Programma najaarsvergadering 8 en 9 oktober 2009

NEDERLANDSE VERENIGING VOOR GASTROENTEROLOGIE

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

NEDERLANDSE VERENIGING VOOR HEPATOLOGIE

NEDERLANDSE VERENIGING VOOR GASTROINTESTINALE CHIRURGIE

NEDERLANDSE VERENIGING VAN MAAG-DARM-LEVERARTSEN

Locatie:

NH KONINGSHOF VELDHOVEN

INHOUDSOPGAVE pag.

Tijdstippen diverse ledenvergaderingen tijdens najaarsvergadering:

Nederlandse Vereniging voor Gastroenterologie	8 oktober, 11.30 uur - Brabantzaal
Nederlandse Vereniging voor Hepatologie	8 oktober, 15.30 uur - Auditorium

INHOUDSOPGAVE pag.

VRIJDAG 9 OKTOBER 2009

Tijdstippen diverse ledenvergaderingen tijdens najaarsvergadering:

Sectie Endoscopie Verpleegkundigen en Assistenten 9 oktober 12.15 uur - Diezezaal
Nederlandse Vereniging Maag-Darm-Leverartsen 9 oktober 13.00 uur - Genderzaal

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

Aandachtspunt voor de sprekers:
u dient zich strikt te houden aan de beschikbare spreektijd! U vindt dit aangegeven bij de betreffende sessie. In **zaal 25** kunt u uw PowerPoint presentatie inleveren tot uiterlijk 30 minuten voor uw voordracht.

VOORWOORD

Hierbij treft u het volledige programma aan van de najaarsvergadering die gehouden wordt op 8 en 9 oktober a.s. 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. Het cursorisch onderwijs vindt plaats op woensdag 7 oktober vanaf 15.00 uur. Het programma zal donderdag 8 oktober om 9.30 uur van start gaan met abstractpresentaties van de Nederlandse Vereniging voor Gastrointestinale Chirurgie in het Auditorium. De abstractpresentaties van de Nederlandse Vereniging van Gastroenterologie en de Nederlandse Vereniging voor Hepatologie beginnen om 10.00 uur in respectievelijk de Brabantzaal en de Baroniezaal. Anders dan voorgaande jaren is de ledenvergadering van de NVGE dit keer op donderdagochtend om 11.30 uur in de Brabantzaal. Na de lunch, in de expositiehal, vindt onder andere een symposium over feacale incontinentie plaats door de Sectie Neurogastroenterologie en Motiliteit en de gebruikelijke mini-battle van de NVGIC over het management van gastro-intestinale bloedingen. De klinische sectie van de Nederlandse Vereniging voor Hepatologie organiseert een symposium over acute hepatologie in chronische leverziekten. Aan het einde van de middag zal in de Brabantzaal het NVH leerboek Leverziekten gepresenteerd worden. Om 17.00 volgt aansluitend hieraan, plenair, de President Select. Om 18.00 uur volgt de uitreiking van de AstraZeneca Gastrointestinale Research Award 2009. De eerste prijswinnaar zal aansluitend aan de uitreiking een erevoordracht houden. Met deze lezing wordt het programma van de donderdag afgesloten. In de avond is er geen programma ingepland. Het diner vindt plaats in de Genderzaal, daarna, vanaf omstreeks 22.30 uur, is er muziek in de Baroniezaal en de gebruikelijke congresborrel in de Limburgfoyer. Op vrijdagochtend starten de abstractpresentaties weer om 8.30 uur. In de Brabantzaal vindt een symposium plaats over diagnostiek van de dunne darm, gevolgd door een State of the Art Lecture door Dr. Roland Valori, een introductie van deze spreker vindt u in het NVGE-nieuwsbulletin. In de Baroniezaal zal voor die tijd nog een mini-symposium plaatsvinden over de Richtlijn Maagcarcinoom. Ook in de Parkzaal zijn er diverse sessies met vrije voordrachten. In respectievelijk de Diezezaal en het Auditorium tenslotte, worden door de Sectie Endoscopie Verpleegkundigen en Assistenten en de Vereniging Maag Darm Lever Verpleegkundigen de gebruikelijke eigen programma's met lezingen verzorgd.

Graag tot ziens in Veldhoven!

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

Let op: *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

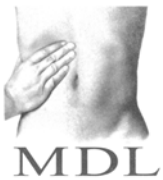
De Nederlandse Vereniging voor Gastroenterologie kent een jarenlange samenwerking met de farmaceutische industrie. De vereniging stelt de farmaceutische industrie in de gelegenheid aanwezig te zijn bij de wetenschappelijke vergaderingen met een stand. Mede hierdoor kan de vereniging haar wetenschappelijke 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. B.B. van Elzen (aios MDL, AMC)
Dr. E. van der Harst (chirurg, Maasstad Ziekenhuis)
Dr. D.J. de Jong (MDL-arts, UMCN)
Prof. dr. J.H. Kleibeuker (MDL-arts, UMCG)
Drs. A.D. Koch (aios MDL, Erasmus MC)
Prof. dr. P.D. Siersema (MDL-arts, UMCU)
Dr. R. Timmer (MDL-arts, Antonius Nieuwegein)



Onderwerp: Oncologie

Voorzitter: *Prof. dr. J.H. Kleibeuker, MDL-arts, Universitair Medisch Centrum Groningen*

15.00 – 15.15	Evaluatie toets oncologie
15.15 – 15.45	In opzet curatieve behandeling van het maagcarcinoom *Prof. dr. D.J. Richel, Academisch Medisch Centrum, Amsterdam*
15.45 – 16.15	Gist: afbakening van diagnose en beleid bij detectie *Dr. S. Sleijffer, Erasmus MC, Rotterdam*
16.15 – 16.45	Carcinoiden en andere endocriene tumoren van de tractus digestivus *Prof. dr. E.G.E. de Vries, Universitair Medisch Centrum Groningen*
16.45 – 17.15	Pauze
17.15 – 17.45	Plaatsbepaling van MRI bij beeldvorming van haarden in de lever *Dr. I.C. Pieters - van den Bosch, VU medisch centrum, Amsterdam*
17.45 – 18.15	Cysteuze pancreastumoren *Dr. M.J. Bruno, Erasmus MC, Rotterdam*
18.15 – 18.45	Chirurgische mogelijkheden en beperkingen bij de behandeling van het cholangiocarcinoom *Dr. O.R.C. Busch, Academisch Medisch Centrum, Amsterdam*
18.45 – 19.45	Dinerbuffet

Cursorisch onderwijs in maag-darm-leverziekten, vervolg **Auditorium**

19.45 – 20.15	Chirurgische en lokale behandelingsmodaliteiten van het coloncarcinoom *Prof. dr. J.F. Lange, Erasmus MC, Rotterdam*
20.15 – 20.45	Palliatieve systemische therapie bij het gemetastaseerd colorectaal carcinoom *Prof. dr. C.J.A. Punt, Universitair Medisch Centrum St. Radboud, Nijmegen*
20.45 – 21.45	Paneldiscussie aan de hand van casuïstiek 1. presentatie van een patiënt met een coloncarcinoom en een levermetastase *aios Universitair Medisch Centrum Utrecht* 2. presentatie van een patiënt met een obstruerend coloncarcinoom *aios Deventer Ziekenhuis* 3. presentatie van een patiënt met een T4 coloncarcinoom *aios Universitair Medisch Centrum St. Radboud Nijmegen*
21.45 – 22.00	Afsluitende kennistoets

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 8 oktober 2009

DONDERDAG	BRABANTZAAL	BARONIEZAAL	AUDITORIUM	PARKZAAL	ZAAL 21
09.30 – 11.30 10.00 – 11.30	Vrije voordrachten Netherlands Society of Parenteral and Enteral Nutrition en Nederlandse Vereniging voor Gastroenterologie p. 10	Vrije voordrachten Nederlandse Vereniging voor Hepatologie p. 11	Vrije voordrachten Nederlandse Vereniging voor Gastrointestinale Chirurgie p. 13	Geen programma in deze zaal donderdag	
11.30 – 12.00	**Ledenvergadering NVGE**				
12.00 – 13.00	Lunchbuffet expositiehal	Lunchbuffet expositiehal	Lunchbuffet expositiehal		
13.00 – 15.30	Vrije voordrachten Nederlandse Vereniging voor Gastroenterologie p. 15 13.30 **Symposium** “Faecale incontinentie” p. 16	Vrije voordrachten Nederlandse Vereniging voor Hepatologie p.19 gevolgd door **Symposium** "Acute hepatologie bij chronische leverziekte" p. 20	14.00 **Minibattle NVGIC** "Management van gastro-intestinale bloedingen " p. 22 Vrije voordrachten Ned. Vereniging voor Gastrointestinale Chirurgie, p. 23		
15.30 – 16.00	Theepauze	Theepauze en **ALV NVH**	Theepauze		
16.00 – 16.30	Vrije voordrachten Nederlandse Vereniging voor Gastroenterologie p. 16	Vrije voordrachten Nederlandse Vereniging voor Hepatologie p. 21	Vrije voordrachten Nederlandse Vereniging voor Gastrointestinale Chirurgie p. 23		
16.30 – 17.00	**Presentatie NVH-leerboek p. 17**	Geen programma in deze zaal			Bijeenkomst werkgroep IBD i.o.
17.00 - 18.00	**President Select** p. 17	Geen programma in deze zaal	Geen programma in deze zaal		
18.00 – 18.30	**Uitreiking AZ-prijs** p. 18	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 Genderzaal	Diner in Genderzaal	Diner in Genderzaal		
22.00 – 01.00	Borrel / Muziek in de foyer	Borrel / Muziek in de foyer	Borrel / Muziek in de foyer		

