept of Gastroenterology and Hepatology and [2]Dept of Pathology, VU University Medical Centre, Amsterdam, The Netherlands

Enteropathy associated T-cell lymphoma (EATL) is associated with adult coeliac disease (CD) and represents the main cause of death in CD patients. Although CD is a common disease (prevalence 0.5%-1% in Western countries), the diagnosis is frequently missed. Consequently, it may be expected that some extra-intestinal T-cell lymphomas, including systemic anaplastic large cell lymphoma (ALCL) are in fact CD-associated. In that case, the frequency of HLA-DQ2 and/or HLA-DQ8 would exceed the 40%, found in the general Caucasian population, and would approach the 98%, observed in CD patients.ALCL can be divided in a systemic and a primary cutaneous subtype. Systemic ALCL can be further subdivided in an anaplastic lymphoma kinase (ALK) expressing type, which has an excellent prognosis, and an ALK-negative type, with a heterogeneous prognosis. Most EATLs are ALK negative and similar to ALCL express CD30. In this study we investigated if the frequency of HLA-DQ2 and/or DQ8 in ALK-positive and –negative ALCL was significantly higher than in the general population. Therefore, genomic DNA was isolated from lymphoma cryosections and DQA1 and DQB1 alleles were amplified using PCR. HLA-DQ typing was subsequently performed using a single strand conformation polymorphism / heteroduplex based method. So far, 16 anaplastic large-cell T-cell lymphomas have been HLA-DQ typed. Nine of these lymphomas (56%) were HLA-DQ2 and/or DQ8 positive, which is a slightly higher prevalence than in the general population. HLA-DQ2 was present in 7 lymphomas, of which 1 was homozygous. HLA-DQ8 was present in 3 samples, all heterozygous. Of all HLA-DQ2 and/or DQ8 positive lymphomas, 89% did not express ALK.
Conclusion: The prevalence of HLA-DQ2 and/or DQ8 observed in the lymphomas approached the 40% found in healthy controls, suggesting that there is not a strong association between extra-intestinal T-cell lymphomas and CD. However, the number of specimens analysed so far is small and currently increased in order to reach a definitive conclusion.

The prognostic value of alarm symptoms for developing chronic abdominal pain in children presenting with abdominal pain in general practice

R.E. Bax, Y. van Leeuwen, M.Y. Berger, Dept of General Practice, Erasmus MC – University Medical Center, Rotterdam, The Netherlands

Abdominal pain is a common pediatric problem in general practice. Short weight, rectal blood loss, vomiting, diarrhea, fever, right upper or right lower quadrant pain and family history of inflammatory bowel disease are believed to be alarm symptoms for underlying disease. Little is known about their epidemiology in general practice. The objective of this study was to estimate the prevalence of alarm symptoms related to chronic gastrointestinal disorders in children presenting with abdominal pain to their general practitioner (GP) and to evaluate whether these alarm symptoms predict the prognosis of abdominal pain. In addition we investigated the association of alarm symptoms with a decreased BMI after 12 months follow-up. We performed a prospective cohort study between May 2004 and March 2006. All consecutive children aged 4-17 years consulting their GP for a new episode of abdominal pain were eligible to participate. At 3 and 12 months follow-up a questionnaire was send and the electronic medical files of all children were checked. Alarm symptoms at baseline were related to chronic abdominal pain as defined by von Baeyer at baseline and 3 and 12 months and to a decreased BMI at 12 months. In total 306 children, mean age 8.3 years (SD 2.95), with a new episode of abdominal pain were included. At baseline, 154 (50.3%) children had chronic abdominal pain and 162 (52.9%) children had one or more alarm symptoms. After one year 103 children (36.4%) had a decreased BMI. Short weight predicted the presence of chronic abdominal pain after one year (odds ratio 11.00, 95% CI 1.64-73.84) and fever decreased the risk of chronic abdominal pain at inclusion (odds ratio 0.43, 95% CI 0.22-0.85). No statistical significant relation was found with alarm symptoms and decreased BMI, but chronic abdominal pain at presentation predicted a decreased BMI.
Conclusion: Alarm symptoms are frequent in children with abdominal pain. Short weight was the only alarm symptom associated with chronic abdominal pain one year after first presentation at a GP. None of the alarm symptoms was related to decreased BMI. The relation between chronic abdominal pain at baseline and a decreased BMI after one year needs further evaluation.

Patients With Early PBC Predominantly Die From Non-Liver Related Causes

E.M.M. Kuiper[1], B.E. Hansen[2], R.A. de Vries[3], J.W. den Ouden-Muller[4], Th.J.M van Ditzhuijsen[5], E.B. Haagsma[6], M.H.M.G. Houben[7], B.J.M. Witteman[8], K.J van Erpecum[9], H.R. van Buuren[1] for the Dutch PBC study group, [1]Dept of Gastroenterology and Hepatology and [2]Dept of Epidemiology and Biostatistics, Erasmus University Medical Center, Rotterdam, [3]Dept of Gastroenterology and Hepatology, Rijnstate Hospital, Arnhem, [4]Dept of Internal medicine, Sint Franciscus Gasthuis, Rotterdam, [5]Dept of Internal medicine, Jeroen Bosch Hospital, Den Bosch, [6]Dept of Gastroenterology and Hepatology, University Medical Center Groningen, [7]Dept of Gastroenterology and Hepatology, Haga Hospital, Den Haag, [8]Dept of Gastroenterology and Hepatology, Hospital Gelderse Vallei, Ede, [9]Dept of Gastroenterology and Hepatology, University Medical Center Utrecht, The Netherlands

Background and Aims: Ursodeoxycholic acid (UDCA) may have a beneficial effect in primary biliary cirrhosis (PBC), particularly in the early stages. If UDCA delays disease progression and prevents end-stage liver disease, death from liver related causes should be uncommon. To test this hypothesis we analyzed the causes of death of patients on long-term UDCA treatment. A secondary aim was to assess the incidence of HCC during long-term UDCA treatment. Methods: Prospective, multicentre cohort study. Inclusion criteria were established PBC, UDCA-therapy 13-15mg/kg/day. Exclusion criteria were Child Pugh class B or C, AIH/PBC overlap syndrome or immunosuppressive drugs. Endpoint was liver transplantation or death. According to serum bilirubin and albumin levels at entry, PBC was classified as early (both bilirubin and albumin normal), moderately advanced (one parameter abnormal) or advanced (both abnormal). Results: Age and sex were comparable for the three PBC stages. Liver related death/-transplantation occurred significantly more often in advanced PBC compared to early PBC ($p<0.001$). After 15 yrs, in 84% of patients with early PBC who died the cause was not liver related. The actuarial 15-yr-risk for HCC in early and moderately advanced PBC was 0.6% and 11.4%, resp. Female/male ratio was 3:1.
Conclusions: UDCA treated patients with early PBC predominantly die from non-liver related causes. This may be explained by therapeutic effects of UDCA, but more prolonged follow-up is necessary to confirm this finding. Given the high incidence of HCC in patients with moderately advanced PBC, surveillance for this tumor could be considered in this subgroup.

Is gluten challenge really necessary for the diagnosis of coeliac disease in children under the age of two years?

V.M. Wolters[1], C.M.F. Kneepkens[2,4], C.F.M. Gijsbers[3], J.J. Schweizer[2,4], M.A. Benninga[7], R.H.J. Houwen[1], Depts of Paediatric Gastroenterology, University Medical Centre, Utrecht[1], VU Medical Centre, Amsterdam[2], Paediatric Gastroenterology, Juliana Children's Hospital/ Haga Teaching Hospital, The Hague[3], Paediatric Gastroenterology, Leiden University Medical Centre, Leiden[4], Paediatric Gastroenterology, Academic Medical Centre, Amsterdam[5], The Netherlands

IntroductionIn the diagnosis of coeliac disease (CD) gluten challenge is recommended for children under the age of two years at initial biopsy.ObjectiveTo investigate the diagnostic yield of gluten challenge in this group of children. MethodsWe included children aged 2 years or younger analysed for possible CD and having villous atrophy at initial small bowel biopsy in the period 1993-2004. We subsequently identified all patients who underwent a complete gluten challenge. ResultsWe identified 334 children with possible coeliac disease. In 100 children (30%) a gluten challenge was performed, with the diagnosis being confirmed in 97. Retrospectively, in two of the three children without mucosal relapse, data available before gluten challenge did not justify the initial diagnosis of CD. In the third patient transient gluten intolerance could not be excluded. At first biopsy, the two children without mucosal relapse had negative serologic parameters, while the third patient had IgA anti-gliadin antibodies, but no IgA anti-endomysium antibodies (EMA). Indeed all patients with EMA at diagnosis had a relapse at gluten challenge.
Conclusion: Routine gluten challenge in children less than 2 years at initial diagnosis of CD has an extremely low diagnostic yield. We suggest that routine gluten challenge in this group of patients is not necessary when patients have villous atrophy in combination with EMA. Therefore, a revision of the current diagnostic criteria has to be considered.

Taurolidine versus heparin lock to prevent catheter-related bloodstream infections (CRBSI) in patients on home parenteral nutrition: a prospective randomized trial

G. Wanten[1], M. Willems[2], T. Bisseling[1], R. Vissers[1], Depts of [1]Gastroenterology and Hepatology and [2]Vascular Surgery, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands

Rationale: CRBSI, mainly occurring in a subset of patients, remain the major threat for the success of any Home Parenteral Nutrition (HPN) program. Taurolidine, an antimicrobial agent without known side effects, holds promise as an effective catheter lock to prevent CRBSI. A randomized controlled trial in HPN patients, however, was lacking so far. Methods: Between April 2006 and March 2008, 30 HPN patients from one referral center, overall harboring 80 patients, were enrolled after developing CRBSI, as proven by positive blood cultures and the absence of other infectious foci. Following adequate treatment of the infection, either with or without a new access device (Hickman catheter or Port-a-Cath), these patients were randomized to continue HPN using heparin (5 mL, 150 U/mL, controls), or taurolidine (5 mL, 2% solution) to lock their access device. Results: Whereas in the heparin control group (14 patients; 4 males; mean age 50 yrs) during the observation period 10 re-infections were observed (73%; mainly due to Staphylococcus sp), in the taurolidine group (16 patients; 4 males; mean age 50 yrs) during 5370 catheter days only 1 re-infection (6%; with Candida) occurred (mean infection-free survival 155 (95% CI 67-243; heparin) versus 641 (95% CI 556-727; taurolidine) days; log-rank $p < 0.0001$). No side effects were reported in either group. Moreover, after crossing-over of the 10 patients with infections on heparin to taurolidine, only 1 re-infection has occurred so far. Of note, neither in controls nor in the taurolidine group, any catheter occlusions were observed.
Conclusion: Taurolidine lock dramatically decreased CRBSI when compared with heparin in this group of HPN patients with proven susceptibility to infections.

Medium-chain triglyceride-induced neutrophil activation is not mediated by the Pertussis Toxin sensitive G-protein coupled receptor GPR84

M.W. Versleijen[1], J. van Esterik[1], H. Roelofs[1], S.E. van Emst-de Vries[2], P.H. Willems[2], G. J. Wanten[1], Depts of Gastroenterology and Hepatology[1] and Biochemistry[2], Radboud University Nijmegen Medical Centre, The Netherlands

Immune modulation by lipids might contribute to the high risk for infections that remains associated with the use of parenteral nutrition. Previously, we have shown that emulsions containing mixed long- and medium-chain triglycerides (LCT/MCT) or pure MCT, but not pure LCT, impair crucial neutrophil functions, modulate cell signaling and induce neutrophil activation in vitro. Others have recently shown that medium-chain fatty acids are ligands for a pertussis toxin (PTX)-sensitive G-protein-coupled receptor (GPCR), which is known as GPR84 and is mainly expressed on neutrophils. The present study was conducted to investigate whether MCT-induced neutrophil activation is mediated by a PTX-sensitive GPCR. In the present study, neutrophils were isolated from 7 healthy volunteers. MCT-induced neutrophil activation was assessed by evaluating stimulus-induced intracellular calcium signaling of cells loaded with the fluorescent probe Fura-2 and oxygen radical (ROS) production by luminol-enhanced chemiluminescence as well as by flowcytometric measurement of the expressions of adhesion (CD11b) and degranulation (CD66b) markers. Neutrophils were pre-incubated with PTX (500-1000 ng/mL, 1.5 hrs) to assess the involvement of a PTX-sensitive GPCR in MCT-induced neutrophil activation. The MCT-dependent modulation of the stimulus-induced biphasic cytosolic calcium increase was not inhibited by PTX. MCT significantly increased ROS production to 146% of unstimulated cells (P=0.018). However, pre-incubation with 500 nor 1000 ng/mL PTX inhibited the MCT-induced ROS production (144% and 150% of unstimulated cells). Furthermore, the MCT-induced increase in CD11b and CD66b expression (196% and 235% of unstimulated cells, respectively) was not inhibited by pre-incubation with 500 ng/mL PTX (222% (CD11b) and 251% (CD66b)) or 1000 ng/mL PTX (199% (CD11b) and 247% (CD66b)).
Conclusion: MCT-induced neutrophil activation appears not to involve the action of a PTX-sensitive GPCR, such as GPR84.

The citrulline generation test in stable ICU patients: optimizing a new enterocyte function test

J.H.C. Peters[1], L.C. Dobrowolski[1], N.J. Wierdsma[2], T. Teerlink[3], A.R.J. Girbes[4], C.J.J. Mulder[1], B. Beishuizen[4], A.A. van Bodegraven[1] , [1]Dept of Gastroenterology, Small Bowel Disease Unit, [2]Dept of Nutrition and Dietetics, [3]Dept of Clinical Chemistry, Metabolic Laboratory, [4]Intensive Care Unit, VU medical center, Amsterdam, The Netherlands

Assessment of small intestinal function is critical in ICU patients with regard to nutritional support and risk of SIRS due to loss of the intestinal barrier function. Recently, we proposed the citrulline generation test (CGT) in which the enterocytes' ability to convert enteral glutamine into citrulline, thus reflecting enterocyte function, could differentiate between healthy subjects and (non-ICU) patients with reduced enterocyte mass. We aimed to assess CGT reference values in 14 'stable' ICU patients with respiratory failure, not dependent on vasopressors, with normal renal function and able to tolerate enteral nutrition meeting full protein-energy requirements. Secondly, we explored four different CGT methods, i.e. following enteral and intravenous (i.v.) glutamine administration, frequently sampling both venous and arterial plasma citrulline up to 3 hours. Glutamine was administered as 100 ml Dipeptiven®, a sterile, aqueous solution containing 20 gram alanine-glutamine. Amino acid analysis was performed using reverse-phase high-performance liquid chromatography. Eight female and 6 male patients had a mean (± SD) age and BMI of 60.1 ± 9 years and 27.1 ± 7.4 kg/m^2, respectively. The incremental area under the curve at 90 minutes during the CGT (iAUCT90) following enteral glutamine was 580 ± 437 µmol/L.min for venous and 680 ± 507 µmol/L.min for arterial citrulline sampling. Performing the CGT with intravenously administered glutamine resulted in an iAUCT90 of 770 ± 235 µmol/L.min for venous and 929 ± 223 µmol/L.min for arterial citrulline sampling. There was a close correlation between venous and arterial citrulline sampling in both enteral (Pearson's $r = 0.96$, $p < 0.0001$) and i.v. (Pearson's $r = 0.91$, $p < 0.0001$) glutamine administration. Thus, in stable ICU patients, the route of glutamine administration in the citrulline generation test clearly favored intravenously administered glutamine for the highest citrulline response and least variation among patients. There was a close correlation between arterial and venous citrulline sampling during the test. The results of this citrulline generation test may be used as reference values for assessing enterocyte function in ICU setting.

Is removal of the fat component from the PN mixture efficient in preventing long-term PN patients from chronic hepatic dysfunction?

L. van der Aa[1], K.S. Vedder[1], C.F. Jonkers-Schuitema[2], H.P. Sauerwein[3], [1]Student Hogeschool van Amsterdam, Nutrition & dietetics, [2]Dietetic Dept/Home parenteral utrition support team, Academic Medical Center, Amsterdam, [3]Dept of Internal Medicine and Endocrinology, Academic Medical Center, Amsterdam, The Netherlands

Background: Liver abnormalities during long-term parenteral nutrition (PN) are reported to occur in adults. When this occurs, nutritional steps could be taken in order to prevent patients from developing chronic hepatic dysfunction.Objective: To assess the prevalence and the contributing factors in the development of PN associated liver disease (PNALD) and to evaluate the effect on liver abnormalities after removal of the fat component from PN. Method: Retrospective analysis of medical records from adults receiving long-term (>3 months) home parenteral nutrition (HPN) between January 1st 1997 and November 1st, 2007. Measurements: Data-follow up assessed the prevalence of PNALD associated with gender, age, primary disease, duration of HPN and nutrient- and patient related factors. Contributing factors to PNALD were assessed by using univariate analysis. Total bilirubin level was (deranged: bilirubin > 20 µmol/l) used to determine occurrence of PNALD. Nutritional management during PNALD was monitored by patients' weight development, total bilirubin level, the return of PNALD and biochemical and clinical signs of nutrient deficiencies. Results: 83 adult patients were included. At the end of follow-up, 33 patients were still receiving HPN, 28 had been weaned from HPN, and 18 had died. None of the patients died of liver failure. PNALD occurred in 20 adults after 11 weeks on HPN (median; range 1 - 51 weeks). Development of PNALD was significantly related ($p<0,05$) to energy overload (> 40 kcal/kg/d) with a relative risk ratio of 2.4 (CI, 1.0 to 5.5). Glucose overload, fat overload and the combination of energy overload and fat overload appeared not to be significantly related to the development of PNALD. In PNALD the fat component was excluded from PN for 12 weeks (median; range 5-44). Total bilirubin levels returned to normal. Clinical signs for essential fatty acid deficiency (EFAD) such as dermatitis, hair loss and impaired wound healing did not occur. EFAD was not diagnosed by biochemical markers. After reintroduction of fat in PN, PNALD returned in four patients.
Conclusion: This study shows that energy intake of 40 kcal/kg per day or more is a significant contributing factor in the development of PNALD in adults on PN. Moreover, this study shows that removing the fat component from PN has a positive influence in normalizing deranged liver function tests. Prospective studies are needed to concerning nutritional prevention and treatment of PNALD.

Nutritional status of patients with de novo coeliac disease

N.J. Wierdsma[1], J.H.C. Peters[2], M.A.E. van Bokhorst-de van der Schueren[1], C.J. J. Mulder[2], A.A. van Bodegraven[2], [1]Nutrition and Dietetics, [2]Gastroenterology, VU University Medical Center, Amsterdam, The Netherlands

Malnutrition is frequently observed in patients with Coeliac Disease (CoD). Knowledge of nutritional status in patients with recently diagnosed CoD is limited.
The aim of this study was to assess an extended nutritional status in patients with de novo CoD. The nutritional status of CoD patients, confirmed by pathognomonic histopathology, was assessed prior to the initiation of a gluten free diet by: 1) length, weight and weight decline; 2) body composition and muscle strength and 3) serum nutrient deficiencies (vitamin A, B6, B12 and folic acid). Fat free mass index (FFMI=kg FFM/height2) was calculated using bio-electric impedance analysis according to Kyle. Muscle strength was measured by a handgripdynamometer and analyzed according to Mathiowitz. Variables were compared to a reference population. hirty-nine patients, 26 women and 13 men, with CoD (aged 18-75 years) were included. Thirteen of the CoD patients were malnourished (mean ± SD BMI (kg/m^2) = 22.9 ± 4.2, % weight loss 6 months = 2.9 ± 5.9). In addition, total nitrogen pool was decreased in 12 (out of 33) patients. This decrease in FFMI (kg/m^2) was more present in woman (mean ± SD = 14.8 ± 1.8 vs 19.2 ± 2.2, $p<0.001$). Long term malnourishment was also determined by handgrip strength, which was subnormal in 24 (out of 37) patients (mean ± SD as % of references = 95.5 ± 28.5). Serum concentration of nutrients (mean ± SD vitamin A = 2.0 ± 1.2mmol/l , B12 = 232 ± 105 pmol/l, B6 = 100 ± 169 nmol/l and folic acid = 17.4 ± 18.2 nmol/l) were reduced in 5-20% of the patients, depending on the studied variable. Vitamin B6 and folic acid were reduced in men compared to women (28.3 ± 19.4 vs 136 ± 198, $p=0.014$, and 8.4 ± 4.3 vs 21.5 ± 20.6, $p=0.004$, respectively).
This study documented malnutrition, decreased nitrogen pool and serum nutrient deficiencies in patients with de novo CoD, leading to functional deficits. Women had less favourable scores of body composition and muscle strength, whereas men showed more serum nutrient deficiencies. Given the high prevalence of energy, protein and serum nutrient deficiencies, extensive nutritional assessment as part of proper treatment, is recommended when CoD is being diagnosed.

A double blind, placebo-controlled trial with escitalopram to prevent psychiatric adverse events during treatment with pegylated interferon-alpha and ribavirin for chronic hepatitis C: The "Prevention Of Psychiatric Side effects (POPS)-study"

G. Bezemer, A.R. van Gool, J.P.H. Drenth, B.E. Hansen, H.A. Droogleever Fortuyn, C.J. Weegink, M.W. Hengeveld, H.L.A. Janssen, R.J. de Knegt, Erasmus MC University Medical Center, Rotterdam, the Netherlands, Depts. Gastroenterology & Hepatology, and Psychiatry. Radboud University Nijmegen Medical Center, Nijmegen, The Netherlands, Dept of Gastroenterology and Hepatology and Psychiatry, Academic Medical Center Amsterdam, The Netherlands, Depts of Gastroenterology and Hepatology and Psychiatry

Title: A double blind, placebo-controlled trial with escitalopram to prevent psychiatric adverse events during treatment with pegylated interferon-alpha and ribavirin for chronic hepatitis C: The "Prevention Of Psychiatric Side effects (POPS)-study" Background/Aim: Treatment with PEG-interferon (PEG-IFN) for chronic hepatitis C is associated with psychiatric side effects, most notably depression and increased irritability, which frequently necessitate dose reduction or cessation of therapy. Methods: We completed an investigator-initiated, randomized, double-blind, controlled trial, in chronic hepatitis C, investigating the efficacy of prophylactic escitalopram (10 mg; n=40) versus placebo (n=39) on psychiatric side effects in patients treated with PEG-IFN α-2a and ribavirin (RBV).Primary outcome measures were an increase of at least two points on reported sadness, inner tension, impaired concentration of the Montgomery-Asberg Depression Rating Scale (MADRS) or on irritability of the Brief Anxiety Scale (BAS). Secondary outcome measure was depression as diagnosed by the Mini International Neuro-psychiatric Interview. Psychometric measurements were performed at baseline, week 4, 12 and 24, together with the completion of self-rating scales (Beck Depression Inventory (BDI) and Symptom Check List-90 (SCL-90)). In case of major psychopathology, study code was broken and open-label escitalopram was started.Results: We observed significantly less psychiatric side effects for those treated with escitalopram as compared to placebo for all primary and secondary outcome measures, except for impaired concentration (Table 1). Regarding the other psychometric measurements, patients treated with escitalopram scored significantly better than placebo on sum scores and all subscales of the BDI and SCL-90 at all different evaluation points ($p \leq 0.04$), except for SCL-90 somatic complaints at week 4 and 12. No (serious) adverse events related to escitalopram were observed. Compliance with PEG-IFN and RBV was similar probably due to the possibility of open-label treatment.
Conclusion: Prophylactic treatment with escitalopram is effective in the prevention of psychiatric side effects during antiviral therapy of hepatitis C and should be considered for all chronic HCV patients who are treated with PEG-IFN based regimens.

Diagnostic accuracy of Transient Elastography: a comparison between chronic hepatitis B and C correlated with optimal-length liver biopsies

C. Verveer[1], B. E. Hansen[2], P.E. Zondervan[3], H.L.A. Janssen[1], R.J. de Knegt , [1]Dept. of Gastroenterology and Hepatology, [2]Dept of Biostatistics [3]Dept of Pathology, Erasmus MC Rotterdam, The Netherlands

Background: Transient elastography (TE) is used to assess hepatic fibrosis non-invasively, mostly in chronic viral hepatitis C (CHC). The efficacy in chronic viral hepatitis B (CHB) is less well established. The diagnostic performance of TE in severe fibrosis and cirrhosis is good, but less reliable in the Metavir fibrosis stages F0-F2. We investigated whether the diagnostic performance and accuracy improved when correlated with liver biopsies of optimal length and whether outcome was influenced by inflammatory activity according to the Ishak HAI score, steatosis and iron. In addition, a comparison between CHC and CHB was made.Methods: 257 consecutive patients with a liver biopsy measuring at least 25mm and concomitant TE (FibroScan) were enrolled. Liver specimens were scored for fibrosis (both Metavir and Ishak classification) with the assessment of necro-inflammatory activity according to the modified HAI system. In addition the amount of steatosis (Brunt classification) and iron were scored. Results: 137 patients with CHB, 117 patients with CHC and 3 patients with combined CHC and CHB were evaluated. Patients were categorized as follows in the Metavir classification: 22 patients F0, 98 F1, 68 F2, 47 F3 and 22 F4. There were no significant differences in the reliability of elastographical measurements between patients with CHB or CHC, when corrected for age, BMI, Metavir classification, steatosis, iron and inflammatory activity.The ROC-curves for the different Metavir classifications were: F1 0.75, F2 0.81, F3 0.90 and F4 0.89.Necro-inflammatory activity, which was significantly correlated with ALT, was an independent factor to influence the TE measurements. With increasing inflammatory activity, the FibroScan outcome can be 1.4 kPa higher than expected. Steatosis and the amount of iron had no significant effect on TE measurement.
Conclusion: Diagnostic accuracy of TE by FibroScan in CHB and CHC is similar. TE correlates very well with severe fibrosis (F3) and cirrhosis (F4) as well with moderate fibrosis (F2). Active inflammation of the liver produces a significant increase in TE outcome and should therefore be taken into account.

Hepatitis C viral kinetics during PEG-interferon alfa-2b and ribavirin therapy in naïve chronic hepatitis C patients

G. Boland[1,10], H. van Soest[1], R.A. de Vries[2], N.A.M. van Ooteghem[3], B. van Hoek[4], J.P.H. Drenth5, R.J. de Knegt[6], R.J. Lieverse[7,] P. Houben[8], A. van der Sluys Veer[9], P.D. Siersema[1], A.M. van Loon[10], K.J. van Erpecum[1] , Depts. of Gastroenterology and Hepatology[1] University Medical Center Utrecht, [2]Rijnstate Hospital Arnhem, [3]St Lucas Andreas Hospital Amsterdam, [4]Leiden University Medical Center, [5]University Hospital Nijmegen, [6]Erasmus Medical Center Rotterdam, [7]Gelre Ziekenhuizen Apeldoorn, [8]Ziekenhuis Zeeuws Vlaanderen, [9]Onze Lieve Vrouwe Gasthuis Amsterdam and [10]Dept of Medical Microbiology, University Hospital Utrecht, The Netherlands

Hepatitis C (HCV) viral kinetics are becoming an increasingly important tool to predict sustained viral response (SVR) to PEG-Interferon/ribavirin treatment of patients with chronic hepatitis C. HCV RNA negativity at week 4 (rapid viral response) is considered highly predictive of sustained viral response (SVR), whereas in case of less than 2-log decrease of viral load at week 12 (no early viral response) the chance of reaching SVR is considered extremely low, and stopping further therapy is advised. We studied HCV kinetics in a subgroup of 94 patients included in the CIRA-study, 67% were HCV genotype 1 or 4, and 33% genotype 2 or 3; 46% had a viral load >6x10^5 IU/mL at start of treatment. Complete data were obtained in 85 of these patients (77 excluding drop-outs). Patients received amantadine hydrochloride 200 mg daily or placebo, in combination with high-dose induction therapy followed by PEG-interferon alfa-2b 1.5 µg/kg/week up to 26 weeks and 1.0 µg/kg/week from week 26 to week 52 (Schering-Plough Maarssen, The Netherlands) and weight-based ribavirin (Schering-Plough: 1000-1200 mg/day). In case of positive HCV RNA at week 24, treatment was discontinued. HCV RNA (bDNA, VERSANT HCV 3.0, Siemens) was measured at T=0, 1, 2, 4, 8 and 12 weeks and related to SVR. HCV kinetics did not differ between amantadine and placebo groups. At T=4 weeks, HCV RNA was negative in 51% of pts (40% of genotype 1-4 and 74% of genotype 2-3) with positive predictive value for reaching SVR of 96% (92% in genotype 1-4 and 100% in genotype 2-3) and negative predictive value for SVR of 76% (74% in genotype 1-4 and 100% in genotype 2-3). Overall, a >2-log decrease in viral load was observed in 81% of pts at week 12 (82% of genotype 1-4 and 79% of genotype 2-3) with positive predictive value for reaching SVR of 78% (69% in genotype 1-4 and 92 % in genotype 2-3) and negative predictive value for SVR of 87% (86% in genotype 1-4 and 100% in genotype 2-3). Two patients with <2 log decrease at week 12 still were HCV RNA positive, but reached SVR (both genotype 1). These patients had a low starting viral load of 3,6x10e4 and 1,4x10e5 IU/mL. Conclusion: HCV RNA negativity at week 4 has high predictive value for reaching sustained viral response, regardless genotype. Negative predictive value of <2-log decline at week 12 is not 100% in patients with low baseline viral load.

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48 Weeks of Peginterferon Alfa-2a alone or in Combination with Ribavirin for HBeAg-negative Chronic Hepatitis B: Addition of Ribavirin does not increase Response Rates

H.L.A. Janssen[1], V. Rijckborst[1], Y. Cakaloglu[2], P. Ferenci[3], F. Tabak[4], M. Akdogan[5], K. Simon[6], M. Raptopoulou-Gigi[7], N. Örmeci[8] ,P.E. Zondervan[9], G.J.J. van Doornum[10], E. Verhey[1], A.J. van Vuuren[1], M.J. ter Borg[1], B.E. Hansen[1,10] for the PARC Study, [1]Dept of Gastroenterology and Hepatology, Erasmus MC, University Medical Center Rotterdam, Rotterdam, The Netherlands, [2]Dept of Gastroenterohepatology, Istanbul University Medical School, Istanbul, Turkey, [3]Dept of Internal Medicine [3], Gastroenterology and Hepatology, Medical University of Vienna, Vienna, Austria, [4]Dept of Infectious Diseases, Istanbul University Cerrahpasa Medical School, Istanbul, Turkey, [5]Dept of Gastroenterology, Turkiye Yuksek Ihtisas Hospital, Ankara, Turkey, [6]Dept and Clinic of Infectious Diseases, Hepatology and Acquired Immune Deficiences, Medical University Wroclaw, Wroclaw, Poland, [7]Second Medical Dept, Aristototle University of Thessaloniki, Thessaloniki, Greece, [8]Dept of Gastroenterology, Ankara University School of Medicine, Ankara, Turkey, [9]Dept of Pathology, Erasmus MC, University Medical Center Rotterdam, Rotterdam, The Netherlands, [10]Dept of Epidemiology and Biostatistics, Erasmus MC, University Medical Center Rotterdam, Rotterdam, The Netherlands

HBeAg-negative chronic hepatitis B (CHB) patients are at high risk for disease relapse after discontinuation of any antiviral therapy. To increase response and further reduce relapse HBeAg-negative patients should be treated with optimized immune modification. The combination of peginterferon alfa (PEG-IFN) and ribavirin could be more effective than PEG-IFN alone or its combination with other nucleos(t)ide analogues, because ribavirin not only inhibits viral replication by interference with viral messenger RNA, but also modulates the immune response. The aim of this international multicenter trial was to investigate whether in patients with HBeAg-negative CHB PEG-IFN alfa-2a and ribavirin combination therapy leads to enhanced response rates in comparison with PEG-IFN alfa-2a monotherapy. Patients were randomized to receive PEG-IFN alfa-2a 180 mcg weekly plus placebo (n=69) or ribavirin 1000-1200 mg daily (n=64) for 48 weeks. Post-treatment follow-up lasted until week 72. A liver biopsy was performed at baseline and week 72. Baseline characteristics were comparable between the two treatment groups, 74% of patients were male, mean age was 42.2±10.9 years and most were genotype D (80%). The primary endpoint, defined by HBV DNA <10,000 cp/ml and ALT normalization at week 72, was achieved in 20% of patients in the PEG-IFN monotherapy group and 16% of patients in the combination group, using intent-to-treat analysis (p=0.485). HBsAg seroconversion occurred in one patient (1.6%) receiving combination therapy and in none treated with PEG-IFN alone. A decrease in necroinflammatory score (≥2 points, Ishak score) was observed in 53% of patients treated with PEG-IFN monotherapy and in 49% treated with combination therapy (p<0.001 for both groups, no significant difference between the two groups). A decrease in fibrosis stage (≥1 point, Ishak score) was reported in 31% of patients receiving PEG-IFN monotherapy and 26% receiving combination therapy (p<0.001 for both groups, no significant difference between the two groups). The number of patients prematurely discontinuing treatment or follow-up did not differ significantly between the two treatment arms. Conclusion: for HBeAg-negative CHB the addition of ribavirin to PEG-IFN alfa-2a for 48 weeks of treatment did not improve response rates compared to PEG-IFN alfa-2a monotherapy.

Early Reduction of Serum HBsAg Levels in HBeAg-negative Chronic Hepatitis B Patients achieving Sustained Virological Response after Peginterferon Alfa-2a ± Ribavirin Treatment

V. Rijckborst[1], M.J. ter Borg[1], U.S. Akarca[2], P. Grima[3], R. Flisiak[4], I. Vafiadis-Zouboulis[5], S. Tripi[6], G.J.J. van Doornum[7], E. Verhey[1], A.J. van Vuuren[1], B.E. Hansen[1,8], H.L.A. Janssen[1], for the PARC Study, [1]Dept of Gastroenterology and Hepatology, Erasmus MC, University Medical Center Rotterdam, Rotterdam, The Netherlands, [2]Dept of Gastroenterology, Ege University Faculty of Medicine, Izmir, Turkey, [3]Dept of Infectious Diseases, S. Caterina Novella Hospital, Galatina, Italy, [4]Dept of Infectious Diseases and Hepatology, Medical University of Bialystok, Bialystok, Poland, [5]First Dept of Propedeutic Medicine, University of Athens Medical School, Athens, Greece, [6]Dipartimento di Medicina, Clinica e della Patologie Emergenti, Universita di Palermo, Palermo, Italy, [7]Dept of Virology, Erasmus MC, University Medical Center Rotterdam, Rotterdam, The Netherlands, [8]Dept of Epidemiology and Biostatistics, Erasmus MC, University Medical Center Rotterdam, Rotterdam, The Netherlands

Hepatitis B surface antigen (HBsAg) seroconversion is the ultimate goal of antiviral therapy, since this state represents control of the virus by the host immune system. Reduction of serum HBsAg levels indicates favourable changes in the virus versus host equilibrium. In a large international multicenter trial HBeAg-negative chronic hepatitis B (CHB) patients received 48 weeks of peginterferon (PEG-IFN) alfa-2a alone or in combination with ribavirin. For the current analysis Sustained Virological Response (SVR) was defined by HBV DNA <10,000 cp/ml 24 weeks after treatment. The aim of the study was to quantify the reduction of HBsAg in patients treated with PEG-IFN ± ribavirin and to compare HBsAg reductions between patients with and without SVR. HBsAg was measured using the ARCHITECT HBsAg assay (Abbott laboratories) at baseline and every 12 weeks during treatment and follow-up in 133 patients treated with 180 mcg peginterferon alfa-2a once weekly plus placebo (n=69) or 1000-1200 mg ribavirin daily (n=64). Patients were categorized as non-responder in case HBV DNA measurement at week 72 was missing. The mean baseline HBsAg level was 4.06 log IU/ml without difference between the treatment groups or between patients with and without SVR. In both treatment groups HBsAg reductions from baseline were significant after 48 weeks of treatment (0.55±1.04 and 0.36±1.00 log IU/ml (mean±SD) in the PEG-IFN monotherapy and combination arm, respectively) and after 24 weeks of follow-up (0.61±1.12 and 0.42±0.67 log IU/ml), without significant differences between the two treatment groups. Therefore, the treatment groups were merged for the analysis of HBsAg quantification in relation to SVR. SVR occurred in 20% of patients. HBsAg reductions from baseline at week 72 were significantly higher in patients achieving SVR (1.30±1.34 versus 0.28±0.57 log IU/ml, p=0.001) and patients achieving SVR already had significant HBsAg reductions compared to baseline at week 12 (0.33±0.62 log IU/ml, p=0.013) in contrast to patients without SVR.

Conclusion: Treatment of HBeAg-negative CHB patients with PEG-IFN alfa-2a alone or in combination with ribavirin induced a significant HBsAg reduction. HBsAg reductions were significantly higher in patients achieving sustained virological response at week 72. Early on-treatment decline of HBsAg levels might become an important tool to predict virological outcome of PEG-IFN treatment.

Impaired Fibrinolysis as a Risk Factor for Budd-Chiari Syndrome

J. Hoekstra[1], F.W. Leebeek[2], A.H.C. Guimarães[2], S. Darwish Murad[1], J.J.M.C. Malfliet[2], A. Plessier[3], P. Langlet4, E. Elias[5], J. Heller[6], M. Primignani[7], J.C. Garcia-Pagan[8], D.C. Valla[3], D.C. Rijken[2], H.L.A. Janssen[1] for the European Network for Vascular Disorders of the Liver (EN-Vie), [1]Dept of Gastroenterology and Hepatology, Erasmus University Medical Center, Rotterdam, The Netherlands, [2]Dept of Hematology, Erasmus University Medical Center, Rotterdam, The Netherlands, [3]Dept of Hepatogastroenterology, Centre Hospitalier Universitaire Brugmann, Bruxelles, Belgium, [4]Liver Unit, Queen Elisabeth Hospital Birmingham, Birmingham, United Kingdom, [5]Dept of Internal Medicine I, University Hospital of Bonn, Bonn, Germany, [6]Gastroenterology and Gastrointestinal Endoscopy Unit, Ospedale Policlinico, Mangiagalli and Regina Elena Foundation, Milan, Italy, [7]Hepatic Hemodynamic Laboratory, Liver Unit, Hospital Clinic, IDIBAPS and Ciberehd, Barcelona, Spain, [8]Dept of Hepatology, Hopital Beaujon, AP-HP, INSERM-U773 & University Paris-7, Clichy, France

In Budd-Chiari Syndrome (BCS) thrombosis develops in the hepatic veins or the inferior vena cava. Disorders leading to a hypercoagulable state can be identified in many BCS-patients. Whether disturbances in the fibrinolytic pathway can also influence the risk of thrombosis in BCS-patients is unknown. In this study we have investigated the relationship between impaired fibrinolysis and BCS. From the EN-Vie study, a prospective multi-center study of patients with BCS, we studied 101 patients and 101 sex- and age-matched, healthy controls. In these two groups, we measured plasma levels of plasminogen activator inhibitor 1 (PAI-1), tissue-type plasminogen activator (t-PA) antigen, thrombin-activatable fibrinolysis inhibitor (TAFI), fibrinogen and factor XIII. As a measure of overall fibrinolytic potential we performed a plasma-based clot lysis assay. In BCS-patients, median levels of PAI-1 and t-PA antigen were significantly higher as compared to controls (6.3 vs. 1.4 IU/ml and 6.8 vs. 2.9 ng/ml, respectively, both $p<0.001$). In contrast, TAFI-levels were decreased in BCS-patients (median 13.8 µg/ml vs. 16.9 µg/ml, $p<0.001$). Plasma fibrinogen concentration was slightly higher in cases than in controls (median 2.9 vs. 2.8 g/l) but this was not statistically significant ($p=0.072$). The median level of factor XIII was lower in BCS-patients as compared to the controls (80 vs. 120%, $p<0.001$). There was no clear association between any of the studied parameters and different liver function tests. Results of the clot lysis assay showed that the median plasma clot lysis time (CLT) was 73.5 min (range 39.6-157.0 min) in cases and 73.0 min (range 53.4-164.5) in controls ($p=0.858$). However, a subgroup of BCS-patients displayed a clearly elevated CLT. When CLT's of the control population were used as a reference, a CLT above the 90th (93.1 min) or 95th (98.0 min) percentile was associated with an increased risk of BCS with an odds ratio of 2.3 (95%CI 1.0-5.3) and 3.2 (95%CI 1.1-9.2), respectively. Using multiple linear regression analysis, only PAI-1 activity was significantly associated with CLT (regression coefficient 1.56, $p<0.001$). Conclusions. This study provides the first evidence that an impaired fibrinolytic potential is related to the presence of BCS. A prolonged CLT, at least partially caused by elevated PAI-1 levels, proves to be a previously unknown etiologic factor that, in combination with other known thrombogenic factors, may potentiate the risk of BCS.

High incidence of histological hepatitis and portal fibrosis at 1 year after pediatric liver transplantation using a tacrolimus-based immunosuppressive regimen

R. Scheenstra[1,4], A.S.H. Gouw[2,4], P.M.J. Peeters[3,4], H.J. Verkade[1,4], [1]Dept of Pediatric Gastroenterology, Beatrix Children's Hospital, [2]Deptartment of Pathology, [3]Dept. of Hepatobiliary Surgery, [4]Liver transplantation Team, University Medical Center Groningen, Groningen, The Netherlands

Introduction: Recent studies show a high incidence of abnormal histological features during follow up after pediatric liver transplantation (LTx). Previously we described portal fibrosis in 30% of first year biopsies after LTx in a group of pediatric patients treated with an immunosuppressive scheme based on cyclosporine (CsA; Transplantation 2000; 70 (11): 1581-7.) It has remained unclear whether the development of fibrosis differs using a tacrolimus (FK) based immunosuppressive regimen, for example due to differences in induction of hepatic TGFβ1 expression and hence stimulation of fibrosis. Aim of this study: To assess development of fibrosis in liver grafts at 1 year after pediatric LTx using a FK based immunosuppressive scheme. Methods: We included patients transplanted between 1999 and 2006, who had a 1 year post LTx survival and were treated with a FK based immunosuppressive scheme (n=77). A 1 year post LTx protocol biopsy was available in 74/77 patients. All biopsies were reviewed by a single pathologist. Histological hepatitis was graded according to the Metavir scoring system. Results: 4 major histopathological categories were found in the biopsies: 1. normal findings (n = 23; 31%), 2. reactive changes (n= 7; 10%), 3. portal fibrosis (n= 25; 34 %), 4. hepatitis (n= 17; 23%). Miscellaneous findings were found in 2 biopsies. Compared with our earlier study using a CsA-based immunosuppressive regimen, the incidence of fibrosis was similar (CsA 31%, FK 34%; NS). The patients with portal fibrosis did have significant higher liver enzymes (AST 49 ± 28 IU/l, ALT 59 ± 40 IU/l) compared with patients with normal histology (AST 36 ±11 IU/l, ALT 30 ± 13 IU/l). Histological hepatitis was more frequently observed in FK treated patients (23%) compared with the CsA group (CsA 1%; $p < 0.05$). This hepatitis was predominantly mild (Metavir score "mild" in 13/17, 76%; "moderate" in 4/17, 24%). Histological hepatitis was not associated with elevated liver enzymes. The etiology of the hepatitis could not be identified: Serology for Hepatitis A, B and C was negative. In situ hybridisation for EBV (EBER) was negative in all hepatitis cases. Serum IgG concentrations were similar in the two groups (hepatitis 11.9 ± 4.5, other 10.2 ± 3.3, NS).

Conclusion: The incidence of graft fibrosis at 1 year after pediatric LTx is similar after a CsA- or a FK based immunosuppressive regimen (~30%). The FK based regimen is specifically associated with a high incidence of histological mild hepatitis of unknown origin.

Efficacy of Nasobiliary Drainage for Refractory Cholestatic Pruritus

E.M.M. Kuiper[1], R.A. de Man[1], H.R. van Buuren[1], [1]Dept of Gastroenterology and Hepatology, Erasmus University Medical Center, Rotterdam, The Netherlands

Background and Aims: Nasobiliary drainage (NBD) has been reported to be effective in pruritus secondary to benign recurrent intrahepatic cholestasis (BRIC) (Stapelbroek et al. Hepatology 2006;43:51-3). The aim of this study was to further explore the feasibility and efficacy of NBD in severe refractory pruritus associated with cholestatic conditions of any etiology. Methods: We selected patients with severe cholestatic pruritus who did not respond to medical treatment including cholestyramine, rifampicin and naltrexon. A nasobiliary drain was inserted during ERCP for 7 days. The effect of drainage was evaluated using visual analogue scales (VAS) for pruritus and fatigue and by laboratory studies including serum bile acids, bilirubin, ALP, AST and ALT before, during and after NBD. Results: 6 consecutive patients (4 females, 2 males; mean age 40 yrs) were included. Causes of cholestatic pruritus were PBC (n=1), PSC (n=1) and BRIC (n=4, based on clinical features, although negative for ATP8B1/ABCB11 mutations). All patients experienced marked improvement of pruritus within 7 days. The absolute difference between median pruritus VAS score before and after NBD was 5 (78%). Laboratory tests all improved markedly. Patients were followed for a median period of 14.6 (range 2.3-26.2) months. Pruritus recurred in one patient with PSC immediately following removal of the drain and recurred after 12 months in another case. Two patients developed mild post-ERCP pancreatitis.
Conclusions: Nasobiliary drainage is an invasive procedure associated with potential complications, but may result in long-term relief of severe, refractory cholestatic pruritus. Our results suggest that beneficial effects of NBD cannot not only be obtained in BRIC but also in other cholestatic conditions and confirm older observations of the utility of surgical biliary drainage to treat cholestatic pruritus.

Detection of Hepatitis B covalently closed circular DNA in paraffin-embedded liver biopsy specimens of chronic hepatitis B patients

R.B. Takkenberg[1], H.L. Zaaijer[2], S. Menting[2], C.J. Weegink[1], V. Terpstra3, M.G.W. Dijkgraaf[4], M. Cornelissen[5], P.L.M. Jansen[1], H.W. Reesink[1] and M.G.H.M.Beld[2],1AMC Liver Center, Dept of Gastroenterology and Hepatology, Academic Medical Center, University of Amsterdam, Amsterdam, [2]Section of Clinical Virology, Dept of Medical Microbiology, Academic Medical Center, University of Amsterdam, The Netherlands, [3]Dept of Pathology, Academic Medical Center, University of Amsterdam, Amsterdam, [4]Dept of Clinical Epidemiology and Biostatistics, Academic Medical Center, University of Amsterdam, [5]Laboratory of Experimental Virology, Dept of Medical Microbiology, Academic Medical Center, University of Amsterdam, The Netherlands

Introduction: In chronic hepatitis B (CHB) infection, covalently closed circular DNA (cccDNA) is responsible for persistence of infection. No studies, in search of the role of cccDNA, have been performed on formalin-fixed, paraffin embedded (FFPE) liver biopsies. The aim of this study was to detect and analyze cccDNA in FFPE liver tissue and compare the results with individual plasma ALT levels and the Histology Activity Index (HAI).