Programma vrijdag 9 oktober 2009

VRIJDAG	BRABANTZAAL	BARONIEZAAL	PARKZAAL	AUDITORIUM	DIEZEZAAL
08.30 – 09.00	Vrije voordrachten Nederlandse Vereniging voor Gastroenterologie p. 25	Vrije voordrachten Nederlandse Vereniging voor Hepatologie p. 28	Vrije voordrachten Nederlandse Vereniging voor Gastroenterologie p. 31		
09.00 – 10.30	Symposium: Diagnostiek van de dunne darm p. 26	Vrije voordrachten Nederlandse Vereniging voor Hepatologie p. 28	Vrije voordrachten Nederlandse Vereniging voor Gastroenterologie p. 32	Programma Vereniging Maag-Darm-Lever Verpleegkundigen p. 35	Programma Sectie Endoscopie Verpleeg-kundigen en Assistenten p. 36
10.30 – 11.00	Koffiepauze	Koffiepauze	Koffiepauze	Koffiepauze	Koffiepauze
11.00 – 13.00	Vrije voordrachten Nederlandse Vereniging voor Gastroenterologie p.26 12.20 State of the Art Lecture Roland Valori: Creating a sustainable quality framework for endoscopy services p. 27	**Symposium rond de richtlijn Maagcarcinoom** p. 30	Vrije voordrachten Nederlandse Vereniging voor Gastroenterologie p. 33	Programma Vereniging Maag-Darm-Lever Verpleegkundigen p. 35	Programma Sectie Endoscopie Verpleegkundigen en Assistenten p. 36
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

NESPEN en NVGE **Brabantzaal**

09.30 Inschrijving, koffie

Voorzitters: W. van Gemert en G. Wanten

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

10.00 Taurine levels are decreased in critically ill patients despite adequate nutrition (p. 38)
S.M.P. Lemmens[1], M.A.R. Vermeulen[1], M. Visser[1], G.C. Ligthart-Melis[2], H.M. Oudemans-van Straaten[3], P.A.M. van Leeuwen[1], Depts of [1]Surgery and [2]Nutrition and Dietetics, VU Medical Centre, Amsterdam, [3]Intensive Care, Onze Lieve Vrouwe Gasthuis, Amsterdam, The Netherlands

10.10 Arginine/ADMA is a predictor for cardiac output in septic shock patients (p. 39)
M.A.R. Vermeulen[1], M. Visser[1], M.C. Richir[1], S.M.P. Lemmens[1], G.C. Ligthart-melis[2], H.M. Oudemans-van Straaten[3], P.A.M. van Leeuwen[1], Depts of [1]Surgery and [2]Nutrition and Dietetics, VU Medical Centre, Amsterdam, [3]Intensive Care, Onze Lieve Vrouwe Gasthuis, Amsterdam, The Netherlands

10.20 Parenteral lipids impair pneumococcal killing by human neutrophils in a structure-dependent manner (p. 40)
M.W. Versleijen[1], H.M. Roelofs[1], R.H. te Morsche[1], E. Simonetti[2], P.W. Hermans[2], G.J. Wanten[1], Depts of [1]Gastroenterology and Hepatology and [2]Laboratory of Pediatric Infectious Diseases, Radboud University Nijmegen Medical Centre, The Netherlands

10.30 Quantification of intestinal absorption capacity in patients with chronic Graft-versus-Host Disease of the digestive tract (p. 41)
B.S. van der Meij[1], O.J. Visser[2], S. Hesselink[1], J.A.E. Langius[1], P.A.M. van Leeuwen[3], A.A. van Bodegraven[4], N.J. Wierdsma[1], Depts of [1] Nutrition and Dietetics, [2] Haematology, [3]Surgery and [4]Gastroenterology and Hepatology, VU University Medical Centre, Amsterdam, The Netherlands

10.40 Preoperative chemotherapy and/or radiation in rectal cancer patients reduces hepatic insulin sensitivity (p. 42)
M.F.M. van Stijn[1], J.J. Atema[1], M.R. Soeters[2], M.J.M. Serlie[2], M.T. Ackermans[2], P.A.M. van Leeuwen[3], A.P.J. Houdijk[1],[1] Dept of Surgery, Medical Centre Alkmaar, [2]Dept of Endocrinology and Metabolism, Academic Medical Centre, Amsterdam, [3] Dept of Surgery, VU University Medical Centre Amsterdam, The Netherlands

10.50 Timing of enteral nutrition in patients with predicted severe acute pancreatitis: an early start is associated with a reduction in bacteremia (p. 43)
O.J. Bakker[1], H.C. van Santvoort[1], M.G. Besselink[1], K. Fischer[2], T.L. Bollen[3], M.A. Boermeester[4], H.G. Gooszen[1], [1]Dept of Surgery, University Medical Centre Utrecht, [2]Julius Centre for Health Sciences and Primary Care, University Medical Centre Utrecht, [3]Dept of Radiology, St. Antonius Hospital, Nieuwegein, [4]Dept of Surgery, Amsterdam Medical Centre, The Netherlands

11.00 The necessity and timing of pancreatic duct visualization in the treatment of pancreatic fluid collections associated with acute pancreatitis (p. 44)
E.M.V. de Cuba, R.P. Voermans, E.A. Rauws, P. Fockens, Dept. of Gastroenterology & Hepatology, Academic Medical Centre, Amsterdam, The Netherlands

11.10 Tropical Calcific pancreatitis is more severe than Western Idiopathic pancreatitis: a comparison between 2 cohorts from India and The Netherlands (p. 45)
M.H.M. Derikx[1], V. Balakrishnan[2], R.H.M. te Morsche[1], J.P.H. Drenth[1], [1]Dept of Gastro-enterology and Hepatology, Radboud University Medical Centre Nijmegen, The Netherlands, [2]on behalf of IPANS (Indian Pancreatitis Study Group), Amrita Institute of Medical Sciences Cochin, Kerala, India

11.20 Risk factors for abdominal arterial atherosclerosis (p. 46)
A. Sana[1], D. van Noord[1], S. Kooij, K. van Dijk, J. Langendonk[2], E. Sijbrands[2], P. Mensink[1], Depts of Gastroenterology and Hepatology[1,] Internal Medicine[2], Erasmus Medical Centre, Rotterdam, The Netherlands

11.30 Einde abstractsessie

11.30 **Ledenvergadering NVGE**

12.00 Lunchbuffet in expositiehal

Nederlandse Vereniging voor Hepatologie — Baroniezaal

09.00 Inschrijving, koffie

Voorzitters: H.J. Metselaar en J.P.H. Drenth

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

10.00 Serum sodium alone is the best predictor of waiting list mortality in patients awaiting liver transplantation (p. 47)
R. Garritsen[1], W.R.R. Farid[1], H.J. Metselaar[2], H.W. Tilanus[1], G. Kazemier[1], Dept. of [1]Surgery and [2]Gastroenterology and Hepatology, Erasmus Medical Centre, Rotterdam, The Netherlands

10.10 Long-term results of liver transplantation with a national protocol for controlled cardiac death donors (p. 48)
J. Dubbeld1a, H. Hoekstra2a, W. Farid3b*, J. Ringers1a*, R.J. Porte2a, H.J. Metselaar3b, A.G. Baranski1a, G. Kazemier3a, M.J. Coenraad1b, A.P. van den Berg2b, B. van Hoek1b, Depts of aSurgery and bGastro-enterology and Hepatology, 1Leiden University Medical Centre, 2University Medical Centre Groningen, [3]Erasmus Medical Centre Rotterdam, The Netherlands*

10.20 Trends in liver transplantation for primary biliary cirrhosis in The Netherlands 1988-2008 (p. 49)

E.M.M. Kuiper[1], B.E. Hansen[1,2], H.J. Metselaar[1], R.A. de Man[1], E.B. Haagsma[3], B. van Hoek[4], H.R. van Buuren[1],[1]Depts of Gastroenterology and Hepatology and [2]Epidemiology and Biostatistics, Erasmus University Medical Centre, Rotterdam, [3]Dept of Gastroenterology and Hepatology, University Medical Centre Groningen, Groningen, [4]Dept of Gastroenterology and Hepatology, University Medical Centre Leiden, Leiden, The Netherlands

10.30 Analysis of incidence and risk factors for chronic renal failure in long term liver transplant recipients (p. 50)

M.E. Azimpour[1], G. Kazemier[2], B.E. Hansen[1,3], H.J. Metselaar[1], Dept. of [1]Gastroenterology & Hepatology; [2]Surgery and [3]Biostatistics, Erasmus MC, University Medical Centre, Rotterdam, The Netherlands

10.40 The long-term effect of ursodeoxycholic acid on liver biochemistries in primary biliary cirrhosis (p. 51)

E.M.M. Kuiper[1], B.E. Hansen[1,2], W. Lesterhuis[3], R.J. Robijn[4], J.C. Thijs[5], L.G.J.B. Engels[6], G.H. Koek[7], M.N. Aparicio[8], M.J. Kerbert-Dreteler[9], H.R. van Buuren[1] for the Dutch PBC study group, [1]Depts of Gastroenterology and Hepatology and [2]Epidemiology and Biostatistics, Erasmus University Medical Centre, Rotterdam, [3]Dept of Gastroenterology and Hepatology, Albert Schweitzer Hospital, Dordrecht, [4]Dept of Gastroenterology and Hepatology, Rijnstate Hospital, Arnhem ,[5]Dept of Internal Medicine, Bethesda Hospital, Hoogeveen, [6]Dept of Gastroenterology and Hepatology, Orbis Medical Centre, Sittard, [7]Dept of Gastroenterology and Hepatology, Maastricht University Medical Centre, Maastricht, [8]Dept of Gastroenterology and Hepatology, Canisius Wilhelmina Hospital, Nijmegen, [9]Dept of Internal Medicine, Medical Spectrum Twente, Enschede, The Netherlands