Material and Methods: As we previously described, cccDNA was quantified by using selective primers that target the gap region between the two Direct Repeat Regions (DR1 and DR2). To quantify cells, we used primers that target the GAPDH gene. Real-time PCR (rt PCR) was performed in the Roche Lightcycler® 480. The number of hepatocytes was calculated as 70% of the total number of cells. From 56 FFPE biopsies of HBeAg positive and HBeAg negative CHB patients (29 HBeAg positive and 31 HBeAg negative CHB patients), 60 μm was cut in coupes of 10 μm each. Paraffin was extracted with 1 mL xyleen, followed by 2 washes with 100% alcohol and one wash with acetone. DNA extraction was performed according the Boom procedure.

Results: The median number of hepatocytes was 9.8x10e6 cells per biopsy (range 2.2x10e6-4.0x10e7 cells) and cccDNA was detectable in 40 FFPE liver biopsies. The median level of cccDNA/10e6 hepatocytes was significantly higher in biopsies from HBeAg positive patients than HBeAg negative patients (183 copies (range 74-755 copies) vs 23 copies (range 8.0-101 copies) (p=0.0013)). The median level of cccDNA was significantly higher in HBeAg positive CHB patients than in HBeAg negative CHB patients (p=0.0036) and significantly higher in CHB patients with active hepatitis (ALT > 45 U/L) than in CHB patients with inactive hepatitis (ALT ≤ 45 U/L) (p=0.0038). Overall there is a significant correlation between the level of cccDNA/10e6 hepatocytes and viral load (p<0.0001) (correlation coefficient (*R*) = 0.6). There was no correlation between the level of cccDNA/10e6 hepatocytes and HAI-score (p=0.10).

Conclusions: we developed a new rt-PCR for detection of cccDNA in FFPE liver biopsies of CHB patients and showed a strong correlation between the number of cccDNA and viral load. Our findings suggest that FFPE liver biopsies can be used for detection of cccDNA, and that the level of cccDNA in FFPE liver biopsies of CHB patients is indicative of viral replication activity.

HBV Genotype is an Important Predictor of Sustained Off-Treatment Response to both Peginterferon Alpha-2b and Entecavir in HBeAg Positive Chronic Hepatitis B

E.H.C.J. Buster[1], B.E. Hansen[1,2], E. Verhey[1], R.A. de Man[1], H.L.A. Janssen[1], Depts of [1]Gastroenterology and Hepatology, [2]Epidemiology and Biostatistics, Erasmus MC University Medical Center Rotterdam, Rotterdam, The Netherlands

Background Choice of initial antiviral therapy is becoming increasingly important in chronic hepatitis B. Knowledge of the predictors of sustained off-treatment response may facilitate choice of therapy. Methods Grouped data from 354 patients treated with entecavir and 266 patients treated with peginterferon alpha-2b (PEG-IFN) for 1 year were evaluated in this retrospective study. Sustained virological response (SVR) was defined as HBeAg loss and HBV DNA <7.0x10^5 copies/ml at 6 months post-treatment (ETV-022 study). Data were stratified by HBV genotype in combination with one of the following factors: ALT (<2, 2-5 or ≥5 x ULN), HBV DNA (<8, 8-9, 9-10 or ≥10 $\log_{10}$ copies/ml), previous treatment with interferon or lamivudine, weight (<55, 50-80 or >80 kg), BMI (<20, 20-25, 25-30 or ≥30 kg/m^2), and necroinflammatory score (<3, 3-6, 6-9, ≥9) and fibrosis score (1-2, 3-4 or 5-6) according to the histological activity index. Predictors of response were identified by logistic regression analysis. Results SVR was observed in 20.2% and 17.2% of patients treated with PEG-IFN and entecavir, respectively. HBV genotype was a predictor of SVR to both PEG-IFN and entecavir (p=0.001 and p=0.03, respectively). In addition, baseline necroinflammatory score predicted response to PEG-IFN (p=0.009), while baseline ALT and HBV DNA were associated with SVR after entecavir therapy (p=0.02 and p=0.02, respectively). PEG-IFN resulted in higher rates of SVR in genotype A infected patients compared to entecavir (OR 1.56 [95%-CI 0.80-3.05], 1.75 [0.88-3.48] and 3.19 [1.41-7.19] after correcting for ALT, HBV DNA or necro-inflammation, respectively), as well as in those with genotype B (OR 4.73 [1.02-22.00], 4.30 [0.86-21.51] and 12.76 [2.55-63.91] after correcting for ALT, HBV DNA or necroinflammation, respectively). Response rates in genotype C infected patients were comparable (OR 0.52 [0.16-1.67], 0.50 [0.15-1.60] and 1.04 [0.27-4.05] after correcting for ALT, HBV DNA or necroinflammation, respectively), while in genotype D infected patients response rates were higher with entecavir compared to PEG-IFN (OR 5.07 [1.84-14.00], 3.27 [1.21-8.87] and 1.86 [0.63-5.45] after correcting for ALT, HBV DNA or necroinflammation, respectively). Conclusion HBV genotype is an important predictor of sustained response to both PEG-IFN and entecavir. When aiming for sustained off-treatment response, determination of HBV genotype is important in order to choose the optimal antiviral agent.

Prediction of response to peginterferon-alfa in HBeAg positive chronic hepatitis B: A model based on 721 patients

E.H.C.J. Buster[1], B.E. Hansen[1,2], G.K.K. Lau[3], T. Piratvisuth[4], P. McCloud[5], P. Button[5], E.W. Steyerberg[6], S. Zeuzem[7], H.L.A. Janssen[1], Depts of [1]Gastroenterology and Hepatology, [2]Epidemiology and Biostatistics, and [6]Public Health, Erasmus MC University Medical Center Rotterdam, The Netherlands, [3]Dept of Medicine, Queen Mary Hospital, University of Hong Kong, Hong Kong SAR, China, [4]Dept of Medicine, Songklanakarin Hospital, Songkla, Thailand, [5]Roche, Dee Why, Australia, [7]Medizinische Klinik I, Klinikum der Johann Wolfgang Goethe-Universität, Frankfurt am Main, Germany

One of the major challenges in the treatment of chronic hepatitis B is to select patients who are likely to respond to peginterferon (PEG-IFN) therapy. In order to develop an optimal model for the prediction of sustained off-treatment response to PEG-IFN in all HBV genotypes, data from the 2 largest global trials investigating PEG-IFN in HBeAg positive chronic hepatitis B were combined. Methods 542 patients treated with PEG-IFN α-2a (180 µg/week for 48 weeks) and 266 patients treated with PEG-IFN α-2b (100 µg/week for 52 weeks) were included. Addition of lamivudine did not influence response rates at the end of follow-up (6 months post-treatment). For this study, sustained virological response (SVR) was defined as HBeAg loss and HBV DNA <10,000 copies/ml at 6 months post-treatment. Logistic regression analysis was used to identify predictors of SVR. Based on results of previous studies and for clinical applicability, the variables investigated were: sex, age, weight, HBV genotype, HBV DNA (copies/ml), ALT (x ULN), treatment allocation and previous antiviral therapy. Results 87 patients were excluded because of missing values or harbouring an HBV genotype other than A-D, leaving 721 patients for analysis. Female sex, older age, high baseline ALT, infection with HBV genotype A, low baseline HBV DNA and absence of previous IFN were found to be associated with an increased likelihood of achieving SVR. A model based on the above mentioned variables had adequate discriminative ability, as shown by an area under the receiver operating characteristics (ROC) curve of 0.72. The area under the ROC curve was 0.75, 0.65, 0.68 and 0.78 for genotypes A to D, respectively. After bootstrap validation, the area under the ROC curve was 0.69. Since the influence of the predictors was significantly different across genotypes, a formula for the prediction of SVR was developed for each HBV genotype separately. In order to facilitate future use of this treatment index for PEG-IFN in HBeAg positive patients, a nomogram for each HBV genotype and an automated (web-based) SVR calculator will be provided.
Conclusion A multivariable model based on the variables sex, age, baseline ALT, HBV genotype, baseline HBV DNA, and previous IFN therapy provides an adequate prediction of sustained off-treatment response to PEG-IFN. The treatment index derived from this model will be a useful tool to guide choice of antiviral therapy in individual HBeAg positive patients in clinical practice.

HBeAg seroconversion induced by nucleos(t)ide analogues in chronic hepatitis B is not durable in a majority of cases

M.J. Perquin[1], J.G.P. Reijnders[1], N. Zhang[1,2], H.L.A. Janssen[1], [1]Dept of Gastroenterology and Hepatology, Erasmus MC University Medical Center Rotterdam, Rotterdam, The Netherlands, [2]Dept of Gastroenterology and Hepatology, Zong Shan Hospital, Fudan University, Shanghai, China

Seroconversion of HBeAg indicates the probable attainment of sustained response in chronic hepatitis B (CHB) patients, currently justifying discontinuation of antiviral therapy after a consolidation period. Yet, long-term durability of HBeAg seroconversion achieved under treatment with nucleos(t)ide analogues (NA) is unclear.In this cohort study, 131 HBeAg positive CHB patients who received more than six months of treatment with any NA were included (69 treated with Lamivudine(LAM), 35 Adefovir(ADV), 18 Entecavir(ETV), 6 Tenofovir(TDF), 1 ADV+LAM, 2 TDF+LAM). Measurement of virologic parameters was done every 3 to 6 months. Seroconversion was defined as loss of HBeAg with appearance of anti-HBe. Relapse of seroconversion was defined as either reappearance of HBeAg or loss of anti-HBe.Baseline characteristics: mean age 35±18 years; m/f 97/34; mean ALT 4.8±6.4 xULN ; mean HBV DNA 8.1±1.6$\log_{10}$ copies/mL. During a median follow up of 98 (24-507) weeks, HBeAg seroconversion was observed in 44 (34%) patients (27 induced by LAM, 12 ADV, 3 ETV, 2 TDF). Four cases were lost to follow-up. Median duration of therapy until HBeAg seroconversion was 28 (7-211) weeks. In multivariate analysis, independent baseline predictors of HBeAg seroconversion were high ALT (OR 1.25, CI 1.11-1.41, P<0.001) and low HBV DNA (OR 0.62, CI 0.45-0.85, P=0.003). Relapse after HBeAg seroconversion occurred in 26 (65%) patients (LAM 19/26 (73%), ADV 6/10 (60%), ETV 1/2 (50%), TDF 0/2 (0%)). Twenty-three (88%) HBeAg relapses occurred during therapy under which sero-conversion was achieved. Fifteen (58%) patients experienced relapse more than 6 months after HBeAg seroconversion, 8 (31%) more than 1 year after HBeAg sero-conversion. Relapse was associated with antiviral drug resistance in 11 (42%) cases. Of 9 patients who stopped therapy after a consolidation therapy of at least 6 months (median duration 67 (25-198) weeks), 3 (33%) experienced off-therapy relapse, 2 (22%) restarted with NA therapy (due to increasing viral load) and 4 (45%) remained HBeAg-negative, anti-HBe positive in absence of therapy.
Conclusion: NA induced HBeAg seroconversion was followed by relapse in a majority of cases, often during treatment. Consolidation treatment of more than 6 months did not induce remission of disease in the majority of cases. Therefore, long-term continuation of treatment with NA after HBeAg seroconversion appears necessary, irrespective of the occurrence of HBeAg seroconversion.

Interferon- rather than ribavirin-related side effects are associated with non-response to peginterferon alfa-2b and ribavirin in naïve chronic hepatitis C patients

L.G. van Vlerken[1], E.J. Huisman[1], H. van Soest[1], G. Boland[1,12], P.J. van der Schaar[2], G.H. Koek[3], R.A. de Vries[4], N.A.M. van Ooteghem[5], B. van Hoek[6], J.P.H. Drenth[7], R.J. de Knegt[8], R.J. Lieverse[9], P. Houben[10], A. van der Sluys Veer[11], P.D. Siersema[1], A.M. van Loon[12], K.J. van Erpecum[1], Depts of Gastroenterology and Hepatology[1] University Medical Center Utrecht, [2]Atrium Medical Center Heerlen, [3]University Hospital Maastricht, [4]Rijnstate Hospital Arnhem, [5]St Lucas Andreas Hospital Amsterdam, [6]Leiden University Medical Center, [7]University Hospital Nijmegen, [8]Erasmus Medical Center Rotterdam, [9]Gelre Ziekenhuizen Apeldoorn, [10]Ziekenhuis Zeeuws Vlaanderen, [11]Onze Lieve Vrouwe Gasthuis Amsterdam and [12]Dept of Virology University Hospital Utrecht, The Netherlands

In the HALT-C trial, less reduction of leucocytes and thrombocytes, and less weight loss at week 20 predicted null-response in hepatitis C patients with advanced fibrosis or cirrhosis retreated with peginterferon alfa-2a and ribavirin, supposedly indicating systemic resistance to interferon. On the other hand, limited decrease of Hb may relate particularly to lower ribavirin levels, with potential relationship to non-response. We treated 244 naïve patients (53% genotype 1-4, 71% viral load >800,000 IU/mL, 33% advanced fibrosis/cirrhosis) with amantadine hydrochloride 200 mg daily or placebo for at least 24 weeks combined with high-dose interferon induction therapy followed by PEG-interferon alfa-2b 1.5 µg/kg/week (Schering-Plough, Maarssen, The Netherlands) and weight-based ribavirin (Schering-Plough: 1000-1200 mg/day). Qualitative measurement of HCV RNA (Cobas Amplicor version 2.0 detection limit 50 IU/ml, Roche Diagnostics) at week 24 was positive in 39 patients (16%: non-responders) and negative in 205 patients (84%: responders). After 24 weeks therapy, average peginterferon dose (1.46±0.17 vs 1.45±0.14 µg/kg/week, p=0.62) did not differ between non-responders and responders, nor did magnitude of interferon-related side effects: decrease from baseline of leucocytes (-4.1±2.9 vs -4.0±2.0x10^9/L), thrombocytes (-50±36 vs -50±51 x10^9/L) or weight loss (-4.8±4.0 vs -5.4±4.9 kg). Average ribavirin dose during 24 weeks therapy (14.0±1.8 vs 15.2±2.5 mg/kg/day, p=0.02) and decrease of hemoglobin (-1.7±0.9 vs -2.0±1.1 mM, p=0.11) were lower in non-responders than responders. Baseline body weight tended to be higher in non-responders (80±15 vs 75±15 kg, p=0.07). Average ribavirin dose (mg/kg/day) correlated negatively with baseline body weight (R=-0.75, P<0.001) and varied from 18.0±1.6 mg/kg/day in case of weight <65 kg to 11.2±1.4 in case of weight >105 kg. Multivariate regression analysis identified HCV genotype 1-4 (OR 65.53, 95%CI 7.01-612.3, p<0.001), age (OR 1.08, 95%CI 1.02-1.15, p=0.01), baseline body weight (OR 1.07, 95%CI 1.03-1.11, p=0.002) and decrease of hemoglobin at T=24 (OR 0.36, 95%CI 0.18-0.70, p=0.003) as independent predicting variables for non-response. We speculate that influences of baseline body weight and hemoglobin drop during therapy are explained in part by their relationship to ribavirin dose. In treatment-naïve patients, ribavirin-related side effects may be better predictors of non-response than interferon-related side effects.

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Early ERCP is only beneficial in predicted severe acute biliary pancreatitis in case of concurrent cholestasis: a prospective multicenter study

H.C. van Santvoort[1], M.G. Besselink[1], A.C. de Vries[2], M.A. Boermeester[3], K. Fischer[4], T.L. Bollen[5], G.A. Cirkel[1], A.F. Schaapherder[6], V.B. Nieuwenhuijs[7], H. van Goor[8], C.H.C. Dejong[9], C.H. van Eijck[10], B.J. Witteman[11], B.L. Weusten[12], C.J. van Laarhoven[13], P.J. Wahab[14], A.C. Tan[15], M.P. Schwartz[16], E. van der Harst[17], M.A Cuesta[18], P.D. Siersema[19], H.G. Gooszen[1], K.J. van Erpecum[19] and the members of the Dutch Acute Pancreatitis Study Group, [1]Dept of Surgery, University Medical Center Utrecht, [2]Dept of Gastroenterology, Erasmus University Medical Center, Rotterdam, [3]Dept of Surgery, Amsterdam Medical Center, [4]Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, [5]Dept of Radiology, St. .Antonius Hospital, Nieuwegein, [6]Dept of Surgery, Leiden University Medical Center, [7]Dept of Surgery, University Medical Center Groningen, [8]Dept of Surgery, Radboud University Nijmegen Medical Centre, [9]Dept of Surgery and NUTRIM, Maastricht University Medical Center, [10]Dept of Surgery, Erasmus Medical Center, Rotterdam, [11]Dept of Gastroenterology, Gelderse Vallei Hospital, Ede, [12]Dept of Gastroenterology, St. Antonius Hospital, Nieuwegein, [13]Dept of Surgery, St. Elisabeth Hospital, Tilburg, [14]Dept of Gastroenterology, Rijnstate Hospital, Arnhem, [15]Dept of Gastroenterology, Canisius Wilhelmina Hospital, Nijmegen, [16]Dept of Gastroenterology, Meander Medical Center, Amersfoort, [17]Dept of Surgery, Medical Center Rijnmond Zuid, Rotterdam, [18]Dept of Surgery, VU medical center, Amsterdam, [19]Dept of Gastroenterology, University Medical Center Utrecht, The Netherlands

We performed a prospective observational study in parallel with a randomized controlled multicenter trial on probiotic prophylaxis in acute pancreatitis to investigate whether early ERCP is associated with reduced complications and mortality in predicted severe acute biliary pancreatitis (ABP) without cholangitis. Between 2003 and 2007, all patients with predicted severe ABP were prospectively followed in 15 hospitals. Patients with potential cholangitis (temp>38.5°C combined with bilirubin >20 µmol/L: n= 23) were excluded. We separately analyzed patients without and with cholestasis (bilirubin >40 µmol/L and/or common bile duct >8 mm with temperature < 38.6°C). Decision to perform early ERCP (<72 hrs after symptom onset) was left to the treating physician and varied among hospitals from 0%-100%. Potential baseline differences (P<0.2) and APACHE-II score were adjusted with logistic regression. 153 patients with predicted severe ABP were included: 78 (51%) exhibited cholestasis. Of the patients with cholestasis, 52 (67%) underwent early ERCP and 26 (33%) conservative treatment. There were no significant baseline differences. Complications were significantly lower after early ERCP than after conservative treatment (25% vs 45%, OR 0.35, 95%-CI 0.13-0.99, P= .049), including >30% pancreatic necrosis (8% vs 31%, P= .010). Mortality was non-significantly reduced after early ERCP (6% vs 15%, OR 0.44, 95%-CI 0.08-2.28, P= .330). Of the patients without cholestasis, 29 (39%) underwent early ERCP and 46 (61%) conservative therapy. The only baseline difference was a slightly higher ASA-class in the conservative group (P= .016). Early ERCP, compared to conservative treatment, did not reduce complications (45% versus 41%, P= .814, adjusted OR 1.36; 95% CI 0.49-3.76; P = .554) or mortality (14% versus 17%, P= .754, adjusted OR 0.78; 95% CI 0.19-3.12, P= .734). In the 81 patients undergoing early ERCP, papillotomy (87% of ERCP's) was associated with reduced complications (adjusted OR 0.24; 95% CI 0.06-0.93; P= .040). Pre-cut papillotomy and cannulation/ contrast injection of the pancreatic duct were not significantly associated with adverse effects. During ERCP, bile duct stones were found in 52% and 41% of groups with and without cholestasis (P= 0.25). ERCP was performed in 7 patients of the conservative group at later stages. Conclusion: Early ERCP was associated with fewer complications in patients with predicted severe ABP, but only in presence of cholestasis.

Endoscopic treatment of ampullary adenomas as an alternative to surgical resection

G.J. de Bruin, J-W. Poley, E.J. Kuipers, Erasmus Medisch Centrum Rotterdam, The Netherlands

Ampullary adenomas can develop into carcinoma through the adenoma-carcinoma sequence. Endoscopic ampullary resection (EAR) is increasingly performed as a less invasive alternative to surgery. However, little is known about the complications and long-term efficacy of EAR. We therefore evaluated the outcome and safety of EAR in a tertiary referral centre. All patients that underwent EAR since 2005 were analyzed. Indications for EAR were high-grade dysplasia (HGD), increase in size during follow-up, bleeding, cholestasis or pancreatitis. Contra indications were proven malignancy and invasion in pancreatic or common bile duct of more than 0.5 centimetres as determined by endoscopic ultrasonography. EAR was performed as follows: after canulation the pancreatic duct is filled with 2-3 ml of diluted methylene blue (1 mg/ml) and contrast. This is followed by lifting of the caudal and lateral parts of the lesion with 0.9% saline. Then the lesion is resected with a snare and removed with a Roth net. To prevent post procedural pancreatitis a 5 french single pigtail unflanged endoprosthesis is placed in the pancreatic duct. The resection margins are treated with Argon plasma coagulation (APC). EAR was performed in 20 patients (M: F 11:9; median age 68; range 34–87 years). Mean size of the lesions was 2.9 cm (range 1–5 cm). Final histopathological examination of resection specimens showed adenoma with HGD and low-grade dysplasia (LGD) in 7 and 11 patients. One specimen contained non-malignant carcinoid. In one patient the resection specimen was lost. During follow-up (range 3-40 months, mean 14 months) no recurrence was observed in 17 patients (85%), two patients were referred for surgery because of persistent HGD after irradical resection, one patient is under endoscopic surveillance because of persistent LGD. Minor complications occurred in three patients: 1 mild pancreatitis and 2 minor bleedings. Major complications were seen in three patients: 1 perforation (treated conservatively), 1 cholangitis (repeat ERCP with stent placement) and 1 patient with pulmonary embolism. No mortality was observed. The overall complication rate was therefore 30% (15% minor; 15% major complications). Although the complication risk of EAR is relatively high, all complications in our series could be managed conservatively without mortality. Since the chance of recurrence after successful resection is low EAR is an attractive alternative to surgical treatment of ampullary adenomas.

Placement of self-expandable stents for non-malignant esophageal perforation

N.C.M. van Heel, V.M.C.W. Spaander, J. Haringsma, E.J. Kuipers, Dept of Gastroenterology and Hepatology, Erasmus MC University Medical Center, Rotterdam, The Netherlands

Esophageal perforation carries a high morbidity and mortality rate. There is no consensus regarding the appropriate treatment modality for this emergency. In the current cohort study we investigated the clinical value of self-expandable metal stents (SEMS) placement for non-malignant esophageal perforation. The aim was to determine the safety and efficacy of SEMS in patients with a non-malignant esophageal perforation. All consecutive patients with a non-malignant esophageal perforation, who were treated by placement of a SEMS at our hospital between 2001 and 2008, were enrolled in this study. Twenty-five patients (72% male; median age 61 years (range: 13-87 months)) were followed after the first placement of SEMS (median follow-up 3 years (range 5-78 months)). Perforation of the esophagus was caused by either Boerhaave's syndrome (n=12) or iatrogenic instrumentation (n=13). Twenty-one patients received a partially-covered stent and 4 patients received a fully-covered metal stent. Placement was technically successful in all patients. Two patients with Boerhaave syndrome required esophagectomy within 2 days. Stent migration was observed in 2 patients and persistent perforation in 5 patients. In these 7 patients (28%), an endoscopic intervention was performed; stent reposition (n=1), stent replacement (n=1), and additional stent insertion (n=5). Stents were removed after a median of 5 weeks post-SEMS insertion (range: 1-37 weeks). No stent-related deaths occurred. Six patients (24%) died within 2 months post-SEMS insertion, due to esophageal perforation (n=4) and to progression of the underlying disease (n=2).
Conclusion: In patients with a non-malignant esophageal perforation, endoscopic placement of a self-expandable metal stent can be effective. The re-intervention rate is considerable, however surgery can be avoided in 92% of patients.

High complication rate in long-term esophageal stenting for non-malignant disease

N.C.M. van Heel, V.M.C.W. Spaander, J. Haringsma, E.J. Kuipers, Dept of Gastro-enterology and Hepatology, Erasmus MC University Medical Center, Rotterdam, The Netherlands

Self-expandable metal stents (SEMS) have been used for a variety of non-malignant esophageal conditions. It is generally advised to remove these stents within 4-8 weeks. Although some of these stents are labelled removable, extraction can be complicated. In this cohort study we investigated the efficacy of SEMS extraction in patients who were treated with a SEMS for a benign esophageal condition for 6 weeks or longer. The aim was to determine the safety and efficacy of esophageal stent insertion for more than 6 weeks in benign diseases. All consecutive patients with a benign esophageal condition who were treated by placement of a SEMS at our hospital between 2001 and 2008, were extracted from a prospective database. Thirty patients were identified. Indications for stent insertion included; Boerhaave's syndrome (n=12), iatrogenic perforations (n=13), mediastinal radiation stenoses (n=1), caustic stenoses (n=2), refractory achalasia (n=1), and fistula after surgery (n=1). Stent removal was peformed within 6 weeks in 23 patients (group I). Stents were removed in 7 patients after 6 to 37 weeks (median: 7 weeks) (group II). Reasons for leaving the stent in place beyond 6 weeks were: persistent symptoms (n=5) and refusal of stent extraction (n=2). SEMS were removed by using a grasping forceps. Stent extraction was successful and without complications in all patients in group I (100%) vs 2 patients in group II (29%).Complications in group II were: self-limiting bleeding (n=1), and stent fracture (n= 4). In 2 patients complete removal was successful after 3 attempts, 1 patient required gastrotomy, and in 1 patient the stent was incompletely removed after 9 attempts. The latter patient subsequently developed a stenosis and a thoracic empyema, 26 and 47 months after incomplete stent extraction respectively.
Conclusions: Self-expandable metal stents for non-malignant esophageal conditions should be removed within 6 weeks after insertion. SEMS longer in place could not be easily removed in the majority of patients and complications occurred in 71%.

Gastrojejunostomy versus duodenal stent placement for the palliation of malignant gastric outlet obstruction: multicenter randomized trial

S.M. Jeurnink[1], E.W. Steyerberg[2], C.H.J. van Eijck[3], E.J. Kuipers[1,4], P.D. Siersema[1,5], Dept. of Gastroenterology and Hepatology[1], Public Health[2], Surgery[3] and Internal Medicine[4], Erasmus MC-University Medical Center Rotterdam and Dept. of Gastroenterology and Hepatology[5], University Medical Center Utrecht, The Netherlands*

Gastric Outlet obstruction (GOO) is a complication of inoperable distal stomach, periampullary or duodenal carcinoma. Although both gastrojejunostomy (GJJ) and duodenal stent placement are commonly used for palliation of obstructive symptoms, it is unclear which treatment is the preferable one. In a multicenter randomized trial 21 hospitals in the Netherlands participated, but only 11 included patients between 2006 and 2008. Thirty-eight patients with malignant GOO were randomized to stent placement or GJJ and were followed-up untill death. Primary outcome was the total area under the survival curve, adjusted for the ability to eat at least soft solids (Gastric Outlet Obstruction Scoring System (GOOSS) score >2). Secondary outcomes were medical effects, quality of life and costs. Analysis was by intention-to-treat. Eighteen patients were randomized for GJJ (mean age 66 + 11 yrs, 50% male) and 20 for stent placement (mean age 66 + 13 yrs, 55% male). Food intake improved more rapidly after stent placement than after GJJ (GOOSS score >2: 4 vs. 7 days; $p<0.01$), but long term (>60 days) relief of obstructive symptoms was better after GJJ. After GJJ, patients had more days with a GOOSS >2 adjusted for survival than after stent placement (72 vs. 50 days; $p=0.05$). More late major complications (5 in 4 pat. vs.0; $p<0.05$) were seen and more reinterventions were indicated (11 in 8 pat. vs. 2 in 2 pat.; $p<0.01$) after stent placement than after GJJ. There was no difference in median survival (46 vs 78 days). Mean hospital stay was 8 days shorter after stent placement than after GJJ ($p<0.05$). Quality of life was maintained after both treatments with no difference between GJJ and stent placement. Total costs for GJJ were higher compared to stent placement (€12325 vs. €8570; $p<0.05$). Despite slow improvement, GJJ gave better long-term relief of obstructive symptoms in patient with malignant GOO. Since GJJ was also associated with fewer complications and reinterventions on the long-term, we recommend it as the primary treatment for relief of obstruction in patients with an expected survival of 2 months or more. Nevertheless, as stent placement was associated with a rapid improvement of food intake, short hospital stay and lower costs, this treatment is preferable for those expected to live shorter than 2 months.

(on behalf of the Dutch SUSTENT study group)*

Feasibility of percutaneous endoscopic jejunostomy (PEJ) and colostomy (PEC) katheters: first results in a Dutch academic centre

T.E.H. Römkens[1], D.J. de Jong[1], J.O. Kristinsson[2], G.J. Wanten[1], [1]Dept of Gastro-enterology and Hepatology, University Medical Centre St. Radboud, Nijmegen, [2]Dept of Gastroenterology and Hepatology, Landspitali University Hospital Reykjavik, Iceland

Introduction:Patients with an indication for post pyloric feeding or colonic lavage or desufflation may be treated by placement of a percutaneous endoscopic jejunostomy (PEJ) or colostomy (PEC), respectively. Information on these relatively novel therapeutic modalities in The Netherlands is lacking so far. We therefore report on our own experience regarding PEJ and PEC-placement. Methods:Twenty two consecutive patients in whom placement of either PEJ or PEC was indicated could be identified between June 2005 and December 2007. All procedures were performed under antibiotic prophylaxis during general anesthesia (PEJ) or conscious sedation (PEC), by a small team of endoscopists. PEJ was performed using a paediatric colonoscope, PEC by means of a standard colonoscope. In all cases either a 15 F poly-urethane or a 20 F silicone PEG catheter was used. Results:In 22 patients (mean age 53 yrs; range 28.2-70.2 yrs; 15 females) PEJ (n = 16; 10 females) or PEC (n = 6; 5 females) placement was attempted The overall technical success rate was 68.1% (15/22), while the overall clinical success rate was 80% (3/15 had to be removed later). Main indications for PEJ were delayed gastric emptying (43.2%) and nonspecific motility disorders (31.2%). The median duration of symptoms before the PEJ-procedure was 10 months (range 1-108). The overall PEJ technical success rate was 9/16 (56,2%); in the first ten procedures 4/10(40%) improving to 5/6 (83.3%) in the last six procedures. In 2 patients (12.5%) the PEJ had to be removed later, because of lacking efficacy or pain at the catheter exit site . Complications were observed in 4/16 (25%) patients, with one major complication (6,25%) in a patient needing acute surgery due to overt perforation. Six patients (5 female) underwent a PEC-procedure. Indications for PEC-procedure were constipation in 5/6 patients (83.3%), or combined constipation and anal sphincter insufficiency in 2/6 patients (33.3%). Median duration of symptoms before PEC-procedure was 48 months (range 16-60). PEC placement was successful in all patients (6/6). Two (33%) PEC's were placed in the descending colon. Apart from pain at the site of the PEC catheter in 2 patients (33%) no complications were seen. In one patient the PEC had to be removed because of this pain (6.25%), this patient received a surgical colonostomy.
Conclusion: In accordance with data in the international literature, PEJ and PEC placement is feasible for the established indications, its clinical success rate (80%) is quite high in difficult to manage patients. However especially for PEJ placement there is a learning curve, and complications do occur.

Endoscopic treatment of pancreatico-cutaneous fistulas after intervention for infected necrotizing pancreatitis

M.C. van Baal[1], O.J. Bakker[1], H.C. van Santvoort[2], M.G. Besselink[2], J.W. Poley[3], J. Heisterkamp[4], H.G. Gooszen[1] and C.H. van Eijck[5] for the Dutch Pancreatitis Study Group., [1]Dept of Surgery, University Medical Center Utrecht, Utrecht, [2]Dept of Surgery, St. Antonius Hospital, Nieuwegein, [3]Dept of Gastroenterology & Hepatology, Erasmus Medical Center, Rotterdam, [4]Dept of Surgery, St. Elisabeth hospital, Tilburg, [5]Dept of Surgery, Erasmus Medical Center, Rotterdam, The Netherlands

Introduction: Pancreatic duct disruption causing a pancreatico-cutaneous fistula is a major cause of morbidity and prolonged hospital stay after intervention for infected necrotizing pancreatitis. The most widely adapted strategy in these patients is conservative treatment. However, endoscopic transpapillary stenting (ETS) of the pancreatic duct may improve ductal outflow and reduce time to fistula resolution. We analyzed the results of ETS for pancreatico-cutaneous fistulas after intervention for necrotizing pancreatitis. Methods: From a prospective cohort of patients with acute pancreatitis admitted in 22 hospitals (2004-till date), all patients that underwent ETS for a pancreatic fistula after percutaneous drainage or surgical necrosectomy for infected necrotizing pancreatitis were identified. A pancreatic fistula was defined as persisting drain production with amylase content greater than 3 times the serum amylase activity. Feasibility, safety and results of ETS were evaluated. Results: Out of 863 patients with acute pancreatitis (varying from mild to very severe), 24 patients underwent ETS for a pancreatic fistula. ETS was not feasible in 4 patients due to papillary edema. The median duration of conservative treatment prior to ETS was 32 days (interquartile range [IQR] 17-76 days). The median number of ETS procedures needed before succesfull stentplacement was 1 (range 1-6). No complications related to ETS were noted. The median duration until fistula resolution was 61 days (IQR 36 – 148 days). Four patients were operated after ETS: two patients received additional necrosectomy and two needed surgical closure of the fistula.
Conclusion: Based on our findings, ETS is a feasible and safe alternative to conservative treatment in patients with pancreatic fistulas after intervention for infected necrotizing pancreatitis and potentially shortens time to fistula resolution. To evaluate the efficacy, future studies comparing endoscopic treatment to conservative and surgical treatment are needed.

Accuracy and interobserver agreement of international experts on a new classification scheme for probe-based confocal fluorescence microscopy

F.J.C. van den Broek[1], A. Meining[2], M.B. Wallace[3], A.M. Buchner[3], J.A. van Es[1], P. Fockens[1], E. Dekker[1], Dept of Gastroenterology and Hepatology, [1]Academic Medical Centre Amsterdam; [2]Klinikum rechts der Isar, Munich; [3]Mayo Clinic, Jacksonville

Probe-based confocal fluorescence microscopy (CFM) enables in-vivo histology during colonoscopy. This technology enables endoscopists to make real time diagnoses and treatment decisions without biopsies. Since probe-based CFM is a new technique, an international collaboration of CFM users was erected to generate a uniform classification for colonic use. The aims of this study were to assess the interobserver agreement and accuracy of this new classification scheme.Patients undergoing colonoscopy for a history of ulcerative colitis (UC) or polyps were included. All detected lesions and random areas of normal colonic mucosa were inspected by probe-based CFM before sampling. Fluorescein i.v. was used to enhance tissue contrast. First, a subset of 10 CFM video sequences was used to generate a uniform classification by an international collaboration of 4 CFM users. Subsequently, the 4 CFM users scored a different set of video sequences by the new classification, as well as by image quality. Histology was used as reference standard.The new CFM classification comprised 3 categories (1-3) concerning vessel-type and 7 categories (1, 2a-e, 3) concerning tissue architecture. In total, 23 patients underwent colonoscopy during which 100 CFM video sequences were made of 46 lesions (5 UC-associated neoplasia, 5 adenomas, 3 sessile serrated adenomas, 30 non-neoplastic, 1 lost for histology) and 56 control areas (non-neoplastic).The inter-observer agreements on vessel-type and tissue architecture were ‘fair’ with kappa-values of 0.39 and 0.35 respectively. When reducing the classification to neoplasia (vessel-type 3 or tissue architecture 3) vs. non-neoplastic only, the agreements became ‘moderate’ (kappa 0.41 and 0.50). Correction for image quality did not change the kappa values.For differentiating neoplasia from non-neoplastic tissue, the consensus diagnosis on vessel-type had a sensitivity and specificity of 80% and 85%. Corresponding figures for tissue architecture were 70% and 93%.
Conclusion: A new classification for probe-based CFM has been generated by an international collaboration group, having a ‘moderate’ interobserver agreement for differentiating neoplasia from non-neoplastic tissue. The sensitivity and specificity were acceptable in this early learning phase. Future research should focus on simplification, learning curve and validation of the CFM classification.

Miniprobe-based confocal fluorescence microscopy is feasible for in-vivo histological differentiation of neoplasia and non-neoplastic tissue in patients with Ulcerative Colitis

J.A. van Es[1], F.J.C. van den Broek[1], P.C.F. Stokkers[1], C.Y. Ponsioen[1], S. van Eeden[2], P. Fockens[1], E. Dekker[1], Depts of [1]Gastroenterology and Hepatology and [2]Pathology, Academic Medical Centre, Amsterdam, The Netherlands

Patients with longstanding Ulcerative Colitis (UC) are advised to undergo colonoscopic surveillance with random biopsies to detect neoplasia. Miniprobe-based confocal fluorescence microscopy (CFM) (GI-CellVizio, Mauna Kea Technologies, Paris) provides in-vivo histology for on-table differentiation of neoplasia and non-neoplastic tissue. The use of CFM may eliminate the need for random biopsies and reduce false positive biopsies during surveillance. The aims of this study are to assess the feasibility of probe-based CFM for surveillance of patients with UC, and to assess histological features of neoplasia and non-neoplastic mucosa in-vivo by using CFM. In this ongoing study, patients with longstanding (>8 yrs) UC undergo colonoscopy. Detected lesions and random areas are examined by CFM. Fluorescein i.v. (10%) is administered for tissue contrast. During CFM imaging, recording time is measured. The video sequences are blindly evaluated afterwards to assess image quality and to describe histological features in-vivo which are compared to final histopathology as reference standard.So far, 14 UC patients have been included (8 male; mean age 56 yrs). In total, 84 CFM video sequences were made. Of 2 areas (2%) no adequate tissue samples were obtained. The remaining 82 video sequences were made of 27 lesions (6 neoplasia), 54 random areas and 1 post-resection scar. One video sequence of a lesion was not usable (1%); the remaining 81 video sequences were evaluated. The median time needed to obtain a video sequence of an area was 68 seconds (IQR: 51-117). During 71% (IQR: 47-90) of this time, actual colonic mucosa was visible on the images. Of all video sequences, 55 (68%) were scored as good or excellent with respect to quality. Assuming CFM-mucosa type 3 (dark epithelial lining and absence of goblet cells) to be associated with neoplasia, the sensitivity of CFM in our learning phase would be 67% (95-CI: 30-90) and the specificity 97% (91-99).
Conclusion: Probe-based CFM is feasible for surveillance in UC, since histological mucosal features can clearly be visualized during 71% of imaging time. CFM has a sensitivity of 67% and a specificity of 97%. However, the learning phase and small number of neoplastic lesions in this study prevent drawing any firm conclusions about sensitivity. Future research should focus on validation of a uniform CFM classification, interobserver agreement and defining the learning curve.

Nurse-administered Propofol (NAP) sedation for endoscopy: first experience in the Netherlands

G. Geerders, J. Haringsma, M. Klimek, E. J. Kuipers, Dept. Gastroenterology & Hepatology and Dept. Anaesthesiology, Erasmus MC Rotterdam, The Netherlands

Propofol is a short acting hypnotic with a rapid onset of action and rapid recovery. It's major adverse effect is severe respiratory depression with apnea. Recent studies have documented the safety of propofol sedation for endoscopic procedures. According to the Dutch CBO guidelines propofol can only be administered by anesthesiologists. In other countries, propofol is also successfully administered by non-physicians under strict monitoring. The aim of this study was to prospectively evaluate the safety of NAP sedation in therapeutic endoscopy. Methods: Over a period of 6 months, patients for interventional gastroscopy, colonoscopy and balloon-enteroscopy received propofol sedation administered by a registered nurse. The dedicated sedation nurse was trained in advanced life-support, mask ventilation, monitoring and specific pharmacology, and certified for the duration of this project. Only patients classified American Society of Anesthesiologists (ASA) class I and II were eligible. Propofol was administered by continuous intravenous infusion with a target controlled infusion (TCI) system (Base Primea, Fresenius/KB Medical). During the procedure, heart rate, ECG, respiration, NIBP and peripheral oxygen saturation was monitored using a Nellcor 5600 (Covidien).Results: Thirty-one patients, median age 45yr (18-75), M/F ratio 8/24, underwent 35 procedures: gastroscopy (10), colonoscopy (6), EUS (1), proximal enteroscopy (9), and distal enteroscopy (9) Average duration of the sedation was 42 minutes, median propofol dose 12,6 mg/kg/hr. Adequate sedation was obtained in all patients, Full recovery of consciousness occurred in 11.2 min (4-24). Neither mask ventilation nor endotracheal intubation was necessary. Hypoxemia (peripheral oxygen saturation < 90%) occurred in 1 patient.
Conclusions: nurse-administered propofol sedation during interventional endoscopy is safe and appropriate, if using an adequately trained dedicated nurse and a strict protocol. Careful selection of patients and adequate monitoring is mandatory.

Incidence of Inflammatory Bowel Disease in the Netherlands 1991-2002: Results of a population based study; the IBD-South Limburg cohort

M.J.L. Romberg-Camps[1,4], M.A.M. Hesselink-van de Kruijs[1], L.J. Schouten[2], P.C. Dagnelie[2], A.D.M. Kester[3], L.P. Bos[4] , J. Goedhard[5], W. Hameeteman[1], F. Wolters[6], M.G.V.M. Russel[7], R.W. Stockbrügger[1], [1]Dept of Gastroenterology and Hepatology, Maastricht University Medical Center, [2]Dept of Epidemiology, University of Maastricht, The Netherlands, [3]Dept of Methodology and Statistics, University of Maastricht, [4]Dept of Internal Medicine and Gastroenterology, Maasland Hospital Sittard, [5]Dept of Internal Medicine and Gastroenterology, Atrium Medical Center Heerlen, [6]Dept of Gastroenterology, Vie-Curi Medical Center Venlo, [7]Dept of Gastroenterology, Medisch Spectrum Twente, Enschede, The Netherlands

An increasing incidence of Inflammatory Bowel Disease (IBD) has been suggested. However, recent data on population based incidence rates within Europe are rare. The primary objective of the IBD-SL registry was to prospectively monitor the incidence of IBD within a stable population of a well-defined geographical and administrative area, namely South Limburg. The incidence was evaluated using standardized registration of all newly diagnosed IBD patients in South-Limburg, the Netherlands, diagnosed between 1-1-1991 and 1-1-2003. Medical records were reviewed in order to verify the diagnosis. To prevent bias because of differences in the age distribution in the IBD-SL region incidence results were corrected using the European Standardized Population figures (ESP). The Estimated Annual Percent Change with confidence interval (EAPC [CI]) was calculated to analyze incidence changes over time. Between 1-1-1991 and 1-1-2003, 1187 patients with IBD (476 Crohn's Disease [CD], 630 Ulcerative Colitis [UC] and 81 Indeterminate Colitis [IC]) were newly diagnosed. The sex distribution (male/female) for CD, UC and IC was 187/289, 350/280 and 43/38, respectively. Mean age was 34 (range: 5.8-79.5) years for CD, 42 (8.2-84.3) years for UC and 42 (13.9-77.7) years for IC. In CD, the incidence peaked between 20-29 years of age, and was higher in females (21.9 per 100.000 person-years [p-y]) than in males (11.6 per 100.000 p-y). In UC, the peak incidence found at 30-39 years of age was not different between males and females (13 per 100.000 p-y), but at older age (60-69 years) a second peak for male patients (12.6 per 100.000 p-y versus female 5.8 per 100.000 p-y) was found. Mean incidence values, per diagnosis were for CD: male 4.8, female 7.6; for UC: male 8.5, female 7.0; and for IC: male 1.1, female 0.9 per 100.000 p-y. The EAPC [95%Confidence Interval] during 1991-2002 was for CD male –3.4% [-10.3%,4.1%], CD female –0.6% [-6.4%,5.5%], UC male –5.3% [-10.6%,0.2%], UC female –4.6% [-10.4%,1.6%], IC male –11% [-24.9%,5.4%], female –1.4% [-16.8%,17.0%] neither of them being statistically significant.

Conclusions: Known age and gender specific differences in incidence were confirmed. We did not observe an increasing incidence for either CD, UC or IC, but we did notice a not statistically significant decrease in the incidence of UC in the study period.

Influence of phenotype on the course of Inflammatory Bowel Disease: A long-term follow-up study of the IBD-South Limburg cohort

M.J.L. Romberg-Camps[1,4], P.C. Dagnelie[2], A.D.M. Kester[3], M.A.M. Hesselink-van de Kruijs[1], M. Cilissen[1], LGJB Engels[4], C. Van Deursen[5], W. Hameeteman[1], F.L. Wolters[6], M.G.V.M. Russel[7], R.W. Stockbrügger[1], [1]Dept of Gastroenterology and Hepatology, Maastricht University Medical Center, [2]Dept of Epidemiology, University of Maastricht, [3]Dept of Methodology and Statistics, University of Maastricht, [4]Dept of Internal Medicine and Gastroenterology, Maasland Hospital Sittard, [5]Dept of Internal Medicine and Gastroenterology, Atrium Medical Center Heerlen, [6]Dept of Gastroenterology, Vie-Curi Medical Center Venlo, [7]Dept of Gastroenterology, Medisch Spectrum Twente Enschede, The Netherlands

Disease course in Inflammatory Bowel Disease (IBD) is highly variable and difficult to predict. To optimize prognostic assessment and therapeutic intervention it is of interest to identify phenotypic characteristics at onset of the disease that could predict future disease course. The aim of this study was to evaluate phenotype at presentation in relation to disease course in a regional population-based IBD patient group followed over a prolonged period of time.IBD patients in South-Limburg, the Netherlands, newly diagnosed between January 1, 1991 and January 1, 2003, were included in a registry (IBD-SL). Medical records were retrospectively reviewed. Patients were classified according to the phenotype at diagnosis. At the end of follow-up (July 1, 2005), disease severity, “surgical” and “non-surgical” recurrence rates, and incidence of recurrence per 100 patient-years, were calculated as outcome parameters. In this study, 1187 patients with IBD (476 Crohn’s Disease [CD], 630 Ulcerative Colitis [UC] and 81 Indeterminate Colitis [IC]) were diagnosed. Ten percent of the patients had no recurrence after diagnosis. In CD, 9.5% of the patients had been operated at diagnosis and, after a mean follow-up of 7.6 years, 50% had undergone at least one resective surgery. In UC, the colectomy rate after a mean follow-up of seven years was 8.3%. In the first year, cumulative total recurrence rates per 100 patient-years for CD, UC and IC were 53, 44 and 42 percent, respectively. Thereafter, approximately one in every three patients had disease recurrence. For CD, small bowel localization and stricturing disease were significant risk factors for surgery; patients who were diagnosed at a young age had a higher risk for all types of recurrent disease. UC patients with extensive colitis were at increased risk for surgery. In UC, older age at diagnosis was an increased risk during the first 2.5 years after diagnosis (HR 1.08), but decreased to 0.77 with longer follow-up. In IC phenotype at presentation was not predictive.
Conclusions: In this population-based study. IBD-recurrence rates were highest in the first year and stabilized subsequently . In CD, phenotype at diagnosis had predictive value for disease recurrence with small bowel localization, stricturing disease and young age, whereas extensive colitis and older age at diagnosis were important predictors in UC. However, in general a relatively benign disease course was observed.