10.50 Malnutrition is an independent risk factor for complications in patients with liver cirrhosis (p. 52)

E.J. Trip[1], E.J. Huisman[1], P.D. Siersema[1], B. van Hoek[2], K.J. van Erpecum[1], Depts of Gastroenterology and Hepatology, [1] University Medical Centre Utrecht and [2]Leiden University Medical Centre, The Netherlands

11.00 Prognosis of neonatal cholestasis due to alpha-1-antitrypsin deficiency * (p. 53)

K.F. Kok[1], L.G. van Vlerken[2], M.A. Benninga[3], J.C. Escher[4], R.A. de Vries[5], R.H.J. Houwen, [1]Dept of Gastroenterology and Hepatology, Radboud Univ. Medical Centre Nijmegen, [2]Dept of Pediatric Gastroenterology, Wilhelmina Children's Hospital, Univ. Medical Centre, Utrecht, [3]Dept of Pediatric Gastroenterology, Emma Children's Hospital, Academic Medical Centre, University of Amsterdam, Amsterdam, [4]Dept of Pediatric Gastroenterology, Erasmus Medical Centre, Sophia Children's Hospital, Rotterdam, [5]Dept of Internal Medicine, Univ. Medical Centre, Groningen, The Netherlands

11.10 Low risk of hepatocellular carcinoma in UDCA-treated patients with primary biliary cirrhosis. Renewed recommendations for surveillance (p. 54)

E.M.M. Kuiper[1], B.E. Hansen[1,2], R.P.R Adang[3], C.M.J van Nieuwkerk[4], R. Timmer[5], J.P.H. Drenth[6], P. Spoelstra[7], J.T. Brouwer[8], J.Ph. Kuyvenhoven[9], H.R. van Buuren[1] for the Dutch PBC study group, Depts of [1]Gastroenterology and Hepatology and [2]Epidemiology and Biostatistics, Erasmus University Medical Centre, Rotterdam, [3]Dept of Gastroenterology and Hepatology, VieCuri Medical Centre, Venlo, [4]Dept of Gastroenterology and Hepatology, VU University Hospital Amsterdam, Amsterdam, [5]Dept of Gastroenterology and Hepatology, St Antonius Hospital, Nieuwegein, [6]Dept of Gastroenterology and Hepatology, Radboud University Hospital Nijmegen, Nijmegen, 7Dept of Gastroenterology and Hepatology, Medical Centre Leeuwarden, Leeuwarden, 8Dept of Gastroenterology and Hepatology, Reinier de Graaf Gasthuis, Delft, 9Dept of Gastroenterology and Hepatology, Kennemer Gasthuis, Haarlem, The Netherlands

11.20 Plasma levels of Apolipoprotein A1 are decreased in patients with Budd-Chiari Syndrome (p. 55)

J. Hoekstra[1], S. Talens[2], S.P.G. Dirkx[2], S. Darwish Murad[1], J. Trebicka[3], E. Elias[4], M. Primignani[5], J-C. García-Pagán[6], D.C. Valla[7], F.W.G. Leebeek[2], D.C. Rijken[2], H.L.A. Janssen[1] for the Eur. Network for Vascular Disorders of the Liver (EN-Vie), [1]Dept of Gastroenterology and Hepatology, Erasmus University Medical Centre, Rotterdam, [2]Dept of Hematology, Erasmus University Medical Centre, Rotterdam, The Netherlands, [3]Dept of Internal Medical, University Hospital of Bonn, Bonn, Germany, [4]Liver Unit, Queen Elizabeth University Hospital, Birmingham, United Kingdom, [5]Gastro-enterology and Gastrointestinal Endoscopy Unit, Ospedale Policlinico, Mangiagalli and Regina Elena Foundation, Milan, Italy, [6]Hepatic Hemodynamic Laboratory, Liver Unit, Hospital Clinic, IDIBAPS and Ciberehd, Barcelona, Spain, [7]Dept of Hepatology, Hôpital Beaujon, AP-HP, INSERM-U773 & Uni-versity Paris-7, Clichy, France

11.30 Ledenvergadering NVGE in de Brabantzaal,
aansluitend lunchbuffet in expositiehal (12.00 uur).

Nederlandse Vereniging voor Gastrointestinale Chirurgie — Auditorium

09.00 Inschrijving, koffie

Voorzitters: B.P.L. Wijnhoven en J.B. Tuynman

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

09.30 Is there a place for preoperative gastroscopy in morbidly obese patients undergoing gastric bypass surgery? (p. 56)

A. Schigt[1], P. Scholten[2], B.A. van Wagensveld[1], [1]afdeling Chirurgie, [2]afdeling Maag-, Darm- en Lever ziekten, Sint Lucas Andreas Ziekenhuis, Amsterdam, The Netherlands

09.40 Liver Transplantation in Polycystic Liver Disease: excellent survival and improvement of quality of life (p. 57)

L. van Keimpema[1], F. Nevens[2], R. Adam[3], R.J. Porte[4], P. Fikatas[5], T. Becker[6], P. Kirkegaard[7], H.J. Metselaar[8], J.P.H. Drenth[1] for the European Liver and Intest Transplant Association (ELITA),[1]Dept of Gastroenterology and Hepatology, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands; [2]Dept of Hepatology, University Hospital Leuven, Leuven, Belgium; [3]Centre Hépato-biliaire, AP-HP Hôpital Paul Brousse, Villejuif, France; [4]Dept of Hepatobiliary Surgery and Liver Transplantation, University Medical Centre Groningen, Groningen, The Netherlands; [5]Dept for General, Visceral an Transplant Surgery, Charite Campus Virchow, Universitätsmedizin Berlin, Berlin, Germany; [6]Dept for General, Visceral and Transplant Surgery, Medizinische Hochschule Hannover, Hannover, Germany; [7]Dept of Surgery and Transplantation, Rigshospitalet, University of Copenhagen, Denmark; [8]Dept of Gastroenterology and Hepatology, Erasmus Medical Centre, Rotterdam, The Netherlands

09.50 Predictors of common bile duct stones during early endoscopic retrograde cholangiopancreaticography in acute biliary pancreatitis (p. 58)

H.C. van Santvoort[1], O.J. Bakker[1], M.G. Besselink[1], T.L. Bollen[2], K. Fischer[3], H.G. Gooszen[1] and K.J. van Erpecum[4] for the Dutch Pancreatitis Study Group, Dept of Surgery[1], Julius Centre for Health Sciences and Primary Care[3] and Gastroenterology[4], University Medical Centre Utrecht, Utrecht, Dept of Radiology, St. Antonius Hospital[2], Nieuwegein, The Netherlands

Donderdag 8 oktober 2009

10.00 Routine preoperative liver function test in patients with uncomplicated symptomatic gallstone disease (p. 59)

M. van den Berg, G.M. van Couwelaar, S.M. Lagarde, P. Joosse, B.A. van Wagensveld, B.C. Vrouenraets, Sint Lucas Andreas Ziekenhuis, Amsterdam, The Netherlands

10.10 Surgical management of submucosal oesophageal cancer: limited or extended lymphadenectomy? (p. 60)

B.A. Grotenhuis[1], M. van Heijl[2], J. Zehetner[3], J. Moons[4], B.P.L. Wijnhoven[1], M. van Berge Henegouwen[2], H.W. Tilanus[1], T.R. DeMeester[3], T. Lerut[4], J.J.B. van Lanschot[1], [1]Dept of Surgery, Erasmus Medical Centre, Rotterdam, The Netherlands, [2]Dept of Surgery, Academic Medical Centre, Amsterdam, The Netherlands, [3]Dept of Surgery, University of Southern California, Los Angeles, USA, [4]Dept of Surgery, University Hospital Gasthuisberg, Leuven, Germany

10.20 Chemoradiation for oesophageal cancer: clinical outcome and pathological assessment of tumour response (p. 61+ p. 62)

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

10.30 Quality of life in long-term survivors after potentially curative treatment for oesophageal cancer (p. 63)

E.F.W. Courrech Staal[1], N.K. Aaronson[2], B.M.P. Aleman[3], H. Boot[4], F. van Coevorden[1], J.W.van Sandick[1],[1]Surgery, [2]Division of Psychosocial Research & Epidemiology, [3]Radiation Oncology, [4]Gastroenterology, The Netherlands Cancer Institute Antoni van Leeuwenhoek Hospital, Amsterdam, The Netherlands

10.40 Impact of delay in diagnostic work-up and treatment of patients with oesophageal cancer (p. 64)

B.A. Grotenhuis, P. van Hagen, B.P.L. Wijnhoven, H.W. Tilanus, J.J.B. van Lanschot, Dept of Surgery, Erasmus Medical Centre, The Netherlands

10.50 Tailored or routine addition of an antireflux fundoplication in laparoscopic hiatal hernia repair; a comparative cohort study (p. 65)

E.J.B. Furnée[1], W.A. Draaisma[2], H.G. Gooszen[1], E.J. Hazebroek[1], A.J.P.M. Smout[3], I.A.M.J. Broeders[2], Dept of Surgery[1], University Medical Centre Utrecht Dept of Surgery[2], Meander Medical Centre, Amersfoort, Dept of Gastroenterology[3], University Medical Centre Utrecht, The Netherlands

11.00 Early Total Parenteral Nutrition (TPN) after rectal surgery implies a shorter length of stay (LOS) than late TPN (p. 66)

M.M.S. van Acht, P.G. Boelens, I.H. de Hingh, G.A.P. Nieuwenhuijzen, H.J.T. Rutten, Dept of General Surgery, Catharina Hospital Eindhoven, The Netherlands