Prognostic factors influencing disease course in Inflammatory Bowel Disease: A long-term follow-up study of the IBD-South Limburg cohort

M.J.L. Romberg-Camps[1,4], P.C. Dagnelie[2], A.D.M. Kester[3], M.A.M. Hesselink-van de Kruijs[1], M. Cilissen[1], LGJB Engels[4] , C. Van Deursen[5], W. Hameeteman[1], F.L. Wolters[6], M.G.V.M. Russel[7], R.W. Stockbrügger[1], [1]Dept of Gastroenterology and Hepatology, Maastricht University Medical Center, [2]Dept of Epidemiology, University of Maastricht, [3]Dept of Methodology and Statistics, University of Maastricht, [4]Dept of Internal Medicine and Gastroenterology, Maasland Hospital Sittard, [5]Dept of Internal Medicine and Gastroenterology, Atrium Medical Center Heerlen, [6]Dept of Gastroenterology, Vie-Curi Medical Center Venlo, [7]Dept of Gastroenterology, Medisch Spectrum Twente Enschede, The Netherlands

Disease course in Inflammatory Bowel Disease (IBD) is highly variable and difficult to predict. To optimize prognostic assessment it is of interest to identify such factors influencing the onset of the disease and disease course. The aim of this study was to evaluate prognostic factors in a regional population-based IBD patient group followed over a prolonged period of time. IBD patients in South-Limburg, the Netherlands, newly diagnosed between January 1, 1991 and January 1, 2003, were included in a registry (IBD-SL). A follow-up questionnaire was developed, and medical records were reviewed. Smoking, appendectomy, family history and educational level were looked at.A total of 1187 patients with IBD (476 Crohn's Disease [CD], 630 Ulcerative Colitis [UC] and 81 Indeterminate Colitis [IC]) were diagnosed. In CD, 53% smoked at diagnosis compared to 20% for UC and 30% for IC ($p < 0.0001$). The percentage of patients having stopped smoking before diagnosis was 16% for CD, 44% for UC and 34% for IC ($p < 0.0001$). With regard to the first three recurrences in CD, "current smoking" had a Hazard Ratio of 1.25 (95%-CI: 1.06-1.48). In UC smoking habits after diagnosis did not significantly influence recurrence rate. Before diagnosis, appendectomy had been performed in 34 CD, six UC and two IC patients. As numbers were small we found no significant influence of appendectomy before diagnosis on disease course in CD, UC and IC. After UC diagnosis, 61 out of 630 patients underwent an appendectomy, there was no significant influence on the disease course in UC. A positive family history was found in 39 CD, 49 UC and 5 IC patients. For second degree family members, this was 17, 13 and 3, respectively, for CD, UC and IC. Even when combining frequencies from the first and second degree family members the figures showed no significant influence on the disease course.Educational level, as retrieved from questionnaire data in 707 patients, did not show any significant influence on the disease course for CD, UC and IC.
Conclusions: In this population-based study, we could confirm the negative influence of smoking in CD. A protective effect of smoking on disease course in UC was not found. Earlier reports on the influence of appendectomy could not be confirmed. Family history and educational level were not of any influence; however, this may be due to small numbers.

Quality of health information on the internet in inflammatory bowel disease

S. van der Marel, D.W. Hommes, H.H. Fidder, Leiden Universitair Medisch Centrum, Leiden, The Netherlands

Background: The Internet is now the largest source of health information and is widely used by patients who are affected by inflammatory bowel disease (IBD). The growing amount of, uncontrolled information available on IBD makes an evaluation necessary.Aims and Methods: To assess the quality of IBD information on the Internet we have searched for health information on IBD, using the phrases 'inflammatory bowel disease', 'Crohn's disease' and 'ulcerative colitis'. The search terms were entered separately into the six most commonly used English language search engines: Google, Yahoo! Search, AOL, MSN search, AlltheWeb, and Altavista. The first 30 results from each search engine were used for initial evaluation. Web sites were broadly categorized as institutional (e.g., government), pharmaceutical, non-pharmaceutical commercial sites (e.g., sponsored site), charitable, support (e.g., personal web), or alternative medicine (e.g., non-orthodox medicine). We evaluated the web sites for content quality using the validated DISCER rating instrument. By using the total DISCERN score, from the 15 questions, the web sites have been grouped into categories of excellent (63–75), good (51–62), fair (39–50), poor (27–38), and very poor (15–26) in content. Word processor Microsoft Word 2003 was used to compute readability statistics of the websites. Free text was scored by using the Flesch Reading Ease and the Flesch-Kincaid Grade Level score. Results: A total of 86 websites were evaluated by two authors: 33% were institutional, 6% pharmaceutical, 29% non-pharmaceutical commercial sites, 5% charitable, 21% support, and 7% alternative medicine. Seventy web sites were excluded from evaluation because they were portals or non-IBD oriented. The DISCERN tool rated 16% of the sites as excellent, 26% good, 38% fair, 12% poor, and 8% very poor. The average rating for institutional websites was 48 (fair), pharmaceutical 38 (poor), non-pharmaceutical commercial sites 51 (good), charitable 57 (good), support 50 (fair) and alternative medicine 35 (poor). Interobserver agreement was good (weighted kappa statistics 0.6 (95% CI 0.41-0.79).
Conclusions: The quality of websites containing information on IBD varies substantially.
Charitable websites appear to have the highest quality of written information and alternative medicine websites the lowest. Most sites have high reading levels, which may compromise the accessibility of the information by broad groups of the population.

Pediatric crohn's disease: the activity at diagnosis, its influence on pediatrician's prescription behavior and clinical outcome five years later

[1]Tamara Mesker, [1]Patrick F. van Rheenen, [2]Obbe F. Norbruis, [3]Jan Uitentuis, [4]Herman J. Waalkens, [5]Gieneke Gonera, [6]Lidy A.T. van Overbeek, [7]Joke Butler, [1]Edmond H.H.M. Rings, [1]Dept of Pediatrics, Beatrix Children's Hospital, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands, [2]Dept of Pediatrics, Isala Clinics, Location Sophia, Zwolle, The Netherlands, [3]Dept of Pediatrics, Medical Center Leeuwarden, Leeuwarden, The Netherlands, [4]Dept of Pediatrics, Martini Hospital, Groningen, The Netherlands, [5]Dept of Pediatrics, Wilhelmina Hospital, Assen, The Netherlands, [6]Dept of Pediatrics, Scheper Hospital, Emmen, The Netherlands, [7]Dept of Pediatrics, Deventer Hospital Location Geertruida, Deventer, The Netherlands

Objectives: Pediatricians tend to treat children with mild CD differently compared to moderate-severe. We hypothesize that the severity of disease at diagnosis does not predict the subsequent clinical course. We compared initial therapies and clinical courses in newly diagnosed children with mild or moderate-severe CD. Patients and Methods: We conducted a retrospective multi-center study in pediatric CD patients (<18 years) that were diagnosed before 2003 with a minimum follow-up of 5 years. Patients were categorized in mild or moderate-severe disease, based on the Pediatric Crohn's Disease Activity Index at diagnosis. We evaluated initial therapies, duration of first remission, number of exacerbations, weight-for-height and height-for-age development and cumulative duration of systemic steroid use after 5 years follow-up.Results: Forty-three children were included (25 mild and 18 moderate-severe disease activity). Amino-salicylate monotherapy was significantly more frequently prescribed in the mild disease group (40% vs.17%, P<0.01). Median total duration of systemic steroid use after diagnosis was 18.3 (range: 9.1-22.6) months in the group with mild disease and 10.4 (5.5-17.9) months in the moderate-severe group (P=0.09). Median time until introduction of immunomodulators was 18.9 months (95% CI 16.3-21.5) in the mild group compared to 12.0 months (95% CI 0-36.9) in the moderate-severe group (P=0.44). Duration of first remission was 15.0 months (95% CI 10.1-19.9) in the mild group and 23.4 months (95% CI 0.1-46.7) in the moderate-severe group (P=0.16). The mean total number of exacerbations in five years was 2.2 (SD 0.9) in the mild group compared to 1.8 exacerbations (SD 1.0) in the moderate-severe group (P=0.28).
Conclusion: This study shows that CD patients with mild disease at diagnosis are treated with less intensive therapies. Unexpectedly, however, these patients tend to have more exacerbations, shorter duration of first remission and longer total duration of systemic steroid use. Our data support the concept that severity of disease at diagnosis does not reliably predict subsequent clinical course. Pediatricians should not guide their therapies according to disease severity at diagnosis.

Infliximab treatment in pediatric IBD: survey of treatment decisions

J.C. Escher, on behalf of the pediatric IBD working group of ESPGHAN,Erasmus MC-Sophia, Rotterdam, The Netherlands

In February 2007, a report on 9 cases of hepatosplenic T-cell lymphoma (HSTCL) in young IBD patients treated with infliximab (IFX) and concomitant immunomodulatory treatment (6-MP or AZA) was published by Mackey et al. (JPGN 2007; 44(2):265-7). Although unknown which treatment is causally related to this fatal malignancy, the report has certainly increased awareness of the risks of long-term complications of immunomodulatory and biological treatment. We evaluated treatment decisions in pediatric IBD patients in Europe after publication of the report. In March 2008, a survey was circulated among members of the IBD working group of the European Society of Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN). Pediatric gastro-enterologists from the United Kingdom, Germany, Belgium, the Netherlands, Sweden, Denmark, Hungary, Czech Republic, Croatia, Italy, and Portugal responded to the survey. Assessing the situation before February 2007, a total of 180 pediatric IBD patients were reported to receive IFX. Of these 180 patients, 157 (87%) were co-treated with 6-MP/AZA, 10% were co-treated with MTX, and 3% had IFX mono-therapy. After the report on HSTCL was published, treatment strategy changed quickly and dramatically: AZA was stopped (after a minimum of 6 months combined treatment) in 89/157 (57%) of the patients, either to continue IFX mono-therapy in 69/157 (44%) or to switch to co-treatment with MTX in 20/157 (13%). IFX was stopped in 19/157 (12%), and in 49 patients (31%), treatment remained unchanged. As such, after Feb 2007, 143 patients were receiving IFX, combined with 6-MP/AZA in 21%, with MTX in 26% and as mono-therapy in 53%. When asked about their current treatment strategy, 63% of pediatric gastroenterologists report to stop AZA in patients with IFX and AZA, either after remission or after 6 months of co-treatment. IFX is stopped by 14%, and IFX is combined with MTX by 18%.
Conclusions: It seems that the recent report of 9 cases of HSTCL has influenced treatment behavior dramatically. Combined treatment of IFX and AZA was common before the report, whereas after its publication, IFX mono-therapy has become the preferred option. At present time there is no data to provide guidance as to what is the safest long-term treatment strategy.

Early occurrence of colorectal carcinoma in IBD patients in non-tertiary cohorts: follow-up on a nation wide long-term survey

J.E. Baars[1], E.J. Kuipers[1], R. Beukers[2], G.W. Erkelens[3], A.C.I.T.L. Tan[4] ,B.L.A.M. Weusten[5], C.J. van der Woude[1], Depts of Gastroenterology and Hepatology, Erasmus MC, Rotterdam[1], Albert Schweitzer ziekenhuis, Dordrecht[2], Reinier de Graaf Gasthuis, Delft[3], Canisius Wilhelmina ziekenhuis, Nijmegen[4], Sint Antonius ziekenhuis, Nieuwegein[5], The Netherlands

Surveillance guidelines in inflammatory bowel disease (IBD) patients (pts) recommend initiating surveillance for IBD after 8-10 yrs of extensive disease and after 15-20 yrs for left-sided colitis. Our aim was to investigate whether these surveillance guidelines reflect the natural history of IBD-related colorectal cancer (CRC) in non-referral centers. IBD related CRC pts in all non-tertiary centers in The Netherlands were identified using the nation wide automated pathology database (PALGA). Pts who had IBD and CRC diagnosed synchronously or metachronously in a pathology report from January 1990 until December 2005 were included. In a 2nd search we included pts < 65 yrs old to minimize interference with sporadic CRC. Further clinical data were obtained to assess the IBD population and to verify the diagnosis of IBD associated CRC. Of selected pts clinical data including age, gender, type of IBD, date of diagnosis of IBD and CRC, follow-up of IBD and CRC and extend of disease were collected from patient charts. Statistical analysis was performed using descriptive statistics, chi-square tests, Kaplan-Meier and log-rank tests. In 40 randomly selected hospitals in The Netherlands, 285 patient charts and pathology reports were assessed to confirm diagnosis and collect clinical data. Overall, in 145 pts < 65 yrs old, diagnosis of IBD related CRC could be confirmed. (92 UC (63.4%), 47 CD (32.4%), 6 indeterminate colitis (4.1%), 66.9% female, mean age 28.74 yrs old (SD 6.39)) Mean time to diagnosis of CRC with entry point confirmed diagnosis of IBD was 9 yrs (SD 6.85), i.e. before the actual start of colonoscopic surveillance. However, mean time to diagnosis from start of IBD related symptoms was 18 yrs (SD 12.33). Location of IBD, type of IBD and gender were not significantly associated with time to diagnosis of CRC. The average IBD population per hospital was 600 pts. On average < 4 pts per hospital developed CRC in a time period of 15 yrs, consistent with a 0.6% CRC risk within 15 yrs follow-up per IBD patient and 0.04% per year per IBD patient, independent of other variables.
Conclusion: IBD related CRC in non-tertiary cohorts generally occurs 9 yrs after diagnosis of IBD and 18 yrs after start of symptoms. The risk for IBD-associated CRC is limited in a regular, secondary IBD population. Therefore, current surveillance strategies need to be adjusted, including equalisation of strategies for left sided- and pancolitis with earlier onset of surveillance.

The role of TNF(-receptor) family members in inflammatory bowel disease

B.J. Olivier[1], M. Greuter [1]and R.E. Mebius[1], [1]Deptartment Mol. Cell Biology and Immunology, Free University Medical Centre, Amsterdam, The Netherlands

Patients with inflammatory bowel disease (IBD) respond to anti-TNF therapy, highlighting the important role played by TNF(-receptor) family members in this chronic inflammatory disease. Inflammatory aggregates found in IBD patients have many characteristics of lymphoid organs; therefore, similar mechanisms for formation and maintenance of these lesions are highly likely. Lymph node formation and structural maintenance is dependant on TNFR1 and LTbR signalling. We have made use of the acute and chronic dextran sodium sulphate (DSS) induced colitis model in C57BL/6 mice. Immunoflourescence stainings were performed for a variety of cell surface receptors and adhesion molecules that are also expressed by stromal subsets in lymphoid organs. These molecules are known to aid in the formation and maintenance of these lymphoid structures. During acute DSS colitis an upregulation of LTbR, TNFR1, TRANCE, PDGFRb and VCAM on stromal cells was observed, which correlated with infiltration of $CD45^+$ cell within the areas of ulceration. At the chronic timepoint of DSS colitis the upregulation of the above mentioned molecules persisted and was accompanied by B cell infiltration and clustering in the ulcerated area. The chronically inflamed areas of ulceration strongly started resembling a tertiary lymph node structure. The area of ulceration within the colon has numerous B-cell follicles, interfollicular areas, lymphatic vessels (Lyve-1+; lymphatic endothelium marker), as well as MAdCAM-1 expressing high endothelial venules. In conclusion, stromal cells within the acutely inflamed colon have the ability to upregulate molecules, which are known to be expressed by stromal cells in secondary lymphoid organs. These stromal cells within the colon can now potentially assist in formation of tertiary structures which occur in chronic colitis through LTbR and TNFR1 triggering.

Serious infections, neoplasms and mortality in association with therapies for Crohn's disease: preliminary results from the ENCORE registry

D.W. Hommes[1], J. Panés[2], J.F. Colombel[3], G. D'Haens[4], P. Rutgeerts[5], A. Ekbom[6], U. Barai[7], H. van Hoogstraten[7], M. Wiekowski[7], C. Antoni[7], [1]Leids Universitair Medisch Centrum, Leiden, Netherlands; [2]Hospital Clinic Provincial, Barcelona, Spain; [3]CHRU Lille, Service d'Hépato-Gastroentérologie, Cedex, Lille, France; [4]Imeldaziekenhuis, Gastro-enterologie, Bonheiden, Belgium; [5]University of Leuven, Division of Gastro-enterology, Leuven, Belgium; [6]Karolinska Institutet, Dept of Medical Epidemiology and Biostatistics, Stockholm, Sweden; [7]Schering-Plough Research Institute, Kenilworth, NJ, United States

Aim: To collect long-term safety data on patients with Crohn' s disease treated with Infliximab (IFX) or Non-Biologic Therapy (NBT). Methods: This is a post-marketing, observational, non-randomized, parallelgroup, safety surveillance registry of CD patients treated with IFX or NBT. The incidence of treatment-emergent adverse events was determined. As of May 2007, a total of 2008 subjects were enrolled: 1166 patients receiving IFX treatment (63% female; mean age 36.4±12.89 years); 842 patients receiving NBT (61% female; mean age 37.5±12.67 years). The median length of follow-up was 13.2 months in the IFX group and 12.7 months in the NBT group. A multivariate Cox's proportional Hazard model was fitted to time to first serious infection, with treatment and prognostic variables based on demographics and disease characteristics in the model. In order to limit the number of variables, prognostic variables were selected based on univariate models (p=0.10). Univariate models included age (continuous), gender, smoking status, draining fistula, disease severity, disease duration, involvement of ileum, and prednisone. Results: At baseline, IFX-treated patients, when compared to the NBT group, had a more severe disease activity index (mean Harvey-Bradshaw index of 8.4±5.55 vs. 6.3±5.16), a higher incidence of draining fistulae (23.3% compared to 9.4%), a longer disease duration (mean time since initial diagnosis 9.1±8.97 vs. 8.0±8.62 years) and increased medical hospitalizations in the 6 months prior to their baseline evaluation (42.8% vs. 37.9%). In addition, more patients in the IFX group were taking narcotic analgesics (8.7% vs. 5.8%), antibiotics (21.5% vs. 13.2%), azathioprine (57.1% vs. 50.4%), 6-mercaptopurine (5.5% vs. 4.0%), and methotrexate (10.9% vs. 5.0%) when compared to the NBT group. Conversely, patients in the IFX group received less corticosteroid treatment at baseline (60% IFX vs. 66% NBT). The multivariate model, which adjusted treatment effect for selected prognostic variables, showed treatment with IFX or NBT was not an independent predictor of serious infection (p=0.30). Factors that were independently associated with serious infection included age (p=0.026), disease severity (p=0.024) and prednisone use (p=0.009).
Conclusions: A Safety Analysis of IFX in CD confirms that corticosteroids, but not IFX, pose an increased risk for serious infection. Additionally, age and severity of disease were associated with occurrence of serious infections.

Breast Cancer Resistance Protein (BCRP/ABCG2) expression is reduced during active colitis and translocated in IBD-related neoplasia

C.L. Koelewijn[1], K.N. Faber[2], M.M. Gerrits[1], H.J. Verhoog[1], H. van Dekken[3], E..J. Kuipers[1], R. Smits[1], C.J. van der Woude[1], Erasmus MC - University Medical Centre Rotterdam, Depts[1] Gastroenterology and Hepatology, [3]Pathology, Rotterdam, The Netherlands[2], University Medical Center Groningen, Dept of Gastroenterology and Hepatology, Groningen, The Netherlands

Introduction: Inflammatory Bowel Disease (IBD) is associated with an increased risk for the development of colorectal cancer (CRC), in which inflammation is thought to play a central role. Breast cancer resistance protein (BCRP/ABCG2) is an active transporter located at the apical membrane of epithelial cells that expels several toxins, carcinogens and drugs from the cells. Consequently, IBD-induced impairment of BCRP could result in unwarranted neoplastic progression due to accumulation of toxic components. Aim & Methods: To investigate the expression of BCRP during inflammation, dysplasia and IBD related CRC. Paired biopsies of both inflamed and non-inflamed colon tissue were collected per patient for quantitative PCR (qPCR). Immunohistochemistry was performed on biopsy specimens collected from the pathology archive of patients with either inactive or active IBD (2 samples per patient), low grade dysplasia (LGD), high grade dysplasia (HGD) or CRC. Expression of BCRP was defined as positive, heterogeneous, or negative if respectively >50%, 15-50%, <15% of the apical membranes of the epithelial cells were positive. Results: qPCR of the paired biopsies of 10 patients displayed an average decrease of BCRP expression of 90% in the inflamed biopsies compared to the non-inflamed biopsies. This result was in accordance with immunohistochemistry in which only 24% (13/54) of the inflamed biopsies showed a positive staining compared to 79% (53/67) of the non-inflamed biopsies ($p<0.001$). Similarly, samples of patients with LGD (n=10), HGD (n=8) and CRC (n=15) showed no expression (0%) of BCRP at the apical membranes of the epithelial cells. However, BCRP was expressed in the cytoplasm of the neoplastic cells in 38% (3/8) of the HGD and 80% (12/15) of the CRC. Conclusion: The expression of BCRP is strongly reduced at the apical membranes of epithelial cells during active inflammation, LGD, HGD and CRC, but not in non-active colitis. Furthermore, BCRP is translocated to the cytoplasm of epithelial cells in IBD-related CRC. This may indicate a decline in protection of the epithelial cells by BCRP in the cascade of inflammation, dysplasia and CRC. However, functional analyses have to be performed.