11.10 The Malone antegrade continence enema in children with defecation disorders, the Amsterdam experience * (p. 67)

L.T. Hoekstra[1], C.F. Kuijper[2], D.C. Aronson[3], R. Bakx[2], M.A. Benninga[1] Dept of Pediatric Gastroenterology, Academic Medical Centre, Amsterdam 2, Dept of Pediatric Surgery, Emma Children's Hospital, Academic Medical Centre, Amsterdam 3, Dept of Pediatric Surgery, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands

11.20 Endoscopic transcolonic specimen removal in laparoscopic ileocolic resection for Crohn's Disease: initial experience (p. 68)
E.J. Eshuis[1,2], R.P. Voermans[1,2], D.P. Hirsch[2], P.C.F. Stokkers[2], M.I. van Berge Henegouwen[1], P. Fockens[2], W.A. Bemelman[1], [1]Dept of Surgery, Academic Medical Centre, Amsterdam, [2]Dept of Gastroenterology and Hepatology, Academic Medical Centre, Amsterdam, The Netherlands

11.30 Einde abstractsessie

11.30 **Ledenvergadering NVGE in de Brabantzaal**

12.00 Lunchbuffet in expositiehal

Nederlandse Vereniging voor Gastroenterologie **Brabantzaal**

Voorzitters: M.A. Benninga en D.P. Hirsch

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

13.00 Impact of anorectal symptoms on quality of life in patients with faecal incontinence (p. 69)
W.P.M. Hopman[1], R-J. Smeenk[2], R. de Vries[1], D.J. de Jong[1], E.N.J.T. van Lin[2], [1] Dept of Gastroenterology and Hepatology and [2] Dept of Radiation Oncology, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands

13.10 The inter-relation between Minimal Distension Pressure, Rectal Capacity and First Sensation in rectal barostat measurements (p. 70)
S. Vanhoutvin[1,2], F. Troost[1,2], P. Lindsey[3], RJ. Brummer[1,2,4], [1]TI Food and Nutrition, Wageningen, [2]Maastricht University, Gastroenterology; [3]Maastricht University, Clinical Genomics and Bioinformatics, Maastricht, The Netherlands; [4]Örebro University, Örebro, Sweden

13.20 Critical reappraisal of anorectal function tests in fecal incontinence: Only anal ultrasound is discriminatory (p. 71)
T.J. Lam[1], C.J.J. Mulder[1], R.J.F. Felt-Bersma[1], [1] Dept of Gastroenterology and Hepatology, VU University Medical Centre, Amsterdam, The Netherlands

13.30 Einde abstractsessie

Symposium Faecale Incontinentie — Brabantzaal

Voorzitters: M.A. Benninga en D.P. Hirsch

13.30 Introduction and epidemiology
Dr. M. Scott, Centre for Academic Surgery, Barts and The London School of Medicine and Dentistry, The Royal London Hospital, Whitechapel, London, UK

14.00 Diagnosis and anorectal function tests
Dr. R.J.F. Felt-Bersma, MDL-arts, VU medisch centrum, Amsterdam

14.30 Conservative treatment
Prof. J.F.W.M. Bartelsman, MDL-arts, Academisch Medisch Centrum, Amsterdam

15.00 Surgical possibilities
Prof. dr. C.G.I.M. Baeten, chirurg, Maastricht Universitair Medisch Centrum

15.30 Theepauze

Nederlandse Vereniging voor Gastroenterologie — Brabantzaal

Voorzitters: M.A. Benninga en D.P. Hirsch

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

16.00 Mortality of biliary atresia in children not undergoing liver transplantation * (p. 72)
W. de Vries[1], Z.J. de Langen[2], D.C. Aronson[3], P.M.J.G. Peeters[2], P. Jansen-Kalma[1], H.J. Verkade[1], also on behalf of NeSBAR.,[1]Dept of Pediatric Gastroenterology, [2]Dept of Surgery, University Medical Centre Groningen, Groningen, and [3]Departement of Surgery / Pediatric Surgery, Radboud University Medical Centre, Nijmegen, The Netherlands

16.10 Concentration of Fecal Calprotectin in Children with Abdominal Pain Presenting in Primary Care – a pilot study * (p. 73)
Y. van Leeuwen[1], J.L. van Gaalen[1], Y.B. de Rijke[2], J.C. Escher[3], M.Y. Berger[1], [1]Dept of General Practice, Erasmus MC, Rotterdam; [2]Dept of Clinical Chemistry, Erasmus MC–Sophia Children's Hospital, Rotterdam;

16.20 Balancing liver homeostasis by modulating c-Myc activity (WO 06-36, MLDS) (p. 74)

T.B. Dansen[1], I.J. van Zutphen[1], J. Whitfield[2], G.I. Evan[2] and B.M.T. Burgering[1], [1]Dept. of Physiological Chemistry, Centre for Biomedical Genetics and Cancer Genomic Centre, UMC Utrecht, The Netherlands, [2]Cancer Research Institute, University of California at San Francisco, CA, USA

16.30 Einde abstractsessie

Presentatie NVH leerboek — Brabantzaal

16.30 Presentatie Leerboek Leverziekten.
H.L.A. Janssen, J.P.H. Drenth en B. van Hoek

President Select (plenaire sessie) — Brabantzaal

Voorzitter: C.J.J. Mulder

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

17.00 Early response assessment of neoadjuvant therapy with Positron Emission Tomography in patients with oesophageal cancer (p. 75)

M. van Heijl[1], J.M.T. Omloo[1], M.I. van Berge Henegouwen[1], O.R.C. Busch[1], H.W. Tilanus[2], P.M.M. Bossuyt[3], O.S. Hoekstra[4], J. Stoker[5], M.C.C.M. Hulshof[6], A. van der Gaast[7], G.A.P. Nieuwenhuijzen[8], H.J. Bonenkamp[9], J.Th.M. Plukker[10], E.J. Spillenaar Bilgen[11], F.J.W. ten Kate[12], R. Boellaard[13], J. Pruim[14], G.W. Sloof [15], J.J.B. van Lanschot[1,2], [1] Dept of Surgery, Academic Medical Centre, Amsterdam, [2]Dept of Surgery, Erasmus Medical Centre, Rotterdam, [3]Dept of Clinical Epidiomiology, Biostatistics and Bioinformatics, Academic Medical Centre, Amsterdam, [4]Dept of Nuclear Medicine, VU Medical Centre, Amsterdam, [5]Dept of Radiology, Academic Medical Centre, Amsterdam, [6]Dept of Radiotherapy, Academic Medical Centre, Amsterdam, [7]Dept of Medical Oncology, Erasmus Medical Centre, Rotterdam, [8]Dept of Surgery, Catharina Hospital Eindhoven, Eindhoven, [9]Dept of Surgery, Radboud University Medical Centre, Nijmegen, [10]Dept of Surgery, University Medical Centre Groningen, Groningen, [11]Dept of Surgery, Rijnstate Hospital, Arnhem, [12]Dept of Pathology, Academic Medical Centre, Amsterdam, [13]Dept of Nuclear Medicine and PET research, VU Medical Centre, Amsterdam, [14]Dept of Nuclear Medicine and Molecular Imaging, University Medical Centre Groningen, University of Groningen, Groningen, [15]Dept of Nuclear Medicine, Academic Medical Centre, Amsterdam, The Netherlands

17.15 Lanreotide reduces the volume of polycystic liver: a randomized, double-blind, placebo-controlled trial (p. 76)

L. van Keimpema[1], F. Nevens[2], R. Vanslembrouck[3], M.G.H. van Oijen[1], A.L. Hoffmann[4], H.M. Dekker[5], R.A. de Man[6], J.P.H. Drenth[1], [1]Dept of Gastroenterology and Hepatology, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands, [2]Dept of Hepatology, University Hospital Leuven, Leuven, Belgium, [3]Dept of Radiology, University Hospital Leuven, Leuven, Belgium, [4]Dept of Radiation Oncology, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands, [5]Dept of Radiology, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands, [6] Dept of Gastroenterology and Hepatology, Erasmus Medical Centre, Rotterdam, The Netherlands

17.30 Lectin complement pathway gene polymorphisms and life-threatening infections after orthotopic liver transplantation (p. 77)

B.F. de Rooij[1], B. van Hoek[1], W.R. ten Hove[1], A. Roos[2], L.H. Bouwman[4], A.F. Schaapherder[4], R.J. Porte[5], M.R. Daha[3], J.J. van der Reijden[1], M.J. Coenraad[1], J. Ringers[4], A.G. Baranski[4], B.G. Hepkema[6], D.W. Hommes[1], H.W. Verspaget[1],[1]Depts of Gastroenterology and Hepatology, [2]Clinical Chemistry, [3]Nephrology and [4]Surgery, Leiden University Medical Centre, Leiden, Depts of [5]Hepatobiliary Surgery and Liver Transplantation and [6]Laboratory Medicine, University Medical Centre Groningen, The Netherlands

17.45 Therapeutic erythrocytapheresis, a new treatment for naïve patients with hereditary hemochromatosis (p. 78)

E. Rombout-Sestrienkova1, P.A.H. van Noord1, C.Th.B.M. van Deursen2, M. Janssen3, G.H. Koek4, 1Sanquin Blood Bank Southeast Region, Maastricht, 2Atrium Medical Centre, Dept of Internal medicine, Heerlen, 3University Hospital, Dept of Internal medicine, Nijmegen, 4Maastricht University Medical Centre, Dept of Internal medicine, division of Gastro-enterology/Hepatology, Maastricht, The Netherlands

18.00 Einde abstractsessie

Prijsuitreiking **Brabantzaal**

18.00 Uitreiking van de **AstraZeneca Gastrointestinale Research Award 2009** door de voorzitter van de jury, prof. dr. J.P.H. Drenth.

Aansluitend aan de uitreikingen van de eerste en tweede prijs, volgt een erevoordracht door de eerste prijs winnaar.

18.30 Congresborrel in expositiehal

19.30 Diner in de Genderzaal

Nederlandse Vereniging voor Hepatologie **Baroniezaal**

Voorzitters: R.J. de Knegt en G.H. Koek

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

13.00 Safety and Antiviral Activity of SCH 900518 Administered as Monotherapy and in Combination with Peginterferon Alfa-2b to Naïve and Treatment-Experienced HCV-1 Infected Patients (p. 79)

J.F. Bergmann[1], J. de Bruijne[2], C.J. Weegink[2], J. van Lier[3], A. van Vliet[3], A. Keung[4], J. Li[4], E. O'Mara[4], M.A. Treitel[4], E.A. Hughes[4], H.L.A. Janssen[1], R.J. de Knegt[1], H.W. Reesink[2], [1]Erasmus MC University Hospital, Rotterdam, [2]Amsterdam Medical Centre, Amsterdam, [3]PRA International, Zuidlaren, The Netherlands; [4]Schering-Plough Research Institute, Kenilworth, New Jersey, USA

13.10 SVR Results in Chronic Hepatitis C Genotype 1 Patients Dosed with SCH 900518 and Peginterferon Alfa-2b for 2 Weeks, Followed by Peginterferon Alfa-2b and Ribavirin for 24/48 Weeks: An Interim Analysis (p. 80)

J. de Bruijne[1], J.F. Bergmann[2], C.J. Weegink[1], R. Molenkamp[3], J. Schinkel[3], M.A. Treitel[4], E.A. Hughes[4], A. van Vliet[5], R.J. de Knegt[2], H.W. Reesink[1], H.L.A. Janssen[2], [1]Amsterdam Medical Centre, Dept of Gastroenterology and Hepatology, Amsterdam, [2]Erasmus MC University Hospital, Dept of Gastroenterology and Hepatology, Rotterdam, [3]Academic Medical Centre, Dept of Medical Microbiology, Amsterdam, The Netherlands; [4]Schering-Plough Research Institute, Kenilworth, New Jersey, USA; [5]PRA International, Zuidlaren, The Netherlands.

13.20 Serotonergic indices and psychiatric symptoms in treatment naïve chronic hepatitis C patients (p. 81)

B.J. Veldt[1], G. Bezemer[1], A.R. van Gool [2], J.P. Drenth[3], D. Fekkes[2], B. Hansen[1], H.L.A. Janssen[1], R.J. de Knegt[1], Erasmus MC University Medical Centre, Rotterdam, Depts of Gastroenterology and Hepatology[1] and Psychiatry & Neuroscience[2], [3]Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands, Dept of Gastroenterology and Hepatology

13.30 On-treatment prediction of sustained response in HBeAg-negative chronic hepatitis B patients treated with pegylated interferon alfa-2a (p. 82+ p. 83)

V. Rijckborst[1], B.E. Hansen[1,2], F. Tabak[3], M. Raptopoulou-Gigi[4], N. Örmeci[5], K. Simon[6], U.S. Akarca[7], R. Flisiak[8], I. Vafiadis-Zouboulis[9], S. Tripi[10], E. Verhey[1], M.J. ter Borg[1], A.J. van Vuuren[1], H.L.A. Janssen[1], for the PARC Study Group,[1]Dept of Gastroenterology and Hepatology, Erasmus MC, University Medical Centre Rotterdam, [2]Dept of Epidemiology and Biostatistics, Erasmus MC, University Medical Centre Rotterdam, The Netherlands, [3]Dept of Infectious Diseases, Istanbul University Cerrahpasa Medical School, Istanbul, Turkey, [4]Second Medical Dept, Aristototle University of Thessaloniki, Thessaloniki, Greece, [5]Dept of Gastroenterology, Ankara University School of Medicine, Ankara, Turkey, [6]Dept and Clinic of Infectious Diseases, Hepatology and Acquired Immune Deficiences, Medical University Wroclaw, Wroclaw, Poland, [7]Dept of Gastroenterology, Ege University Faculty of Medicine, Izmir, Turkey, [8]Dept of Infectious Diseases and Hepatology, Medical University of Bialystok, Bialystok, Poland, [9]First Dept of Propedeutic Medicine, University of Athens Medical School, Athens, Greece, [10]Dipartimento di Medicina, Clinica e della Patologie Emergenti, Universita di Palermo, Italy

13.40 Early ribavirin levels predict steady state concentration in hepatitis C patients (p. 84)

H.W.H.A. Huntjens-Fleuren[1], S. Slavenburg[2], A.S.M. Dofferhoff[3], C. Richter[4], P.P. Koopmans[5], C.P.W.G.M. Verwey-Van Wissen[6], J.P.H. Drenth[2], D.M. Burger[6], [1]Dept of Pharmacy, Canisius Wilhelmina Hospital, Nijmegen, [2]Dept of Gastroenterology and Hepatology, Radboud University Nijmegen Medical Centre, [3]Dept of Infectious Diseases, Canisius- Wilhelmina Hospital, Nijmegen, [4]Dept of Infectious Diseases, Rijnstate Hospital, Arnhem, [5]Dept of Infectious Diseases, Radboud University Nijmegen Medical Centre, [6]Dept of Pharmacy, Radboud University Nijmegen Medical Centre, The Netherlands

13.50 Psychiatric side-effects and the fluctuation in serotonergic parameters during treatment of chronic hepatitis C-infection with peginterferon and ribavir (p. 85)

G. *Bezemer[1], B. Veldt[1], A.R. van Gool[1], J.P.H. Drenth[2], D. Fekkes[1], B. Hansen[1], H.L.A Janssen[1], R.J. de Knegt[1], [1]Erasmus MC University Medical Centre, Rotterdam, Depts of Gastroenterology and Hepatology, Psychiatry, Neuroscience [2]Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands, Dept of Gastroenterology and Hepatology*

14.00 Einde abstractsessie

Symposium Nederlandse Vereniging voor Hepatologie **Baroniezaal**

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

"Acute hepatologie bij chronische leverziekte"

14.00 De huidige behandeling van acute varicesbloedingen bij chronische leverziekte
Dr. E.A.J. Rauws, MDL-arts, Academisch Medisch Centrum Amsterdam

14.20 Pathofysiologie en therapie van hepatorenaal syndroom en spontane bacteriële peritonitis
Dr. K.J. van Erpecum, MDL-arts, Universitair Medisch Centrum Utrecht

14.40 Hepatische encephalopathie bij chronische leverziekte
Dr. S.W.M. Olde Damink, chirurg, Maastricht Universitair Medisch Centrum

15.00 Transplantatie bij hoge MELD-score:
uitkomsten bij patiënten met zeer ernstige leverziekte
Prof. dr. H.J. Metselaar, MDL-arts, Erasmus Medisch Centrum Rotterdam

15.15 Transplantatie van gecompromitteerde donor-levers:
de rol van leeftijd (80+), vet (steatosis hepatis) en ischemie (non-heart beating)
Prof. dr. R.J. Porte, chirurg, Universitair Medisch Centrum Groningen.

15.30 Einde programma

Dit symposium is mede mogelijk gemaakt door Ferring B.V.

Nederlandse Vereniging voor Hepatologie **Baroniezaal**

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

Nederlandse Vereniging voor Hepatologie **Baroniezaal**

Voorzitters: F.H.J. Wolfhagen

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

16.00 Long-term follow-up of patients with portal vein thrombosis and myelo-proliferative disease (p. 86)
E.L. Bresser[1], J. Hoekstra[1], J.H. Smalberg[2], M.C.W. Spaander[1], F.W.G. Leebeek[2], H.L.A. Janssen[1],[1]Dept of Gastroenterology and Hepatology, Erasmus MC, University Medical Centre Rotterdam, [2]Dept of Hematology, Erasmus MC, University Medical Centre Rotterdam, The Netherlands

16.10 Octreotide reduces liver volume in patients with a polycystic liver (p. 87)
L. van Keimpema, J.P.H. Drenth, Dept of Gastroenterology and Hepatology, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands

16.20 Outcome of pregnancy in women with chronic portal vein thrombosis (p. 88)
E.L. Bresser[1], J. Hoekstra[1], M.C.W. Spaander[1], H.R. van Buuren[1], H.L.A. Janssen[1], [1]Dept of Gastro-enterology and Hepatology, Erasmus MC, University Medical Centre Rotterdam, The Netherlands

16.30 *Voor de presentatie van het Leerboek Leverziekten, de plenaire sessie (President Select) en de uitreiking van de AstraZeneca Gastrointestinale Research Award 2009 kunt u zich begeven naar de Brabantzaal*

Werkgroep IBD **Zaal 21**

16.30 Oprichtingsvergadering werkgroep

agenda
a. structuur van de werkgroep
b. gemeenschappelijke research

17.00 Einde bijeenkomst

Mini-battle Nederlandse Vereniging voor Gastrointestinale Chirurgie **Auditorium**

Voorzitters: E.J.Th. Belt en R. van Hillegersberg

"Management van gastro-intestinale bloedingen"

13.00 Oorzaken van GI bloedingen
Dr. C.IJ. Ponsioen, MDL-arts, AMC, Amsterdam

13.20 Endoscopische interventies bij GI bloeding.
Prof. dr. C.J.J. Mulder, MDL-arts, VUmc, Amsterdam.

13.40 Radiologische Interventies bij GI bloeding.
Dr. M.A. van den Bosch, interventie-radioloog, UMCU, Utrecht

14.00 Chirurgische interventies bij GI bloedingen
Dr. M.H.A. Bemelmans, chirurg, MUMC, Maastricht

14.20 Discussie

14.30 Einde symposium

Nederlandse Vereniging voor Gastrointestinale Chirurgie **Auditorium**

Voorzitters: E.J.Th Belt en L.P.S. Stassen

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

14.30 Results of patients with haemorrhoids treated with Doppler-guided haemorrhoidal artery ligation (p. 89)
R.A. Pol[1], W.C. van der Zwet[2], D. Hoornenborg[1], L. Lodewijk[1], B. Makkinga[1], B.M. Wallis de Vries[1], M. Kaijser[1], M. Eeftinck Schattenkerk[1], E.H. Eddes[1], [1]Dept of Surgery, Deventer Hospital, Deventer, [2]Dept of Epidemiology, Deventer Hospital, Deventer, The Netherlands