Progression rate of flat low-grade dysplasia to advanced neoplasia in IBD

F.D.M. van Schaik[1], F.P. Vleggaar[1], G.J.A. Offerhaus[2], M.E.I. Schipper[2], P.C.F. Stokkers[3], C.J. van der Woude[4], D.W. Hommes[5], A.A. van Bodegraven[6], P.D. Siersema[1], B. Oldenburg[1] ,[1]University Medical Center Utrecht, Dept of Gastroenterology and Hepatology, [2]University Medical Center Utrecht, Dept of Pathology, [3]Academic Medical Center Amsterdam, Dept of Gastroenterology and Hepatology, [4]Erasmus Medical Center Rotterdam, Dept of Gastroenterology and Hepatology, [5]Leiden University Medical Center, Dept of Gastroenterology and Hepatology, [6]VU University Medical Center Amsterdam, Dept of Gastroenterology and Hepatology, The Netherlands

Low-grade dysplasia in flat mucosa (fLGD) is frequently detected in patients with Inflammatory Bowel Disease (IBD). Reported rates of progression to advanced neoplasia differ. The aim of our study was to determine the progression rate of fLGD to advanced neoplasia (dysplasia-associated lesion or mass (DALM), high-grade dysplasia (HGD) or colorectal cancer (CRC)) in clinical practice. A nationwide pathology database was consulted to identify patients diagnosed with IBD-associated dysplasia in five university medical centers in the Netherlands between 1990 and 2006. Medical records and endoscopy, pathology and surgery reports of patients found to have definite flGD were reviewed. The progression rate of fLGD to advanced neoplasia was assessed and proportional hazards regression was used to assess potential clinical risk factors. Eighty-three patients (67 ulcerative colitis, 13 Crohn's disease, 3 indeterminate colitis; 46 males; median age at IBD diagnosis, 29 [7-78] years; median age at fLGD diagnosis, 42 [15-78] years) were identified; most patients (60.2%) were found to have unifocal fLGD. In 7 patients (8.4%) fLGD was identified at the moment of IBD diagnosis. Advanced neoplasia was found in 12 patients (14.5%) during follow-up (1 DALM, 3 HGD, 2 CRC, 2 HGD with concurrent CRC, 4 HGD with subsequent CRC). In 37.5% of the patients who developed CRC during follow-up, CRC was only diagnosed in the colectomy specimen. The progression rate to advanced neoplasia was 11.4%, 19.5% and 39.0% after 5, 10 and 15 years of follow-up, respectively. No clinical characteristics were found to predict the progression to advanced neoplasia.
Conclusion: Based on data in clinical practice, LGD in flat mucosa progresses to advanced neoplasia in 14.5% of patients with a progression rate up to 39.0% after 15 years of follow-up.

Active transcellular Ca^{2+} transport in the intestine during health and disease
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S. Huybers, R. Bindels, J. Hoenderop. , Department of Physiology, Radboud University Nijmegen Medical Centre, The Netherlands

Ca^{2+} is a very important cation in the body and is involved in many physiological functions. Therefore, the maintenance of the body's serum Ca^{2+} is of crucial importance and is tightly controlled by the concerted action of the intestine, kidney and bone. Besides passive paracellular transport, fine-tuning of Ca^{2+} homeostasis takes place via active transcellular Ca^{2+} fluxes. In the intestine, active Ca^{2+} absorption can be described as a three-step process consisting of apical entry of Ca^{2+} into the cell via the Ca^{2+} selective channel TRPV6, buffering of cytosolic Ca^{2+} and diffusion to the basolateral membrane via the Ca^{2+}-binding protein calbindin-D_{9k}, and finally extrusion into the blood compartment mediated by the plasma membrane Ca^{2+}- ATPase (PMCA1b). This active Ca^{2+} transport is under strong hormonal regulation, mainly by vitamin D.

Understanding of the expression and regulation of these intestinal Ca^{2+} transporters is necessary to gain knowledge about Ca^{2+} absorption in general and more specifically during disease-related Ca^{2+} disturbances, such as in Crohn's Disease (CD). Using real-time PCR, Western blot and *in vivo* $^{45}Ca^{2+}$ absorption techniques, active intestinal Ca^{2+} transport was investigated in different animal studies. First, the exact localization of Ca^{2+} transporters was thoroughly mapped in mouse and human intestinal samples. Thereafter, the possible effect of prednisolone, a drug frequently prescribed in CD, on active Ca^{2+} transport was determined. Finally, Ca^{2+} balance was analysed in TNF$\Delta$are mice, a model for human CD.

We identified that TRPV6 and calbindin-D_{9k} are exclusively located at the first part of the duodenum and rapidly decrease in abundance towards the jejunum. This confirms that the duodenum is the main site of active Ca^{2+} transport. Prednisolone treatment can significantly affect expression of these transporters, leading to intestinal Ca^{2+} malabsorption and ultimately can contribute to bone disorders as described in CD. The TNF$\Delta$are CD model showed a dysregulated Ca^{2+} balance characterized by reduced vitamin D serum levels, downregulation of Ca^{2+} transporters and a severe decline in bone mineralization.

In conclusion, we identified the duodenum as the main site of active Ca^{2+} transport. A decrease in the expression of active Ca^{2+} transport proteins plays a major role in prednisolone-induced Ca^{2+} malabsorption. Finally, the TNF$\Delta$are CD model can be a suitable model to further study CD-related Ca^{2+} disorders.

Severe malnutrition in Dutch patients with liver cirrhosis

E.J. Huisman[1], B. van Hoek[2], P.D. Siersema[1], K.J. van Erpecum[1], Depts. of Gastro-enterology and Hepatology[1], University Medical Center Utrecht, [2]Leiden University Medical Center, The Netherlands

Prevalence of malnutrition among Dutch cirrhotic patients has not yet been reported. We aimed to explore in detail nutritional state of Dutch cirrhotics. Exclusion criteria were malignancy, acquired immunodeficiency syndrome and other interfering non liver-related diseases. 107 consecutive consenting cirrhotic patients (age 54 ± 12 yrs: 69% male: 32% viral, 23% alcoholic and 45% other causes) in two academic hospitals were evaluated. Child Pugh class A, B and C occurred in 42, 44 and 14 % of cases. We obtained a detailed dietary history of 5 week days and two weekend days with check. Also, three separate tools for assessing malnutrition were used: the subjective global assessment (SGA) adjusted for patients with liver disease by Hasse et al., and two parameters for muscle mass: hand grip strength and mid arm muscle circumference. Body mass index corrected for fluid retention (i.e. ascites and edema) did not differ significantly between Child Pugh classes (CP A 25.8 ± 0.79, CP B 26.2 ± 0.78, CP C 25.5 ± 1.4), nor did caloric intake (CP A 2230 ± 108, CP B 2059 ± 97 and 1978 ± 176). In contrast, protein intake decreased progressively with increasing severity of the disease (CP A 98 ± 5, CP B 90 ± 5 and 81 ± 9, $p = 0.016$). Serum IgA levels (as marker of gut permeability) clearly depended on Child Pugh score (CP A 2.97 ± 0.33, CP B 5.13 ± 0.33, CP C 7.5 ± 0.6 G/L, $p < 0.0001$). Caloric intake did not meet requirements in 39% of patients. Protein and fibre requirements were not met in 55% and 56% of cases. According to the subjective global assessment, 44% of patients were well nourished, 50% classified as mild to moderate malnutrition and 6% were severely malnourished. Hand grip strength (marker for muscle mass) was low in 65% of patients. Mid arm muscle circumference (also marker of muscle mass) revealed that 43% of patients were well nourished, 19% mildly, 24% moderately and 14% severely malnourished. More advanced stages of malnutrition were associated with lower energy (EN) and protein (P) intake (correlation of SGA to both En and P, $p < 0.0001$: hand grip strength to both En and P, $p < 0.0001$: and MAMC to P, $p = 0.04$). Prevalence of moderate or severe protein-calorie malnutrition was higher in patients with more severe liver disease ($p < 0.0001$).

Conclusion: Protein-calorie malnutrition is a frequent event in Dutch cirrhotic patients, especially in advanced stages of the disease. Routine dietary guidance should be considered in cirrhotics.

Increased predicted colorectal cancer survival in asymptomatic patients detected by population-based screening with FOBT

L.G. van Rossum[1], A.F. van Rijn[2], I.P. van Munster[3], J.B. Jansen[1], R.J. Laheij[1], P. Fockens[2], E. Dekker[2], [1]Dept of Gastroenterology and Hepatology, Radboud University Nijmegen Medical Center, Nijmegen, The Netherlands, [2]Dept of Gastroenterology & Hepatology, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands, [3]Dept of Gastroenterology & Hepatology, Jeroen Bosch Hospital, 's-Hertogenbosch, The Netherlands

Introduction and Aim: The aim of colorectal cancer screening is to improve prognosis by the detection of early cancer and precursor stages. Measuring improvement of prognosis directly would take many years. In the mean time there is need for intermediate outcome measures to estimate the improvement of prognosis. We aimed to compare characteristics of asymptomatic colorectal cancer patients and a positive faecal occult blood test with symptomatic colorectal cancer patients. Methods: TNM-classification and tumour stages were assessed in 41 asymptomatic colorectal cancer patients (mean age 64.9 years, 56% male), and in 144 symptomatic colorectal cancer patients (mean age 69.3 years, 56% male). Of the 41 asymptomatic CRC patients, 11 were detected with Hemoccult-II and 30 with OC-Sensor. Tumour staging was performed according to the American Joint Committee on Cancer (AJCC) system, also called the TNM system. According to data from the Surveillance, Epidemiology, and End Results (SEER) program, the five-years predicted survival was estimated by TNM stage and analysed with Wilcoxon log rank test. Results: Predicted 5-years survival was considerably lower in symptomatic patients (59.1%) compared to asymptomatic patients (76.6%, $p<0.0001$). Treatment could be confined to colonoscopy in 27% of the asymptomatic patients compared to 4% of the symptomatic patients ($p<0.0001$). The difference in predicted 5-years survival between colorectal cancer patients with a positive Hemoccult-II® (60.5%) did not significantly differ ($p=0.18$) from symptomatic patients (59.1%), whereas the difference in predicted 5-years survival between colorectal cancer patients with a positive OC-Sensor® (82.4%) and symptomatic patients (59.1%) was highly significant ($p<0.0001$). The distribution of tumours over the colon was comparable between symptomatic and asymptomatic patients ($p=0.3$).
Conclusions: Colorectal cancers were detected at significantly earlier stages in asymptomatic patients with a positive faecal occult blood test compared to symptomatic patients and treatment could significantly more often be confined to colonoscopy in the asymptomatic patients. In this respect, the OC-Sensor® performed better than the Hemoccult-II®. There was no difference in cancer localisation over the colon between screened patients and symptomatic patients, indicating that faecal occult blood tests are capable to detect cancers throughout the entire colon.

Immunochemical faecal occult blood testing is more cost-effective than guaiac faecal occult blood testing and no screening in colorectal cancer screening when implementing randomised controlled data according to intention to screen

L.G. van Rossum[1], A.F. van Rijn[2], E.M. Adang[3], M.G. van Oijen[1], R.J. Laheij[1], P. Fockens[2], J.B. Jansen[1], E. Dekker[2], [1]Dept of Gastroenterology and Hepatology, Radboud University Nijmegen Medical Center, Nijmegen, The Netherlands, [2]Dept of Gastroenterology & Hepatology, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands, [3]Dept of Epidemiology, Biostatistics and MTA, Radboud University Nijmegen Medical Center, Nijmegen, The Netherlands

Introduction and Aim: Cost-effectiveness studies in colorectal cancer(CRC) screening comparing different screening tests have been performed, based on combined data from different studies and different populations. Also assumptions about many aspects of screening, like for example participation rates, are made without scientific data. Generalizability of the results is therefore questionable. We aimed to perform a cost-effectiveness study using data from a screening trial with random FOBT testing.Methods: A screening population of 20,623 persons between 50 to 75 years of age was randomly assigned a guaiac based faecal occult blood test (Hemoccult-II, G-FOBT), or an immunochemical FOBT (OC-Sensor, I-FOBT). We used a Markov model for analysis and the randomised controlled trial was the primary source of data. The model was completed with data from the national cancer registry database and literature. For the quantitative I-FOBT we used the standard cut-off value of 100ng/ml. I-FOBT screening was compared with G-FOBT screening and no screening. Costs were discounted with 4% per year and effects with 1.5% per year. Analyses were performed in accordance with intention to screen. Costs and effects were calculated on a population level and presented per 100,000 persons in respectively euros and life years gained.Results: In the base case, with and without discounting, I-FOBT dominated both G-FOBT and no screening, i.e. I-FOBT resulted in life years gained and cost less than G-FOBT and no screening. Per 100,000 persons, after discounting, I-FOBT resulted in 286 life-years gained and € 4,409,000 less costs compared to G-FOBT screening, and 268 life-years gained and € 5,106,000 less costs compared to no screening. The difference in I-FOBT compared with G-FOBT and no screening was robust for sensitivity analysis of all major cost drivers.
Conclusions: CRC screening with I-FOBT is cost-effective resulting in both life years gained and lower costs compared with both G-FOBT and no screening. Therefore colorectal cancer screening should be implemented in all Western European countries and I-FOBT screening should be preferred over G-FOBT screening.

Cutoff value determines colorectal cancer screening performance with a semi-quantitative immunochemical faecal occult blood test.

L.G. van Rossum[1], A.F. van Rijn[2], R.J. Laheij[1], M.G. van Oijen[1], P. Fockens[2], A.L. Verbeek[3], J.B. Jansen[1], E. Dekker[21]Department of Gastroenterology and Hepatology, Radboud University Nijmegen Medical Center, Nijmegen, The Netherlands, [2]Department of Gastroenterology & Hepatology, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands, [3]Department of Epidemiology, Biostatistics and MTA, Radboud University Nijmegen Medical Center, Nijmegen, The Netherlands.

Introduction and Aim: Some immunochemical faecal occult blood tests (I-FOBTs) are semi-quantitative allowing changing the cutoff value, which can considerably influence the detection rate of CRC and advanced adenomas in CRC screening. However the success of CRC screening is also determined by continued compliance with repeated FOBTs over many years. Participation in primary colonoscopy screening programs is usually quite poor. Therefore at least part of continued compliance with FOBT screening will be determined by the proportion of participants that have to have a colonoscopy. A lower cutoff value will usually result in both more true positive and more false positive FOBTs. We studied the performance of a semi-quantitative I-FOBT, OC-Sensor®, to determine the optimal cut-off value for CRC screening in Western European countries. Methods: Average risk subjects between 50 and 75 years of age with ≥50ng haemoglobin per ml sample solution (≥50ng/ml) were invited for colonoscopy. Advanced adenomas(AA) were defined as adenomas with a size ≥10mm, a villous component ≥20% or high grade dysplasia. Detection rate was defined as the percentage of participants with CRC or ≥1 AA. The ratio between true and false positives was illustrated with the number needed to scope (NNTScope) and defined as the number of persons that have to have a colonoscopy to find one person with CRC or ≥1 AA. In this study the cutoff value was defined to be optimal if the NNTScope was ≤2.0, which means every other colonoscopy a person with CRC or ≥1 AA was found.Results: In total 6,157 patients participated, 526 had an OC of ≥50ng/ml of which 430 underwent colonoscopy. CRC was found in 28 patients and 161 patients had ≥1 AA. At the standard cut-off value of 100ng/ml the detection rate was 2.4%(95% CI 2.0-2.7). The NNTScope was 2.0 at a cutoff value of 76ng/ml, with a detection rate of 2.7%(95% CI 2.3-3.1). One patient with stage I sigmoid cancer, had a test result below this level (59ng/ml).Conclusions: The optimal cutoff value for the semi-quantitative OC-Sensor® in a screening population between 50 and 75 years of age in the Netherlands was 76ng/ml. At this level the detection rate was higher than at the standard level of 100ng/ml and every other colonoscopy a patient with CRC or ≥1 AA was found. We suggest a lower cutoff value than the standard 100ng/ml, that is 75ng/ml for application in population based CRC screening programs in Western European countries.

False negative immunochemical faecal occult blood tests due to delay between test execution and laboratory receipt

L.G. van Rossum[1], A.F. van Rijn[2], J.B. Jansen[1], R.J. Laheij[1], P. Fockens[2], E. Dekker[2], [1]Dept of Gastroenterology and Hepatology, Radboud University Nijmegen Medical Center, Nijmegen, The Netherlands, [2]Dept of Gastroenterology & Hepatology, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands

Introduction and aim: Degradation of haemoglobin in the faecal sample solution of the immunochemical faecal occult blood test, OC-Sensor, might increase false negative test results. This is important, because delay between executing occult blood tests at home and receipt at the laboratory is difficult to control. We aimed to study degradation of haemoglobin in faecal sample solutions of OC-Sensor tests of colorectal cancer screening participants.Methods: Screening participants were asked to self-report the date of home testing. Of 6157 screening participants the proportion of positive OC-Sensor tests (≥50ng haemoglobin per ml sample solution, i.e. ≥50ng/ml) in a group without delay (<5 days) between self-reported home testing and laboratory receipt, was compared with a group having ≥5 days delay and a group having ≥7 days delay. Also we retested 170 tests of positive patients 5 times within 10-14 days. The sample tube capacity is more than sufficient for 5 retests. After each series, tests were resealed and stored at room temperature (±20ºC). Results: Of 6157 participants 3767(61%) reported the date of home testing: in 19% delay was ≥5 days and in 5% ≥7 days. OC-Sensor tests were positive (≥50ng/ml) in 8.7% without delay and in 5.8% with a delay ≥5 days (p=0.01) and in 4.1% with a delay ≥7 days (p=0.03). Quantifiable haemoglobin in the faecal sample solution was on average reduced with 28ng/ml per day (SD 36) with a median of 12ng/ml per day. Of the 170 participants with a positive OC-Sensor test(≥50ng/ml), of whom the tests were retested, 139(82%) had a colonoscopy: 45(32%) had at least one advanced adenoma (but not colorectal cancer) and 8(6%) had colorectal cancer. Within 5 days 5(11%) and within 7 days 10(22%) of the patients with at least one advanced adenoma would have been missed, because quantifiable haemoglobin decreased below the cutoff value of 50ng/ml. After 7 days delay 2 of the 8 cancer patients (25%) would have been missed. Both had stage I cancer and a low initial test value <100ng/ml, where stage I cancer patients on average had 532ng/ml.
Conclusions: The performance of the immunochemical faecal occult blood test, OC-Sensor, is decreased by delay between home testing and laboratory receipt. Cancer patients will probably not often be missed due to this delay, but at least a relevant proportion of patients with advanced adenomas might be missed even with a delay of a few days.

In vivo differentiation between neoplastic and non-neoplastic colorectal polyps by chromoendoscopy-guided confocal laser endomicroscopy: an ongoing prospective study

S. Sanduleanu[1], A. Driessen[2], W. Hameeteman[1], A. de Bruïne[2], A. Masclee[1], Dept of Gastroenterology and Hepatology[1], Dept of Pathology[2], University Hospital Maastricht, The Netherlands

Neoplastic and non-neoplastic colorectal polyps usually share clinical presentation and endoscopic appearance. During conventional endoscopy, distinction is not possible and all identified polyps are removed. This results in increase of endoscopic workload, additional costs and higher rate of complications. Confocal laser endomicroscopy (CLE) is a new image enhanced technique in which real-time histology is generated during endoscopical examination. The combination with chromoendoscopy enables characterization of lesions and allows targeted biopsy sampling. This study aimed i) to analyze differential features between neoplastic and non-neoplastic colorectal polyps by chromoendoscopy-guided confocal laser endomicroscopy (C-CLE); ii) to assess the predictive value of this technique for discrimination between colorectal polyps. Patients undergoing screening or surveillance colonoscopy were prospectively investigated using C-CLE. Chromoendoscopy was performed using indigo-carmine and the pit-pattern was assessed according to the Kudo classification. Hereafter, CLE images were obtained following iv administration of fluorescein 10% and topical use of acriflavin hydrochloride 0.05%. Ex vivo histopathology of colorectal polyps was assessed. In total, 68 colorectal polyps in 56 patients were examined. Ex vivo histology showed 30 neoplastic (12 high-grade dysplasia or beyond, 18 low-grade dysplasia) and 38 non-neoplastic polyps (16 hyperplastic, 22 inflammatory). C-CLE of neoplastic polyps revealed type III-V pit pattern, lack of epithelial surface maturation, crypt destruction, mucin-depleted goblet cells, loss of nuclear polarity, altered vascular pattern, with interstitial leakage of fluorescein. By contrast, C-CLE of non-neoplastic polyps revealed type I-II pit pattern, epithelial surface maturation, minor abnormalities of crypt architecture, preserved appearance of goblet cells, maintained nuclear polarity, and minor vascular abnormalities. Inflammatory infiltrates were detected in all inflammatory (pseudo)polyps. In vivo histology predicted the ex vivo data with a sensitivity of 90.0%, specificity of 94.7% and accuracy of 92.6%.

Conclusion: C-CLE enables differentiation between neoplastic and non-neoplastic colorectal polyps during ongoing endoscopy. Standardized classifications may help to accurately distinguish between different forms of colorectal polyps. This approach may ultimately save time, reduce pathology costs and refine the endoscopic management.

Population preferences for different screening strategies for colorectal cancer in the Netherlands; a discrete choice experiment

L. Hol[1], E. de Bekker-Grob[2], L. van Dam1, B. Donkers[3], E. J. Kuipers[1], D.J.F. Habbema[2], E.W. Steyerberg[2], M.E. van Leerdam[1], M. Essink-Bot[4], [1]Gastroenterology and Hepatology, [2]Public Health, Erasmus MC, [3]Marketing and Organisation, Faculty of Economics, Erasmus University, Rotterdam, [4]Public Health, Academic Medical Center, Amsterdam, The Netherlands

Introduction: Randomized controlled trials provided evidence for the effectiveness of CRC screening. However, the decision to participate or not in any screening program is based on an individual deliberative decision-making process of weighting the test burden (certainty) against the potential (at the individual level uncertain) benefits of CRC screening. Data on individual preferences for CRC screening strategy are lacking. Aims & Methods: We therefore conducted a discrete choice experiment (DCE) to determine individual screening strategy preference and the relative importance of the screening attributes. A DCE questionnaire was designed in which subjects had to choose between fecal occult blood test (FOBT), flexible sigmoidoscopy (FS) and total colonoscopy (TC) (alternatives). Each alternative was characterized by two attributes (screening interval, CRC mortality reduction) with three levels. DCE questionnaire contained three-alternative questions including one opt-out (no screening). DCE questionnaire was sent to 2268 individuals aged 50-75 years old including 770 participants of a FOBT or FS screening program and 1498 individuals from a random population sample. Results: In total 870 of 2268 (37%) of subjects (men 52%; mean age 61±7yrs) returned the questionnaire. 720 questionnaires were analyzable (81 incomplete, 69 invalid). All alternatives and attributes proved to be important for the respondents' preferences. Respondents preferred screening to no screening irrespective of the screening test. Endoscopy screening was preferred over FOBT screening. FS screening at a five year interval with a 70% CRC mortality reduction demonstrated the highest utility followed by colonoscopy screening at a five year interval with a 97% CRC mortality reduction. This suggests that the high burden of TC screening prevents subjects to go for maximal CRC mortality reduction. FOBT screening with 10% mortality reduction was the least preferred screening strategy.
Conclusion: Screening strategy, interval and CRC mortality reduction influence subject's preferences for CRC screening. Subjects in the target population prefer endoscopy screening over FOBT screening irrespective of screening interval and mortality reduction. In contrast, uptake of endoscopy screening in population based screening programs remains low, despite a potential higher CRC mortality reduction. Increasing subjects' knowledge on CRC mortality reduction of different screening strategies is warranted to optimize informed choice.