14.40 Ex vivo comparison of current colotomy closure modalities for Natural Orifice Transluminal Endoscopic Surgery (NOTES) (p. 90)
R.P. Voermans[1,2], F. Vergouwe[1,2], P. Fockens[1], M.I. van Berge Henegouwen[2], Depts of [1]Gastroenterology and Hepatology and [2]Surgery, Academisch Medisch Centrum, Amsterdam, The Netherlands

14.50 Randomised, blinded comparison of transgastric, transcolonic and laparoscopic peritoneoscopy for the detection of peritoneal metastases in a human cadaver model (p. 91)
R.P. Voermans[1,2], M.I. van Berge Henegouwen[2], E. de Cuba[1], F. van den Broek[1],G. van de Acker[2], R. Timmer[3], P. Fockens[1], Depts of [1]Gastroenterology and Hepatology and [2]Surgery, Academical Medical Centre, Amsterdam, [3]Dept of Gastroenterology and Hepatology, St. Antonius hospital, Nieuwegein, The Netherlands

15.00 Liver mobilization during liver resection induces immediate and profound hepatocellular damage in humans (p. 92)
M.A.J. van den Broek[1], J.G. Bloemen[1], M.C.G. van de Poll[1], M.H. Bemelmans[1], R.M. van Dam,[1] W.A. Buurman[2], C.H.C. Dejong[1,2], S.W.M. Olde Damink[1,2,3], Depts of Surgery, [1]Maastricht University Medical Centre, Maastricht, [2]Nutrition and Toxicology Research Institute Maastricht, Maastricht University, The Netherlands and [3]University College London Hospital, University College London, London, United Kingdom

15.10 Fasting protects against hepatic ischemia/reperfusion injury via up-regulation of HO-1 and antioxidant defence (p. 93)
M. Verweij[1], T. van Ginhoven[1], J.R. Mitchell[3], S. van den Engel[1], F. Bonthuis[1], E. Torabi[1], J.N.M. IJzermans[1], J.H.J. Hoeijmakers[2], R.W.F. de Bruin[1], Depts of [1]Surgery and [2]Cell Biology and Genetics, Erasmus MC – University Medical Centre, Rotterdam, The Netherlands, [3]Dept of Genetics and Complex Diseases, Harvard School of Public Health, Boston, USA

15.20 Adjuvant radioimmunotherapy improves survival of rats after resection of colorectal liver metastases (p. 94)
G.M. de Jong, W.J.G. Oyen[1], T. Hendriks, O.C. Boerman[1] and R.P. Bleichrodt, [1]Radboud University Nijmegen Medical Centre, The Netherlands, Depts of Surgery and Nuclear Medicine

15.30 Einde abstractsessie, theepauze in de expositiehal

Nederlandse Vereniging voor Gastrointestinale Chirurgie **Auditorium**

Voorzitters: L. Stassen en A. Menon

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

16.00 Atherosclerosis: a new risk factor for anastomotic leakage? (p. 95)
J. Slieker[1], N. Komen[1], P. Klitsie[1], J. Hermans[1], K. Havenga[2], M. Oudkerk[2], G.J. Kleinrensink[1], J. Jeekel[1], J.F. Lange[1], [1]Erasmus MC, Rotterdam, [2]University Medical Centre Groningen, The Netherlands

16.10 Sentinel node procedure of the sigmoid using indocyanine green: feasibility study in a goat model (p. 96)
M.H.G.M. van der Pas[1], G.A.M.S. van Dongen[2], F. Cailler[3], A. Pèlegrin[3], W.J.H.J. Meijerink[1], [1]Dept of Surgery, VU University Medical Centre, Amsterdam, [2]Dept of Otolaryngology, Head and Neck Surgery, VU University Medical Centre, Amsterdam, The Netherlands, [3]Institut de Recherche en Cancérologie de Montpellier, France

16.20 Isolated tumor deposits in colorectal cancer predict an adverse outcome (p. 97)
E.J.Th. Belt[1], M.F.M. van Stijn[1], H. Bril[2], E.S.M. de Lange-de Klerk[3], G.A. Meijer[4], S. Meijer[1], H.B.A.C. Stockmann[5], [1]Dept of Surgery, VU University Medical Centre, Amsterdam, [2]Dept of Pathology, Kennemer Gasthuis, Haarlem, [3]Dept of Epidemiology and Biostatistics, VU University Medical Centre, Amsterdam, [4]Dept of Pathology, VU University Medical Centre, Amsterdam, [5]Dept of Surgery, Kennemer Gasthuis, Haarlem, The Netherlands

16.30 Incisional Hernias in Old Stoma Wounds: a Cohort Study (p. 98)
M.H.F. Schreimacher[a], G.H.E.J. Vijgen[a], P.C. Dagnelie[b], J.G. Bloemen[a], B.F. Huizinga[a], N.D. Bouvy,[a,] [a]Dept of General Surgery, Maastricht University Medical Centre, Maastricht, [b]Dept. of Epidemiology, Maastricht University Medical Centre, Maastricht, The Netherlands

16.40 Histological identification of epithelium in perianal fistulas (p. 99)
P.J. van Koperen[1], F.J.W. ten Kate[2], W.A. Bemelman[1], J.F.M. Slors[1], [1]Dept of Surgery, Academic Medical Centre, Amsterdam, [2]Dept of Pathology, Academic Medical Centre, Amsterdam, The Netherlands

16.50 The anal fistula plug treatment compared to the mucosal advancement flap for cryptoglandular high transsphincteric perianal fistula: A double blinded multicentre randomized trial (p. 100)
P.J. van Koperen[1], W.A. Bemelman[1], M.F. Gerhards[2], L.W.M. Janssen[3], W.F. van Tets[4], A.D. van Dalsen[5], J.F.M. Slors[1], [1]Dept of Surgery, Academic Medical Centre, Amsterdam, [2]Dept of Surgery, Onze Lieve Vrouwe Gasthuis, Amsterdam, [3] Dept of Surgery, Zuwe Hofpoort Hospital, Woerden, [4]Dept of Surgery, Sint Lucas Andreas Hospital Amsterdam, [5]Dept of Surgery, Isala Clinics, Zwolle, The Netherlands

17.00 *Voor de plenaire sessie (President Select) en de uitreiking van de Astra-Zeneca Gastrointestinale Research Award 2009 kunt u zich begeven naar de Brabantzaal*

Nederlandse Vereniging voor Gastroenterologie **Brabantzaal**

Voorzitters: J.J.G.H.M. Bergman en M.A.J.M. Jacobs

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

08.30 Autofluorescence endoscopy improves the targeted detection of early Barrett's neoplasia but subsequent detailed inspection with Narrow-Band Imaging is of limited value. A randomized cross-over study comparing endoscopic tri-modal imaging with standard endoscopy (ISRCTN 68328077) (p. 101)

W.L. Curvers[1], L. Alvarez-Herero[1,2], M.B. Wallace[3], K. Ragunath[4], L.M. Wong Kee Song[5], H.C. Wolfsen[3], V. Subramanian[4], K.K. Wang[5], B.L.A.M. Weusten[2], J.J.G.H.M. Bergman[1],[1]Academisch Medisch Centrum, Amsterdam, [2]St Antonius, Nieuwegein, The Netherlands, [3]Mayo Clinic, Jacksonville, USA, [4]Queen's Medical Centre, Nottingham, UK, [5]Mayo Clinic, Rochester, USA

08.40 A randomized prospective trial in 74 patients comparing the ER-cap technique and multi-band mucosectomy technique for piecemeal endoscopic resection in Barrett esophagus (p. 102)

R.E. Pouw1, L. Alvarez Herrero1, 2, F.G. van Vilsteren1, F.J.W. ten Kate3, B.E. Schenk4, E.J. Schoon5, F.T.M. Peters6, R. Bisschops7, B.L. Weusten2, J.J. Bergman1, 1Dept. of Gastro-enterology, Academic Medical Centre, Amsterdam, 2Dept. of Gastroenterology, St. Antonius Ziekenhuis, Nieuwegein, 3Dept. of Pathology, Academic Medical Centre, Amsterdam, 4Dept. of Gastroenterology, Isala Clinics, Zwolle, [5]Dept. of Gastroenterology, Catharina Ziekenhuis, Eindhoven, 6Dept. of Gastroenterology, University Medical Centre, Groningen, The Netherlands, 7Dept. of Gastroenterology, University Hospital Leuven, Leuven, Belgium

08.50 Do we still need endoscopic ultrasound (EUS) in the work-up of patients with early esophageal neoplasia for endoscopic treatment? A retrospective analysis of 131 cases (p. 103)

P.E. Pouw[1], N. Heldoorn[1], L. Alvarez Herrero[1], F.J.W. ten Kate[2], K.K. Krishnadath[1], P. Fockens[1], J.J. Bergman[1],[1]Dept. of Gastroenterology, Academic Medical Centre, Amsterdam, [2]Dept. of Pathology, Academic Medical Centre, Amsterdam, The Netherlands