Colorectal cancers within 3 years after colonoscopy or sigmoidoscopy: frequency and causes

N.D.H. Esveldt[1], H. Geldof[2], W.A. Bode[2], D.R. de Vries[1], P.D. Siersema[1] , [1]Dept of Gastroenterology and Hepatology, University Medical Center Utrecht; [2]Dept of Gastroenterology, IJsselland Hospital, Capelle aan den IJssel, The Netherlands

Tandem colonoscopy studies have estimated miss rates of 15-25% of adenomatous polyps. Colorectal cancer (CRC) with 3 years after previous lower GI endoscopy is suggested to be a measure for missed CRCs. All patients with CRC in a general hospital between 1999 and 2005 were identified. Patients with a previous colono- or sigmoidoscopy within 3 years of CRC detection were subdivided into group A, in which endoscopy reached the CRC site but did not visualise it, group B, in which intubation depth was insufficient to reach the CRC site, group C, in which the bowel was insufficiently prepared, and group D with only previous sigmoidoscopy in which the CRC was localized proximal to the descending colon. Group A was classified as missed CRC. In group B and C, follow-up (FU) was evaluated by studying the pathology database, endoscopy reports and patient charts. Group D was classified as inadequate indication for sigmoidoscopy if at least one alarm symptom for CRC was present.In total, 566 patients with CRC were identified (55% male, mean age 71 ± 11.3 yr). Ninety-one (16%) patients had previous colonoscopy (n=33) or sigmoidoscopy (n=58). In 4 of the previous colonoscopies (12%) and 1 of the previous sigmoidoscopies (1.7%) CRC was not detected within 3 years of CRC detection (group A). In 1 of the previous colonoscopies (3%) and 1 of the previous sigmoidoscopies (1.7%), the site of CRC was not reached and FU did not detect CRC (group B). In 1 patient with previous colonoscopy, FU was not performed due to patient-related factors (3%) (group B). No FU was performed in 3 patients with poor bowel preparation with CRC being detected within 3 years of colonoscopy (9%). Reasons were health organization-related in 2 and patient-related in 1 (group C). In 6 cases (10%), in which the CRC was not reached during sigmoidoscopy, no FU was performed due to health organization-related factors (group B+C). In 4 patients following sigmoidoscopy, the site of the following CRC was proximal to the descending colon (6.9%). All these patients were older than 50 years and had at least one alarm symptom (group D).
Conclusion: Detection of CRC within 3 years of previous colonoscopy (12%) or sigmoidoscopy (1.7%) is comparable to findings from the literature. If a lower GI endoscopy is insufficient (technical reasons, poor bowel preparation), it is important to organize adequate FU. Finally, colonoscopy and not sigmoidoscopy should be considered in patients older than 50 years with at least one alarm symptom for CRC.

Effect of a fish intervention on markers of colorectal carcinogenesis: the FISHGASTRO study

G. Pot [1], G. Majsak-Newman, A. Geelen[1], L. Harvey, FISHGASTRO Study team gastro-enterologists, P. van 't Veer[1], G. Schaafsma[1], E. Kampman[1], E. Lund[2] FISHGASTRO Study team gastroenterologistsF. Nagengast[3], B. Witteman[4], J. Uil[4], J. van Bergeijk[4], P. van de Meeberg[5], R. Timmer[6], A. Tan[7], E. Witteman[7], P. Wahab[8], A. Hart[9], Williams[10], [1]Dept of Human Nutrition, Wageningen University, Wageningen, The Netherlands; [2]Dept of Nutrition, Institute of Food Research, Norwich, United Kingdom, [3]UMC St Radboud, Nijmegen, The Netherlands; [4]Gelderse Vallei Hospital, Ede, The Netherlands; [5]Slingeland Hospital, Doetinchem, The Netherlands, [6]St Antonius Hospital, Nieuwegein, The Netherlands, [7]Canisius Wilhelmina Hospital, Nijmegen, The Netherlands, [8]Rijnstate Hospital, Arnhem, The Netherlands [9] Norfolk & Norwich University Hospital, United Kingdom, [10]James Paget University Hospital, United Kingdom

Several observational studies have indicated that fish consumption is inversely associated with the occurrence of colorectal adenomas and progression of ulcerative colitis (UC), both risk factors for colorectal cancer. N-3 fatty acids in oily fish may favourably influence inflammatory processes involved in colorectal carcinogenesis. Also, other constituents of fish, such as vitamin D and selenium may be involved. It is unknown whether the protective effect of fish is associated only with the consumption of oil-rich fish or also with lean fish consumption. Until now no intervention studies on fish and gastrointestinal health have been performed. The aim of FISHGASTRO is to assess whether oily and/or lean fish consumption reduces the risk of intermediates of colorectal cancer as assessed by mitotic rate, apoptosis, and crypt length in colonic biopsies. The study is a randomised, parallel, multi-centre six months intervention trial. In total, 242 volunteers were randomly allocated to receive one of three interventions: oil-rich fish (salmon) (n=82), lean fish (cod) (n=78), or no extra fish (n=82). Colonic biopsies were collected before and after the six month intervention. Results were analysed using analysis of covariance (ANCOVA) including baseline values of the studied measure. Preliminary results show that after intervention, the number of mitotic cells per crypt was more reduced, although not statistically significant, after intervention with salmon (-1.44 ±3.16) or cod (-1.53 ±3.66) compared to the dietary advice group (-0.83 ±2.50). Colonic apoptosis rates per crypt were less reduced in the salmon (-0.12 ±0.69) and cod group (-0.01 ±0.86, p=0.06) compared to the dietary advice group (-0.21 ±0.59). Crypt length was more reduced in the salmon (0.3 ±3.4) and cod group (1.0 ±3.8), compared to the dietary advice group (2.0 ±12.3). Although results from this study were not statistically significant, they do show a trend that increased fish consumption can contribute to lower mitotic and apoptosis rates, and shorter crypt length, which are all indicators of a reduced colorectal cancer risk. Additional analyses on gene expression and inflammation are ongoing.

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Cumulative risk of developing colorectal adenomas during colonoscopic surveillance in MLH1, MSH2 or MSH6 mutation carriers

M.J.M. Broes[1,2], V. Duif[1,2], N.T.M.Saksens[1,2], N.C.M. Visser[1,2], Y. Woliner[1,2], I.D. Nagtegaal[2], M.C.V van Kouwen[1], F.M. Nagengast[1], Depts of Gastroenterology[1] and Pathology[2], Radboud University Nijmegen Medical Centre, The Netherlands

Lynch syndrome is an autosomal dominant disease caused by a mutation in one of the DNA mismatch repair genes: MLH1, MSH2, MSH6 or PMS2, leading to an increased risk of colorectal tumors. Our aim was to assess the cumulative risk of developing colorectal adenomas and carcinomas during colonoscopic surveillance in MLH1, MSH2 or MSH6 mutation carriers. Clinical and pathologic data of 88 mutation carriers, without previous colorectal tumors or colorectal tumors discovered at first screening, were collected (38 men, 50 women, mean age 37.4 years, range 19-63). Of these patients, 29 had an MLH1 mutation, 35 an MSH2 mutation and 24 an MSH6 mutation. In total, these patients underwent 289 colonoscopies between August 1981 and March 2008. The total follow-up time was 432.5 years (median 3.4y/patient). Survival analyses were used to determine the cumulative risk of developing colorectal adenomas or carcinomas. During screening, 39 adenomas were found in 17 patients (10 men, 7 women, mean age 43.1 years). The mean age of first adenoma diagnosis was 42.5 (MLH1), 44.3 (MSH2) and 46.8 years (MSH6). The cumulative risk of developing adenomas by age 40 was 12% in men (95% CI: 1-24%) and 6% in women (95% CI: 0-14%), but this difference was not significant (OR 0.41, 95% CI: 0.15-1.08). By age 40, the cumulative risk of adenomas was 16% (95% CI: 1-32%) in MLH1 mutation carriers, 8% (95% CI: 0-16%) in MSH2 mutation carriers and 0% (95% CI: 0-0%) in MSH6 mutation carriers. MLH1 mutation carriers had a four times higher risk of developing adenomas compared with MSH2 mutation carriers (OR 4.09, 95% CI: 1.30-12.85). MSH6 mutation carriers had a significant lower risk of developing adenomas compared with MLH1 and MSH2 mutation carriers combined (OR 0.11, 95% CI: 0.01-0.83). Most adenomas were located proximal to the splenic flexure (77%), had tubular histology (77%) and showed low-grade dysplasia (72%). Adenomas found in men showed more often high-grade dysplasia (HGD) than in women (38% vs. 8%, p>0.10). In only 3 patients, colon cancer was found; during previous colonoscopies, no adenomas were detected in these patients.
Conclusions: MLH1 gene carriers have a higher risk than MSH2 carriers in developing colonic adenomas while MSH6 carriers have the lowest risk. Men have a higher risk of HGD adenomas than women. Larger prospective studies should be done to establish whether our findings have consequences for surveillance in Lynch syndrome gene carriers.

Bone morphogenetic protein signaling activity as a predictive marker for survival of patients with colorectal cancer

R.J. Jacobs[1], L. Kodach[1], N. de Miranda, D.W. Hommes[1], G.R. van den Brink[1], H. Morreau[2], J.C. Hardwick[1], [1]Dept of Gastroenterology & Hepatology, [2]Dept of Pathology, Leiden University Medical Center, Leiden, The Netherlands

Background: The ability to identify stage II colonic cancer subgroups with a high risk of recurrence would improve treatment strategies for stage II disease. Therefore predictive markers are needed. Signaling pathways play a central role in tumorigenesis and may be used in the future as independent survival prognosticators. Bone Morphogenetic Proteins (BMPs) are members of the TGFβ superfamily of multifunctional cytokines. We have shown that intact BMP signaling is important for normal homeostasis of the intestinal epithelium and that loss of BMP signaling correlates tightly with progression of adenoma to cancer and occurs relatively early during cancer progression. Previous studies have shown that loss of expression of TGFβ pathway elements such as SMAD4 correlates significantly with poor survival. Although in the early stages of cancer TGFβ exerts a tumor suppressor function, there is considerable evidence that in later stages activity of this pathway correlates with worse clinical outcome. Whether elements of the BMP pathway can be used as predictive markers for survival of patients is not known. Aims and methods: In this study we aimed to investigate whether activity of BMP signaling could predict survival outcome in patients with CRC. We used a large array of 300 colon cancers and performed immunohistochemical (IHC) analysis of BMP signaling components: pSMAD1/5/8, SMAD4 and BMP-Receptor-2 (BMPR2). The IHC staining was scored blinded, quantifying activity of BMP signaling by cytoplasmatic BMPR2, nuclear localization of SMAD4 and nuclear localization of pSMAD1/5/8. The correlation between pSMAD1/5/8 staining, Dukes classification and clinical outcomes, including disease-free survival and overall survival, was analyzed with SPSS version 14 for Windows. Results: The BMP pathway is inactivated, as judged by nuclear pSMAD1,5,8 expression, in 75% of CRCs and this correlates with BMPR2 and SMAD4 loss ($p<0.010$, Fisher's Exact Test). Analysis of Kaplan-Meier survival curves revealed a significant difference in active BMP signaling between patient groups. ($p<0,05$). Conclusion: Our data suggests that BMP signaling plays different roles during colon cancer progression. At an early stages (Dukes A+B) loss of BMP signaling is associated with worse 5 year outcome, while, on the contrary, at a later stage (Dukes C+D) patients with active BMP signaling have worse survival. This implies that BMPs play a dual role in colon cancer progression similar to TGF-β.

Hyperplastic polyps and sessile serrated adenomas as a phenotypic expression of MYH-associated polyposis (MAP)

K.S. Boparai[1, 2], E. Dekker[1], S. van Eeden[2], M.M. Polak[2], J.F.W.M. Bartelsman[1], E.M.H. Mathus-Vliegen[1], J.J. Keller[1], C.J.M. van Noesel[2], [1]Dept of Gastroenterology & Hepatology, Academic Medical Center, Amsterdam, The Netherlands, [2]Dept of Pathology, Academic Medical Center, Amsterdam, The Netherlands

Introduction: MYH-associated polyposis (MAP) is an autosomal recessive disorder caused by a bi-allelic germline MYH mutation and characterised by the presence of multiple colorectal adenomas. These adenomas harbour G:C→T:A transversions in the APC and K-ras genes caused by defective base-excision repair due to MYH deficiency. Occasional hyperplastic polyps (HPs) have been described in MAP patients but a causal relationship has never been investigated. Aims and Methods: We examined the presence of HPs and sessile serrated adenomas (SSAs) in a cohort of 17 MAP patients and studied the occurrence of G:C→T:A transversions in the APC and K-ras gene in these polyps.MAP patients were analysed for the presence of HPs and SSAs. APC and K-ras mutation analysis was performed in adenomas (n=22), HPs (n=63) and SSAs (n=10) from these patients and from a control group of sporadic adenomas (n=17), HPs (n=24) and SSAs (n=17). Results: HPs and SSAs were detected in 8/17 (47%) patients of which 3 (18%) met the criteria for hyperplastic polyposis syndrome (HPS). APC mutations were only detected in adenomas and comprised exclusively G:C→T:A transversions. In HPs/SSAs, 48/51 (94%) K-ras mutations comprised G:C→T:A transversions, compared to 2/7 (29%) sporadic HPs/SSAs in the control group ($p<0.0001$).
Conclusions: HPs and SSAs are a common finding in MAP patients. The detection of almost exclusively G:C→T:A transversions in the K-ras gene of HPs/SSAs strongly suggests that these polyps are causally related to MYH deficiency. This implies that distinct oncogenic pathways, i.e. APC-gene related and non-related, appear to be operational in MAP. Genetic analysis of the MYH gene in patients with HPS and multiple adenomas therefore seems justified.

A complete in vitro assay to diagnose Variants of Uncertain Significance in presumed Lynch syndrome patients (Final report Maag Lever Darm Stichting projectno. MWO 05-16)

M. Drost[1], J.B.M. Zonneveld[1], L. van Dijk[1] and N. de Wind[1], [1]Dept. Of Toxicogenetics, Leiden University Medical Centre, Leiden, The Netherlands

Lynch syndrome (Hereditary Non Polyposis Colorectal Cancer, HNPCC) is an inherited cancer susceptibility characterized by a high risk for the development of colorectal cancer and other cancers, such as endometrium, stomach and ovary cancer. Lynch syndrome is caused by mutations in genes involved in the mismatch repair (MMR) pathway. Determination of the disease-causing mutation within families is important, as this enables to discriminate between family members who are or are not at risk. This liberates the latter from extensive cancer screening procedures, including colonoscopies. Overall, in half of all suspected Lynch syndrome patients an alteration in one of the MMR genes is identified. About half of these mutations are so-called Variants of Uncertain Significance (VUS), generally missense mutations. This class of mutations forms a problem since it is hard to distinguish between pathogenic, disease-causing, mutations and benign polymorphisms. We have developed a complete in vitro assay in which we can measure the mismatch repair activity of a VUS of a MMR gene as found in a presumed Lynch syndrome patient. Sequence data of the VUS is obtained from diagnostic laboratories and used as a basis to create a mutant protein in vitro. Activity of these mutant proteins is measured in a completely in vitro assay and can be accurately quantified on an automated fragment analyzer. Total loss of mismatch repair activity is diagnostic for Lynch syndrome. Our assay has been tested against established pathogenic mutations. In addition we have tested panel of VUS that were assayed never before.This assay does not require patient material, is relatively easy, reproducible and can therefore be carried out in any lab equipped for molecular genetic diagnostics. For these reasons this assay may greatly contribute to the classification of VUSs and therefore to Lynch Syndrome diagnosis.

Additional value of jejunal measurements during 24 hours tonometry in patients suspected of chronic gastrointestinal ischemia

D. van Noord[1], P.B.F. Mensink[1], P.M.T. Pattynama[2], H.J.M. Verhagen[3], E.J. Kuipers[1], Depts. of Gastroenterology and Hepatology[1], Intervention Radiology[2], Vascular Surgery[3], Erasmus MC University Medical Center, Rotterdam, The Netherlands

At our institution twenty-four hour tonometry (24hrTM) in combination with CT angiography (CTA) is the standard diagnostic work-up for patients referred for evaluation of possible chronic gastrointestinal ischemia (CGI). 24hrTM consists of a gastric and jejunal measurement, based on the theory that stomach and jejunum are vascularized by 2 different vessels. The common variant of abdominal vascular anatomy dictates that Treitz ligament divides the supply of the celiac artery (CA) and the superior mesenteric artery (SMA). Compared to the placement of the gastric tonometry catheter, the placement of the jejunal catheter is more invasive, and is usually performed under fluoroscopy and/or endoscopic guidance. In this study we evaluated the additional value of jejunal 24hrTM in patients evaluated for CGI. All patients referred for evaluation of CGI were included. Patients with non-occlusive mesenteric ischemia (NOMI) were excluded. The definition of a pathologic (positive) 24hrTM was a peak >10.6 – 13.6 kPa (depending on the test meal) occurring < 2 hours postprandial. Gastric and jejunal 24hrTM were scored each separately as negative, positive or inconclusive. All diagnostics were discussed in a multidisciplinary team. The outcome of the gastric and jejunal 24hrTM was compared to the consensus diagnosis (CGI or not). In 18 months, 86 patients were analyzed: 13 had no 24hrTM, 9 only had gastric 24hrTM and 13 patients were diagnosed NOMI. So, 51 patients were eligible for evaluation: F 37, mean age 56 (range 17-87) yrs. CGI was diagnosed in 32 patients: 1-vessel (CA 19, SMA 3) in 22, 2-vessel in 6 (CA+SMA 5, CA+ IMA 1) and 3-vessel stenosis in 4 patients. In 16 patients with isolated CA stenosis an abnormal jejunal 24hrTM was found; in 2 with isolated SMA stenosis an abnormal gastric 24hrTM was found. Compared to the consensus diagnosis the sensitivity and specificity for gastric and jejunal 24hrTM were respectively 55% and 100%, and 90% and 94%.

Conclusions: Jejunal 24hrTM seems more sensitive for ischemia as compared to gastric 24hrTM in patients suspected of CGI. This is in contrast with the small additional value of jejunal exercise tonometry as reported before. The higher sensitivity might reflect the limited oxygen reserve of the small bowel mucosa, with a possible superposed mesenteric steal phenomenon. The latter is illustrated by the fact that in patients with CA stenosis frequently jejunal ischemia is measured during 24hrTM.

Properties of the neosquamous epithelium after radiofrequency ablation of Barrett esophagus with early neoplasia

R.E. Pouw[*1], J.J. Gondrie[1], A.M. Rygiel[1], W.D. Rosmolen[1], C.M. Sondermeijer[1], P. Fockens[1], F.J. Ten Kate[2], M. Vieth[3], K.K. Krishnadath[1], J.J. Bergman[1], [1]Gastroenterology, Academic Medical Center, Amsterdam, The Netherlands, [2]Pathology, Academic Medical Center, Amsterdam, The Netherlands, [3]Pathology, Klinikum Bayreuth, Bayreuth, Germany*

Radiofrequency ablation (RFA) is safe and effective for eradication of Barrett esophagus (BE) and associated dysplasia. But, it has been suggested that the neosquamous epithelium (NSE) that regenerates after RFA may retain genetic abnormalities of the baseline BE and may harbor buried Barrett glands (BB) that can not be adequately sampled with standard biopsies. At baseline and 2 months after final ablation, the pre-RFA BE and post-RFA NSE were sampled by brush cytology. Multi-color fluorescent in-situ hybridization (FISH) was performed on cytology brushes using probes for centromeric regions of chromosome 1 and 9, and locus-specific probes for 9p (p16) and 17p (p53). At least 12 months after the last RFA, 4Q biopsies were obtained for every 2 cm of the NSE, and from untreated squamous mucosa. Keyhole biopsies were taken from all NSE biopsy sites. An endoscopic resection (ER) specimen was obtained from the NSE. Two expert pathologists, blinded to the origin of the specimens, scored histological depth for each biopsy and ER fragment and determined if BB was present. 23 consecutive BE patients with HGD (n=20)/LGD (n=3) were included. Complete removal of dysplasia and intestinal metaplasia was achieved in all patients. All pre-RFA BE cyto-brushes showed FISH abnormalities: numerical chromosomal changes (60%), loss of p16/p53 (90%), both (50%). All post-RFA NSE cyto-brushes, however, showed a normal diploid signal count for all FISH probes. Of the 23 patients included, 15 participated in the histology depth evaluation (exclusions: unrelated death (1), co-morbidity (3), initial BE < 2 cm (4)). There was no difference in biopsy depth between NSE and untreated squamous mucosa. Keyhole biopsies sampled sub-epithelial structures more often than standard biopsies (59% vs. 39%). All ER-specimens included submucosa. No BB was found in any of the NSE biopsies or ER specimens.
Conclusion: RFA of BE-dysplasia results in eradication of all oncogenic abnormalities and results in endoscopically and histologically normal appearing NSE. Biopsies from NSE after RFA contain full epithelium in all cases and ~40% of biopsies contain lamina propria, comparing favorably to biopsies from normal untreated squamous mucosa. No biopsies or ER specimens had BB. The hypothesis that absence of BB after RFA reflects insufficient biopsy sampling depth is, therefore, invalid.

Optimising patient's flow undergoing esophagectomy for carcinoma with reconstruction by predicting the durations of surgical procedure and length of stay at the intensive care unit

D.T. Nguyen[1,2], M. Van Houdenhoven[1], M.J. Eijkemans[2], E.W. Steyerberg[2], G. Wullink[1], H.W. Tilanus[3], G. Kazemier[1,3], Dept of Operating Rooms[1], Center for Clinical Decision Sciences, Dept of Public Health[2], Dept of Surgery[3], Erasmus MC - University Medical Centre, Rotterdam, The Netherlands

Nowadays it is no exception that patients must be rescheduled as there is no space at the surgical schedule or no available intensive care bed.. Accurate durations of a patient's stay at the operation room (OR) and intensive care unit (ICU) are a prerequisite for efficient planning to prevent patient cancellations, idle time, and under and over utilization. We aim to develop models to predict session times and length of stay at the ICU of the surgical procedure esophagectomy for carcinoma with reconstruction using individual patient characteristics. Methods: Data of 518 consecutive patients, who underwent esophagectomy for carcinoma with reconstruction between January 1997 and April 2005, were included to construct and validate the models. Multivariable linear regression models for session times and length of stay at the ICU were developed and bootstrap methods were used to validate the models. The models were applied on 65 patients in the period May 2005 and April 2006 to realize the actual effect of the models. Results: The model for session times had a validated R2 of 38%. In this model significant variables were: patient's age, sex, body mass index, type of carcinoma, summed age of the two surgeons, type of approach, and type of reconstruction. The prediction model allows for at least 5.2% gain in OR utilization. The model for length of stay at the ICU had a validated R2 of 45%. Significant variables were patient's age, sex, comorbidities, type of approach, preoperative respiratory minute volume, complications within 72 hours occurring at the ICU. This model reduced the number of deficit ICU days with 65 and increased the number of excess ICU days with 23.
Conclusions: Accurate individual predictions for session times can be calculated with a model that include patient, tumor, and procedural characteristics. A conservative calculation shows that 7% more esophagectomies can be performed and up to 15% less patient cancellations.

Morbidity in immigrants of Turkish descent undergoing upper gastrointestinal endoscopy

A.I. Wegman, R.J.L.F. Loffeld, Dept of Internal Medicine, Zaans Medisch Centrum Zaandam, The Netherlands

Introduction: Upper GI-endoscopy is widely used in cases of dyspepsia and reflux. From earlier studies it is known that the morbidity in upper GI-abnormalities in Turkish patients differs from authentic Dutch patients.Aim: Study the yearly yield of upper GI-endoscopy in relation to gender and H.pylori in patients of Turkish descent.Methods: The results of endoscopy done in all consecutive Turkish patients, in a period of 16 years, were included. All repeated endoscopies were excluded. Results were noted in a standardised report. H.pylori detection was done with HE-, immuno-, and Gram's stain, and culture. Significant diagnoses were ulcers, oesophagitis and cancer.Results: In the sixteen years 23251 consecutive endoscopies were done. Of these 2427 procedures were done in patients of Turkish descent. After exclusion of repeated endoscopies 842 first endoscopies in Turkish women and 827 procedures in Turkish men remained. Peptic ulcer disease was seen in 101 (6%) patients, reflux disease in 97 (5.8%). Seven patients had cancer. In 749 patients (64%) no macroscopic abnormalities were seen.Of the men 522 (64%) was H.pylori-positive, 202 (24%) was H.pylori-negative, and from 103 (12%) no data were available. For Turkish women these data were 506 (60%), 252 (30%) and 84 (10%) respectively. Turkish men harboured significantly more often H.pylori ($p=0.03$). This did not change if al missing data were considered H.pylori-positive. In the course of the years there was a clear decrease in prevalence of H.pylori in both men and women. The number of peptic ulcers in men decreased while the number of men with reflux oesophagitis increased. Women had a lower prevalence of ulcers and oesophagitis during each year. H.pylori-positive Turkish men were significantly younger than H.pylori-negative men, mean age 38.7 years (standard deviation 12) and 42.5 years (SD 15) respectively ($p<0.0001$). H.pylori-positive Turkish women had the same age as H.pylori-negative women, 39.2 years (SD 12.8) and 40.4 (SD15) respectively. The prevalence of H.pylori decreased with increasing age.
Conclusion: The prevalence of H.pylori in Turkish patients decreases. There a clear differences in morbidity between men and women. Prevalence of H.pylori decreases with increasing age. This is in discordance with the well-known age cohort effect. Reflux oesophagitis, being rare in this population, is increasing in prevalence, ulcer disease is becoming rare.