09.00 Einde abstractsessie

Vrijdag 9 oktober 2009

Symposium - Diagnostiek van de dunne darm — Brabantzaal

Voorzitter: M.A.J.M. Jacobs

09.00 VCE indications and outcome
Dr. E. Rondonotti, University of Milan, Department of Medical Sciences and Gastroenterology, Milaan, Italy

09.25 Enteroscopie van de dunne darm - de gouden standaard
Dr. P.B.F. Mensink, maag-darm-leverarts, Erasmus MC, Rotterdam

09.50 Radiologische beeldvorming van de dunne darm; huidige ontwikkelingen
Drs. S.J.B. van Weyenberg, maag-darm-leverarts, VUmc, Amsterdam

10.15 Samenvatting en discussie
Dr. M.A.J.M. Jacobs, maag-darm-leverarts, VUmc, Amsterdam

10.30 Koffiepauze

Nederlandse Vereniging voor Gastroenterologie — Brabantzaal

Voorzitters: J.J.G.H.M. Bergman en M.A.J.M. Jacobs

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

11.00 Risk of lymph node metastases in late early adenocarcinoma of the oesophagus and cardia diagnosed by endoscopic resection (p. 104)
L. Alvarez Herrero[1, 2], R.E. Pouw[2], F.G.I. van Vilsteren[2], F.J.W. ten Kate[3], B.L.A.M. Weusten[1], J.J. Bergman[2], [1]Dept of Gastroenterology and Hepatology, St Antonius, Nieuwegein, [2]Dept of Gastroenterology and Hepatology and [3]Pathology, Academic Medical Centre, Amsterdam, The Netherlands

11.10 Surveillance of individuals at high risk of pancreatic cancer; preliminary results of a multicentre prospective study (p.105 + p. 106)
F. Harinck[1], I. Kluijt[6], J-W. Poley[1], A. Cats[7], C.M. Aalfs[4], M.G.W. Dijkgraaf[8], R. Timmer[9], H.J. van Dullemen[10], D.J. Gouma[3], C.Y. Nio[5], P. Fockens[2], M.J. Bruno[1] Gastro, [1]Dept of Gastroenterology and Hepatology, Erasmus Medical Centre Rotterdam, [2]Dept of enterology and Hepatology, Academic Medical Centre Amsterdam, [3]Dept of Surgery, Academic Medical Centre Amsterdam, [4]Dept of Clinical Genetics, Academic Medical Centre Amsterdam, [5]Dept of Radiology, Academic Medical Centre, Amsterdam, [6]Dept of Clinical Genetics, Netherlands Cancer Institute Amsterdam, [7]Dept of Gastroenterology and Hepatology, Netherlands Cancer Institute Amsterdam, The Netherlands

11.20 Safety and efficacy of the Trans-Oral Endoscopic Restrictive System (TERIS) for the treatment of obesity (p. 107)

K. de Jong[1], E.M.H. Mathus-Vliegen[1], J.H. Eshuis[2], P. Fockens[1], [1]Dept of Gastroenterology and Hepatology, [2]Dept of Anesthesiology, Academic Medical Centre, Amsterdam, The Netherlands

11.30 Polyp location is a risk factor for delayed type post-polypectomy hemorrhage: a multi-centre case-control study (p. 108)

T. Herngreen[1], K.T. Buddingh[1], J. Haringsma[2], F.P. Vleggaar[3], R. Breumelhof[4], F. ter Borg[1] [1]Dept of Gastroenterology and Hepatology, Deventer Hospital, Deventer, [2]Dept of Gastro-enterology and Hepatology, Erasmus Medical Centre, Rotterdam,[3]Dept of Gastroenterology and Hepatology, University Medical Centre Utrecht, Utrecht,[4]Dept of Gastroenterology and Hepatology, Diakonessenhuis Utrecht, Utrecht, The Netherlands

11.40 Third eye retroscope randomized clinical evaluation ("TERRACE" study): Initial results (p. 109)

A.M. Leufkens[1], A. Repici[2], P. Deprez[3], B. Saunders[4], F.P. Vleggaar[1], G. Rando[2], K. Azzouzi[3], O. Dewit[3], J. East[4], A. Ignjatovic[4,] P.D. Siersema[1], [1]Dept of Gastroenterology and Hepatology, University Medical Centre, Utrecht, The Netherlands; [2]Dept of Digestive Endoscopy, Istituto Clinico Humanitas, Milan, Italy; [3]Dept of Gastroenterology, Cliniques Universitaires Saint-Luc, Brussels, Belgium; [4]Wolfson Unit for Endoscopy, St. Mark's Hospital, London, UK

11.50 Is ileoanal pouch surveillance indicated after restorative proctocolectomy for neoplasia in ulcerative colitis? (p. 110)

T. Kuiper[1], M. Vlug[2], F.J.C. van den Broek[1], K.M.A.J. Tytgat[1], S. van Eeden[3], P.C.F. Stokkers[1], P. Fockens[1], W.A. Bemelman[2], E. Dekker[1], Depts of Gastroenterology and Hepatology[1], Surgery[2] and Pathology[3], Academic Medical Centre, Amsterdam, The Netherlands

12.00 Nurse endoscopists doing colonoscopy: a prospective study on performance in clinical practice of a general hospital (p. 111)

M. van den Kerkhof[1], A. van Neerven[1], P. Friederich[2], K. Ocran[2], dr. F. L. Wolters[2], dr. R.P.R. Adang[2], [1]Nurse endoscopists and [2]gastroenterologists, VieCuri MC, Venlo, The Netherlands

12.10 Einde abstractsessie

State of the Art Lecture **Brabantzaal**

12.20 **'Creating a sustainable quality framework for endoscopy services'**
Dr. R. Valori, UK., National Lead in Endoscopy en National Advisor on Colorectal Cancer Screening.

13.00 Lunchbuffet in expositiehal

Voorzitters: B. van Hoek en J.F. Monkelbaan

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

08.40 Single nucleotide polymorphisms (SNPs) in C-type lectin genes, clustered in the IBD2 and IBD6 susceptibility loci, may play a role in the pathogenesis of Inflammatory Bowel Diseases *(WO06-16)*(p. 112)

S.C.S.Wolfkamp[1], M.I. Verstege[1], S. Meisner[1], A.A. te Velde[1], P.C.F. Stokkers[2], [1]Centre for Experimental and Molecular Medicine, Academic Medical Centre, Amsterdam, The Netherlands, [2]Dept of Gastroenterology and Hepatology, Academic Medical Centre, Amsterdam, The Netherlands

08.50 Affinity capturing of autoantibodies using synthetic ganglioside epitopes for the treatment of the Guillain-Barré Syndrome (MWO 05-27, MLDS)(p. 113)

A. Heikema[1], K. Tetala[2], V. de Matteis[2], A. Tio[3], B. Jacobs[3], H. Endtz[1,4], A. Pukin[2], M. Gilbert[5], G. Visser[2], H. Zuilhof[2] and A. van Belkum[1], [1]Dept of Medical Microbiology and Infectious Diseases, University Medical Centre Rotterdam, [2]Laboratory of Organic Chemistry, Wageningen University, [3]Dept of Neurology, University Medical Centre Rotterdam, The Netherlands, [4]International Centre for Diarrhoeal Disease Research, Dhaka, Bangladesh, [5]Institute for Biological Sciences, National Research Council of Canada, Ottawa, Canada

09.00 Complement activation in human non-alcoholic fatty liver disease (p. 114)

S.S. Rensen[1], F.J. Verdam[1], Y. Slaats[1], A. Driessen[2], C.J. Peutz-Kootstra[2], J. Nijhuis[1], J.W. Greve[1,3], W.A. Buurman[1,][1]Dept of Surgery and [2]Dept of Pathology, Nutrition and Toxicology Research Institute Maastricht, Maastricht University Medical Centre, Maastricht, [3]Dept of Surgery, Atrium Medisch Centrum, Heerlen, The Netherlands

09.10 Baseline and on-treatment HBsAg level as a predictive marker in chronic hepatitis B patients treated with a combination of Peginterferon alfa-2a and Adefovir: an interim analysis (p. 115 + p. 116 + p. 117)

R.B. Takkenberg[1], H.L. Zaaijer[2], A. de Niet[1], C.J. Weegink[1], M. Koot[3], V. Terpstra[4], M.G.W. Dijkgraaf[5], P.L.M. Jansen[1], H.L.A. Janssen[6], M.G.H.M. Beld[7], H.W. Reesink[1], [1]AMC Liver Centre, Dept of Gastroenterology and Hepatology, Academic Medical Centre, University of Amsterdam, Amsterdam, [2]Medical Microbiology and Karl Landsteiner Laboratory, Academic Medical Centre, Centre for Infectious Disease and Immunology (CINIMA), University of Amsterdam, Amsterdam, [3]Sanquin, Dept of Virus Diagnostic Services, Amsterdam, [4]Dept of Pathology, Academic Medical Centre, University of Amsterdam, Amsterdam, [5]Dept of Clinical Epidemiology and Biostatistics, Academic Medical Centre, University of Amsterdam, [6]Dept of Gastroenterology & Hepatology, Erasmus MC, University Medical Centre Rotterdam, Rotterdam, [7]KIT Biomedical Research, Amsterdam, The Netherlands

09.20 Five year tenofovir therapy is associated with maintained virologic response, but significant decline renal function in HIV/HBV coinfected patients (p. 118)

J.G.P. Reijnders1, T.E.M.S. de Vries-Sluijs2, B.E. Hansen1, H.L. Zaaijer3, J.M. Prins4, M. Schutten5, R.A. de Man1, M.E. van der Ende2, H.L.A. Janssen1,1Dept of Gastroenterology and Hepatology, Erasmus MC University Medical Centre Rotterdam, 2Dept of Internal Medicine -Infectious Diseases, Erasmus MC University Medical Centre Rotterdam, 3Dept of fMedical Microbiology (CINIMA), Academic