The influence of socioeconomic status on proton pump inhibitor (PPI) use in a large population in the Netherlands

O.S. van Boxel[1], M.P. Hagenaars[2], A.J.P.M. Smout[1], P.D. Siersema[1], [1]Dept of Gastro-enterology and Hepatology, University Medical Center Utrecht, The Netherlands [2]Achmea Health Insurance, Leiden, The Netherlands

PPIs are the standard treatment for symptomatic gastro-oesophageal reflux disease (GORD). It has been demonstrated that medical reasons for the first-time prescription of PPIs are inappropriate in 20% of prescriptions. The socio-demographic environment of prescribers and patients may well affect decisions related to drug therapy. The aim of this study was to investigate whether a correlation exists between socio-economic status (SES) and PPI use in the Netherlands. Data was collected retrospectively from a large anonymized computerized database of a Dutch health insurance company. Patients having had at least one prescription for a PPI in the year 2006 were classified as PPI users. The remaining patients were classified as non-PPI users. The date of the first dispensation was set as the index date. The Medical Possession Rate (MPR) was calculated to further subdivide PPI users into chronic users, defined as an MPR ≥80%, and intermittent users, defined as an MPR <80%, during a 6-month follow-up period after the index date. SES was based on neighbourhood level of residence. Logistic regression was performed to determine socioeconomic factors associated with PPI use.A total of 1,972,529 insured were included, 233,819 (11,9%) subjects had reimbursed minimal one PPI prescription, of whom 74,456 were chronic- and 83,951 were intermittent users. 75,412 subjects filled out only one prescription. In a multivariable analysis, adjusting for age, sex, urbanisation and medical confounders, low SES [OR 1.18, CI 1.16-1.20] was positively associated with PPI use. Concurrent nonsteroidal anti-inflammatory drug (NSAID) use was also a positive predictor of PPI use [OR 5.31, CI 5.23-5.40] as was the use of promotility drugs [OR 9.24, CI 8.65-9.87] which are frequently prescribed as second-line therapy in GORD, and polypharmacy [OR 3.58,CI 3.38-3.80], a measure of comorbidity. Positive predictors for chronic PPI use, compared to intermittent PPI use, were increasing age [OR 4.22, CI 3.93-4.52] and low SES [OR 1.07, CI 1.04-1.11] Females were less likely to be chronic users than males [OR 0.89, CI 0.87-0.90] as were patients using NSAIDs [OR 0.69, CI 0.66-0.71].
Conclusion: Patients with a low SES use PPIs more frequently and more chronically. Even in a health care system in which medical care is performed according to well established guidelines, social differences seem to exist in prescription behaviour of PPIs.

Does extended proton pump inhibitor therapy after H. pylori eradication increase cure rates of H. pylori positive peptic ulcers? a systematic review

M.J.R. Janssen[1,2], D. Huis in 't Veld[1], L. Stikkelbroeck[1], W.A. de Boer[3], [1]Dept of Internal Medicine, Slingeland Hospital, Doetinchem, The Netherlands, [2]Dept of Nuclear Medicine, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands, [3]Dept of Gastroenterology, Bernhoven Hospital, Oss, The Netherlands

Background: Many patients with H. pylori positive peptic ulcer disease receive additional proton pump inhibitor therapy after finishing therapy for H. pylori eradication in the assumption that this is necessary for adequate ulcer healing. However, several small studies suggest that H. pylori eradication alone may suffice. However, these results may be due to type II error caused by the small sample size. In order to overcome this problem we performed a systematic review. Methods: The literature (until March 2008) was searched in order to identify randomized clinical trials investigating patients with peptic ulcer disease and comparing ulcer healing rates for modern triple therapies for H. pylori eradication with prolonged PPI-treatment with exactly the same regimen without prolonged PPI-treatment. The overall risk difference (with - without prolonged PPI--treatment) was calculated by pooling the risk differences of the individual studies weighted by the inverse of their variances. Results: Nine studies, investigating a total of 1,564 patients with (nearly all) duodenal ulcers were identified. No studies focused on patients with gastric ulcers. There was only little variation regarding therapy regimen and duration of the extended PPI-treatment. Pooled duodenal ulcer healing rates were 85.3% (658/771) for patients with extended PPI-treatment and 84.2% (668/793) for patients without extended PPI-treatment. The (weighted) overall risk difference was 0.7% (95%CI: -2%;4%).
Conclusion: Extended treatment with a proton pump inhibitor after therapy for H. pylori eradication does not increase cure rates of H. pylori positive duodenal ulcers. There are insufficient data for gastric ulcers.

Serum level of leptin: a potential marker for patients at high risk of gastric cancer?

L.G. Capelle[1], A.C. de Vries[1], J. Haringsma[1] , C.W.N. Looman[2], N.M.A. Nagtzaam[1], H. van Dekken[3], F. ter Borg[4], R.A. de Vries[5], E. J. Kuipers[1], [1]Depts of Gastroenterology and Hepatology, [2]Public Health, and [3]Pathology, Erasmus MC University Medical Center, Rotterdam, [4]Dept of Hepato-gastroenterology, Deventer Hospital, Deventer, [5]Dept of Hepato-gastroenterology, Rijnstate Hospital, Arnhemm The Netherlands

Surveillance of patients with premalignant gastric lesions remains dependent on biopsy sampling. This approach is hampered by its invasive nature, potential sampling error and interobserver variation. Serological markers are of interest as a screening tool to detect patients at high risk of gastric cancer. Leptin is produced by adipocytes and the stomach lining and have been linked with several types of cancer. Therefore leptin could be suggested as a new serological marker for the gastric carcinogenesis. The aim of this case-control study was to evaluate whether serum leptin levels are associated to intestinal metaplasia (IM) and could therefore serve as an early prognostic tool for gastric cancer. Patients with previously diagnosed IM were considered to be cases, patients with no diagnosis of IM were considered to be controls. All patients underwent endoscopy. Fasting serum was collected and random biopsies were obtained from at least four intragastric locations. IM was defined according to the updated Sydney Classification. Serum levels of leptin, pepsinogens (PG), gastrin and H. pylori antibodies were measured using enzyme immunoassays. Multivariate regression analyses were performed to estimate the association between IM and serum leptin levels and other serological markers. In total, 123 cases (M/F 67/56, mean age 60, 23 to 81 yrs) and 98 controls (M/F 42/56, mean age 48; 18 to 76 yrs) were included. Fasting serum was collected in 218 patients. Serum leptin levels were correlated with age and BMI (both $p<0.001$) in all subjects. Males demonstrated significantly lower leptin levels as compared to females ($p<0.001$). In cases, the median level of leptin was 116.6 pg/ml (interquartile range(IQR) 75.0-207.5) versus 81.9 pg/ml (IQR 32.9-207.0) in controls ($p=0.01$). After adjustment for age, sex and BMI, leptin levels were significantly higher in male cases than in male controls ($p<0.001$) in females no association was found ($p=0.13$). Male sex, age, pepsinogen I<28 ug/l, H. pylori status and a high serum leptin concentration were identified as the most accurate predictors of intestinal metaplasia. Conclusions: High serum leptin levels are associated with an increased risk of intestinal metaplasia in males and not in females, independently of BMI. Therefore high serum leptin levels may serve as an early prognostic tool for progression to gastric neoplasia in males.

Exploring the causative role of MYCN in esophageal atresias

(Final report Maag Lever Darm Stichting projectno. MWO 05-71)

A.P.M. de Brouwer[1], C. Marcelis[1], E. van Beusekom[1], P. Rieu[2], H. Brunner[1], H. van Bokhoven[1], [1]Dept of Human Genetics and [2]Pediatric Surgery, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands

Introduction & objective: Feingold syndrome (FS) is the most frequent cause of familial syndromic gastrointestinal atresia and follows an autosomal dominant mode of inheritance. FS is caused by mutations in exon 3 or deletions of the *MYCN* gene, resulting in haploinsufficiency of both the canonical MYCN protein and the shorter isoform, ΔMYCN. In this project, the role of *MYCN* in gastrointestinal atresia is explored in depth by screening a large cohort of patients with FS and related disorders for *MYCN* mutations. Patients with a mutation have been used to establish a distinct phenotype-genotype correlation, facilitating a molecular diagnosis of FS patients. In addition, other genes that are closely related to *MYCN* have been screened for deletions and/or duplications. Finally, the isoform-specific expression pattern of *MYCN* in human development has been established.
Methods: Mutations were identified by direct DNA sequencing, multiplex ligation-dependent probe amplification, and quantitative real-time PCR (QPCR). The *MYCN* expression pattern has been established by QPCR in 11 human fetal tissues.
Results and conclusions: We identified novel *MYCN* mutations in 17 families with FS, including seven mutations in exon 2 that result in a premature termination codon (PTC) solely in the long *MYCN* transcript. Moreover, we have identified a PTC in exon 1 that only affects the ΔMYCN isoform, and did not have a phenotypic effect. This suggests that mutations in *ΔMYCN* do not contribute to the Feingold syndrome. In addition, we found three novel deletions encompassing *MYCN*. No deletions or duplications were identified in genes closely related to *MYCN*, such as *SHH*, *FAM58A*, *MAD*, *GLI-2*, and *GLI-3*. In total, we have now four missense mutations in the DNA binding domain, 19 PTCs of which six render the transcript subject to nonsense-mediated decay, and five larger deletions in a total of 77 patients. We have reviewed the clinical features of these 77 patients, and found that digital anomalies (brachymesophalangy, toe syndactyly) are the most consistent features and are present in 100% and 97% of the patients, respectively. Only two FS patients with digital anomalies did not have a *MYCN* mutation. Small head circumference was present in 89% of the cases. Gastrointestinal atresia remains the most important major congenital anomaly in FS (55%), but cardiac and renal anomalies are also frequent. The isoform-specific expression pattern in human fetal tissues supports this clinical phenotype.

Distribution of small intestinal fat delivery influences satiety and food intake

P.W.J. Maljaars[1], E.H. Haddeman[2], H.P.F. Peters[2], A.A.M. Masclee[1], [1]Division of Gastro-enterology-Hepatology, Dept of Internal Medicine, University Hospital Maastricht, Maastricht, The Netherlands, [2]Unilever Food and Health Research Institute, Unilever Research & Development Vlaardingen, Vlaardingen, The Netherlands

Ileal delivery of fat more potently decreases hunger and food intake compared to both duodenal and oral fat delivery. Animal data suggests that the length of intestinal segment exposed to fat may also affect hunger and food intake. The objective of this study was to test whether increasing the luminal surface exposed to fat will lead to a decrease in hunger and food intake versus oral consumption or a purely ileal infusion. Methods: 15 volunteers (9 female, mean age 22 yr, BMI 23 kg/m2) were intubated with a naso-ileal tube. Each subject received 4 treatments on 4 consecutive days in balanced order Oral control (control) was a liquid meal (145 kcal , carbohydrates and proteins) with 6 g of high oleic rapeseed oil added (190 kcal in total). This meal was ingested at t=0 min, and the ileum was perfused with saline from t=30-120 min. This was compared to the fat-free liquid meal (145 kcal) at t=0 min, with 6g of oil delivered in the intestine, either sequentially (Seq) (2g to duodenum at t=30-60 min, 2g to jejunum at t=60-90 min, 2g to ileum at t=90-120 min), simultaneously (Sim) at t=30-120 min (2g ileum, 2g jejunum and 2 gram duodenum simultaneously from 30-120 min), or 6g to ileum only (Ileum) at t=30-120 min. Satiety scores (VAS, AUC) were collected throughout the test day at regular intervals. Food intake was assessed with an ad libitum meal at t=180 min. Data were analyzed using ANOVA with subjects as blocks and treatments as factors, and baseline values as covariates, followed by Dunnett test. Results: Ileum and Sim more significantly reduced hunger compared to Control ($p<0.05$), while Seq did not differ from Control (AUC was 51, 49, 44 and 44 mm/min, Se=5.4 for Control, Seq, Sim and Ileum, respectively). The other satiety parameters (except for fullness) showed similar results. Food intake: Ileum reduced food intake significantly over Control ($p<0.01$) while Seq and Sim did not differ from Control (499, 480, 458 and 422 grams, Se=40 for Control, Seq, Sim and Ileum, respectively).
Conclusions: Continuous ileal fat infusion has the most pronounced effect on food intake and satiety, pointing to the efficacy of the ileal brake in affecting eating behaviour. Increasing the areas of intestinal fat exposure only affects eating behaviour when fat is delivered simultaneously but not sequentially over the exposed areas. Intestinal, especially ileal, feed back mechanisms offer excellent opportunities for regulation of caloric intake and weight management.

Magnetic resonance enteroclysis in the diagnosis of small bowel neoplasms. Diagnostic accuracy and interobserver variance

S.J.B. Van Weyenberg[1], M.R. Meijerink,[2], M.A.J.M. Jacobs,[1], D.L. Van der Peet[3], C. Van Kuijk,[2], C.J.J. Mulder[1], J.H.T.M. Van Waesberghe[2], [1]Dept of Gastroenterology and Hepatology, [2]Dept of Radiology, [3]Dept of Surgery, The Netherlands

Small bowel neoplasms are rare entities and are often difficult to diagnose. We evaluated the diagnostic accuracy and interobserver variance of magnetic resonance enteroclysis in diagnosing small bowel neoplasms. Magnetic resonance enteroclysis studies of 91 were retrospectively evaluated by two radiologists blinded to clinical details. Radiological findings were compared with findings of double balloon endoscopy (n=45), surgery (n=18), esophagogastroduodenoscopy (n=3), ileocolonoscopy (n=2), autopsy (n=2), and clinical follow-up > 1 year. Efficacy parameters were calculated with 95% confidence intervals. The number of magnetic-resonance-enteroclysis-studies interpreted as depicting small bowel neoplasm was 31 (reader 1) and 33 (reader 2). The number of studies interpreted as depicting small bowel malignancy was 19 (reader 1) and 17 (reader 2). In 32 patients the presence of small bowel neoplasm was histopathological confirmed. In 19 of these patients the neoplasm was malignant. Sensitivity, specificity and weighted kappa values of MRE in diagnosing small bowel neoplasms were 0.91-0.94, 0.95-0.97 and 0.928 respectively. For diagnosis of small bowel malignancy these values were 0.79-0.90, 0.97 and 0.931 respectively.

In conclusion, the overall diagnostic accuracy of magnetic resonance enteroclysis in detecting small bowel neoplasms is 0.95. For small bowel malignancy diagnostic accuracy is 0.93-0.96. Kappa values for MRE diagnosis of neoplasm and malignancy were 0.928 and 0.931 respectively. Therefore magnetic resonance enteroclysis seems a promising tool in the diagnosis of benign and malignant small bowel neoplasms.

Regional and temporal stability of the intestinal microbiome

M.E. Grasman[1], A.E. Budding[2], C.J. Mulder[1], C.M.J.E. Vandenbroucke-Grauls[2], P.H.M. Savelkoul[2], A.A. van Bodegraven[1], Dept of Gastroenterology and Hepatology[1], Dept of Medical Microbiology and Infection Control[2], VU University Medical Centre, Amsterdam, The Netherlands

The intestinal microbiome is implicated as an essential factor in the pathogenesis of IBD, although the exact role remains elusive. Since most intestinal bacteria are uncultivable, we developed a rapid, highly reproducible molecular method for high throughput bacterial profiling. Our aim was to determine the regional and temporal stability of the intestinal microbiome adherent to colonic mucosa (MAM) and in faeces by means of IS-pro. This method is based on two features of the bacterial genome: the length of the interspace (IS) region between the 16s and the 23s rDNA and specific primer sequences by which all species belonging to the Firmicutes and Bacteroidetes, the two major phyla in the human colon, can be discriminated. The IS region is conserved within each species, but varies between species in length and sequence. Using specific primer sequences, unknown species, constituting more than 60% of the intestinal microbiome, can be directly sorted into their phylum. Size and colour sorting of amplified fragments was performed thus creating a specific bacterial profile. One faecal sample and five mucosal biopsy specimens throughout the colon were collected from 20 individuals and subsequently analyzed. Intra- and interpatient variation of bacterial profiles was determined by means of Pearson's correlation. In addition, eight faecal samples from one individual were analysed over a two-week period to determine short-term temporal microbiome variation. Each individual had a unique bacterial profile, sharing only a few identical fragments with other individuals. The obtained fragments corresponded to well known colonic bacteria such as Faecalibacterium prausnitzii and Bacteroides thetaiotao-micron. Patterns from different locations throughout the colon of a single individual were almost identical (76-98% identity). Intraindividual faecal profiles showed significant differences compared to mucosal profiles, but were still host specific (50-68% identity). Bacterial profiles from faecal samples were stable in time (75-92% identity). Especially the Bacteroides-profiles revealed high temporal stability (87-96% identity).
Conclusion: IS-pro is a rapid and highly suitable method for bacterial profiling purposes. With this method every individual has a unique intestinal microbiome. In addition, MAM is stable throughout the entire colon allowing general sampling. The faecal microbiome differs from the MAM, but is still host specific and is stable in time.

Genetic and morphological characteristics in Dutch hereditary pancreatitis patients

M.H. Derikx[1], R.H.M. te Morsche[1], J.B.M.J. Jansen[1], J.P.H. Drenth[1], [1]Dept of Gastro-enterology and Hepatology, Radboud University Medical Center Nijmegen, The Netherlands

Background: Hereditary pancreatitis (HP) is a rare form of early onset chronic pancreatitis caused by gain-of-function PRSS1 gene mutations. The actual prevalence of HP in the Netherlands is unknown. We set out to assess genetic, epidemiological, clinical and morphological characteristics of HP. Material and methods: The study population consisted of 411 patients who were referred for molecular diagnosis of HP from 2001-2007. We selected 52 patients with a positive family history for HP. Analysis for PRSS1 gene mutations was performed by direct sequencing or mutation analysis. All patients received a symptom questionnaire. Results: We included 52 patients from 23 families (follow-up 1,847 person-years). PRSS1 mutations were detected in 84% (R122H 66%, N29I 14%, E79K 2%, N29T 2%). Mean age at first presentation was 10 years (range 1-42 years). Pain was reported in 80% of patients, but most patients had incidental attacks (45%: 1 per year), and chronic pain was seen in 15%. The mean length of pain attacks was 4,8 days (range 0-12 days). Exocrine and endocrine dys-function was seen in a minority (35% respectively 20%). Some 17% gave a family history of pancreatic carcinoma.
Conclusion: Yield of PRSS1 testing is high among a Dutch population that is selected on basis of a positive family history for HP. The HP phenotype in this cohort is relatively mild as most patients had infrequent painful attacks.

Chymotrypsinogen C (CTRC) variants as a genetic susceptibility factors in tropical calcific pancreatitis

M.H.M. Derikx[1], M. Sahin-Tóth[2], R.H.M. te Morsche[1], R. Szmola[2], S. Santhosh[3], A. Chacko[3], J.P.H. Drenth[1], [1]Dept of Gastroenterology and Hepatology, Radboud University Medical Center Nijmegen, The Netherlands [2]Dept of Molecular and Cell Biology, Boston University Goldman School of Dental Medicine, 715 Albany Street, Evans-433, Boston, MA 02118, USA, [3]Dept of Gastrointestinal Sciences, Christian Medical College and Hospital, Vellore, India

Background: Tropical calcific pancreatitis (TCP) is common in parts of Asia and Africa. The SPINK1 variant p.N34S is strongly associated with TCP, but other genetic factors remain to be defined. Mutations in the chymotrypsinogen C (CTRC) gene were detected in two European cohorts of chronic pancreatitis (CP). Preliminary data on a small cohort of patients with TCP indicated that CTRC variants might be risk factors. Here we extended these studies and investigated the significance of CTRC variants in TCP. Materials and methods: We performed mutational screening of the 8 CTRC exons and the SPINK1 p.N34S allele. Results: We detected the heterozygous p.A73T variant in 4/146 patients (2.7%) and in 1/144 controls (0.7%). The heterozygous p.V235I variant was present in 3/148 patients (2%) and 2/150 (1.3%) controls, and 1/148 (0.7%) patient was homozygous for this variant. A novel p.G61R variant was found in one patient. Functional analysis showed that p.G61R caused complete loss of chymotrypsinogen C secretion from transiently transfected HEK 293T cells. The variant p.K172E was observed in controls (2/146; 1.4 %) and in patients (1/149; 0.7 %) and a novel p. G227S variant was also identified in one control subject. Carriage of CTRC variants was independent of SPINK1 p.N34S.
Conclusions: We replicated the enrichment of the p.A73T and p.V235I variants in an independent cohort of TCP patients and identified the novel loss-of-function p.G61R variant.

Plattegrond

Alfabetische lijst van standhouders *B = Beneluxhal K = Kempenhal* Standnr.

Abbott B.V.	K 6
Acertys B.V.	B 3
Alvleeskliervereniging	B 27
AstraZeneca B.V.	K 10
Baxter	K 4
Boston Scientific Benelux B.V.	K 3
Bristol Myers Squibb	B 36
Campro Scientific GMBH	B 30
Cobra Medical B.V.	B 17
Cook Medical	B 35
Crohn en Colitis Ulcerosa Verereniging Nederland	B 26
Danica Nederland B.V.	B 6
Datascope Patient Monitoring	B 34
ECCE Dutoit	B 18
Endomed B.V.	K 7
Endotechniek	B 12
Ferring B.V.	B 1
FMH Medical B.V.	B 9
Fresenius Kabi Nederland B.V.	B 31
Getinge B.V.	K 11
Hitachi Medical Systems	B 11
Janssen-Cilag B.V.	K 5
Lans Medical B.V.	B 2
Medical Measurements Systems B.V.	B 32
Medicor	B 8
Minntech	K 2
Nationaal Hepatitis Centrum	B 24
Nederlandse Coeliakie Vereniging	B 22
Norgine B.V.	B 15
Novartis Pharma B.V.	K 12
Nutricia Nederland B.V.	B 19
Nycomed B.V.	B 20
Olympus Nederland B.V.	K 13
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Roche Nederland B.V.	K 8
Schering-Plough B.V.	B 21
Shire Pharmaceuticals Benelux	B 14
Solvay Pharma B.V.	K 9
Stichting Opsporing Erfelijke Tumoren	B 28
Surgical Technologies B.V.	B 33
TMI	B 5
Tramedico B.V.	K 1
Vereniging Ziekte van Hirschsprung	B 25
Wassenburg Medical Devices B.V.	B 10
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