Medical Centre, Amsterdam, 4Dept of Internal Medicine, Division of Infectious Diseases, Tropical Medicine and AIDS, Academic Medical Centre, Amsterdam, 5Dept of Virology, Erasmus MC University Medical Centre Rotterdam, The Netherlands

09.30 Intrahepatic Hepatitis B virus (HBV) covalenty closed circular DNA (ccc-DNA) is a predictor of response in chronic HBV patients treated with a combination of peginterferon-alfa 2a and adefovir (p. 119)

R.B. Takkenberg[1], H.L. Zaaijer[2], A. de Niet[1], C.J. Weegink[1], M. Koot[3], V. Terpstra[4],M.G.W. Dijkgraaf[5], P.L.M. Jansen[1], M.G.H.M. Beld[6], H.W. Reesink[1], [1]AMC Liver Centre, Dept of Gastroenterology and Hepatology, Academic Medical Centre, University of Amsterdam, [2]Medical Microbiology and Karl Landsteiner Laboratory, Academic Medical Centre, Centre for Infectious Disease and Immunology (CINIMA), University of Amsterdam, [3]Sanquin, Dept of Virus Diagnostic Services, Amsterdam, [4]Dept of Pathology, Academic Medical Centre, University of Amsterdam, [5]Dept of Clinical Epidemiology and Biostatistics, Academic Medical Centre, University of Amsterdam, [6] KIT Biomedical Research, Amsterdam, The Netherlands

09.40 Focal nodular hyperplasia and adenoma of the liver: contrast enhanced ultrasound performance (p. 120)

P. Taimr, R.J. de Knegt, R.S. Dwarkasing, H.L.A. Janssen, Dept. of Hepato-gastroenterology, Erasmus MC, Rotterdam, The Netherlands

09.50 Prevalence of HCV among former and current drug users and marginally housed people: results of a multidisciplinary approach on screening and antiviral treatment (p. 121)

D.M. Hotho[1], J.N. Breemer[2], G.J. van Doornum[1], H. Voeten[2], O. de Zwart[2], H.L.A. Janssen[1], R.J. de Knegt[1], [1]Erasmus Medical Centre, Rotterdam, [2]Public Health Service, Rotterdam, The Netherlands

Koffiepauze

Symposium **Baroniezaal**

Voorzitters: A. Cats en R.L.H. Jansen

Richtlijn Maagcarcinoom

11.00 Inleiding: what's new?
Dr. R.L.H. Jansen, medisch oncoloog, Maastricht Universitair Medisch Centrum, Voorzitter van de richtlijnwerkgroep

11.15 Dr. Early gastric cancer in Nederland: hoe verder?
Dr. J.J.G.H.M. Bergman, MDL-arts, Academisch Medisch Centrum, Amsterdam

11.35 Wat is een curatieve maagresectie en is er plaats voor een palliatieve resectie?
Dr. H.H. Hartgrink, chirurg, Leids Universitair Medisch Centrum

12.00 Welke peri-operatieve behandeling is nu standaard?
Dr. A. Cats, MDL-arts, NKI Antoni van Leeuwenhoekhuis, Amsterdam.

12.20 Einde programma in deze zaal.
In de Brabantzaal start om 12.20 de lezing van Dr. R. Valori 'Creating a sustainable quality framework for endoscopy services'

13.00 Lunchbuffet in expositiehal

Nederlandse Vereniging voor Gastroenterologie **Parkzaal**

Voorzitter: G. Bouma en B. Oldenburg

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

08.30 Fatigue in Inflammatory Bowel Disease, results of a population based study in the Netherlands; the IBD-South Limburg cohort (p. 122)

M.J.L. Romberg-Camps[1,5], Y. Bol[2], P.C. Dagnelie[3], M.A.M. Hesselink-van de Kruijs[1], A.D.M. Kester[4], L.G.J.B. Engels[5], C. van Deursen[6], W.H.A. Hameeteman[1], M. Pierik[1], F. Wolters[7], M.G.V.M. Russel[8], R.W. Stockbrügger[1], [1]Dept of Gastroenterology and Hepatology, Maastricht University Medical Centre, [2]Dept of Medical Psychology, Orbis Medical Centre, Sittard, [3]Dept of Epidemiology, Maastricht University, [4]Dept of Methodology and Statistics, Maastricht University, [5]Dept of Internal Medicine and Gastroenterology, Orbis Medical Centre, Sittard, [6]Dept of Internal Medicine and Gastroenterology, Atrium Medical Centre, Heerlen, [7]Dept of Gastroenterology, Vie-Curi Medical Centre, Venlo, [8]Dept of Gastroenterology, Medisch Spectrum Twente, Enschede, The Netherlands

08.40 Factors determining the severity of fatigue in Crohn's disease patients (p. 123)

L. Vogelaar, A. van 't Spijker, Z. Zelinkova, E.J. Kuipers, C.J. van der Woude, Dept of Gastroenterology & Hepatology, Erasmus MC, Rotterdam, The Netherlands

08.50 Peri-conceptional use of medication for inflammatory bowel diseases in a referral centre (p. 124)

Z. Zelinkova, P.B.F. Mensink, J. Dees, E.J. Kuipers, C.J. van der Woude, Dept of Gastroenterology and Hepatology, Erasmus MC, Rotterdam, The Netherlands

09.00 Bone Mineral Density in IBD: a 5- year follow-up study (p. 125)

A.G.L. Bodelier[1], A.C. Heijckmann[2], B. Dumitrescu[3], D. Jonkers[1], E. de Boer[1], M. van Kroonenburgh[4], W. Hameeteman[1], A.A.M. Masclee[1], M.J. Pierik[1], [1]Dept of internal Medicine, Division Gastroenterology-Hepatology, Maastricht University Medical Centre, [2]Dept of Internal Medicine, Bernhoven Hospital, Veghel, [4]Dept of Nuclear Medicine, Maastricht University Medical Centre, The Netherlands

09.10 6-Thioguan is an effective and tolerable rescue drug in the treatment of ulcerative colitis (p. 126)

D.P. van Asseldonk[1], B. Jharap[1], N.K.H. de Boer[1], D.J. Kuik[2], B.D. Westerveld[3], F.J.G.M. Kubben[4], M.G.V.M. Russel[5], C.J.J. Mulder[1] and A.A. van Bodegraven[1], [1]Dept of Gastroenterology and Hepatology, VU University Medical Centre, Amsterdam; [2]Dept of Epide-miology and Biostatistics, VU University Medical Centre, Amsterdam, [3]Dept of Gastro-enterology and Hepatology, Isala Clinics, Zwolle; [4]Dept of Gastroenterology and Hepatology, Maasstad Hospital, Rotterdam; [5]Dept of Gastroenterology and Hepatology, Twente Medical Spectrum, Enschede, The Netherlands

09.20 Microsatellite status of colorectal cancer in patients with primary sclerosing cholangitis and concurrent Inflammatory Bowel Disease (p. 127)

M.M.H. Claessen[1], F.P. Vleggaar[1], M.E.I. Schipper[2], F.H.M. Morsink[2], J.W.J. Hinrichs[2], P.D. Siersema[1], G.J. A. Offerhaus[2], [1]Dept of Gastroenterology and Hepatology, University Medical Centre Utrecht, [2]Dept of Pathology, University Medical Centre Utrecht, The Netherlands

Nederlandse Vereniging voor Gastroenterologie — Parkzaal

Voorzitter: A.A.M. Masclee en A. Cats

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

09.30 The outcome of longterm surveillance of families with dominant clustering of colorectal cancer (p. 128)

M. Abdirahman[1,2], H.F.A. Vasen[1,2], J. Kleibeuker[3], M. van Kouwen[4], J.J. Koornstra[3], A. Cats[5], E. Dekker[6], A.M.J. Langers[2], S. Sanduleanu[7], J-W. Poley[8], J.C.H. Hardwick[2], W.H. de Vos tot Nederveen Cappel[2], A.E. van der Meulen-de Jong[2], F.N. Nagengast[4], [1]The Netherlands Foundation for the Detection of Hereditary Tumours, Leiden, [2]Dept of Gastroenterology and Hepatology, Leiden University Medical Centre, [3]Dept of Gastroenterology and Hepatology, University Medical Centre Groningen, [4]Dept of Gastroenterology and Hepatology, Radboud University Medical Centre Nijmegen, [5]National Cancer Institute, Amsterdam, [6]Dept of Gastroenterology and Hepatology, Academic Medical Centre, Amsterdam, [7]Dept of Gastroenterology and Hepatology, University Medical Centre, Maastricht, [8]Dept of Gastroenterology and Hepatology, Erasmus Medical Centre Rotterdam, The Netherlands

09.40 First-degree relatives of hyperplastic polyposis patients have an increased colorectal cancer risk (p. 129)

K.S. Boparai[1], J.B. Reitsma[2], V. Lemmens[3], J.J. Koornstra[4], F.M. Nagengast[5], M. Jacobs[6], J.J. Keller[1], E. Dekker[1], [1]Dept of Gastroenterology and Hepatology, Academic Medical Centre, Amsterdam, [2]Dept of Clinical Epidemiology & Biostatistics, Academic Medical Centre, Amsterdam, [3]Dept of Research, Comprehensive Cancer Centre South, Eindhoven, [4]Dept of Gastroenterology and Hepatology, University Medical Centre Groningen, Groningen, [5]Dept of Gastroenterology and Hepatology, Radboud University Medical Centre, Nijmegen, [6]Dept of Gastroenterology and Hepatology, VU Medical Centre, Amsterdam, The Netherlands

09.50 Adenomatous and hyperplastic polyps: co-factors in colorectal carcinogenesis?(p. 130)

E. Rondagh[1], M. Bouwens[1], R. Riedl[2], B. Winkens[3], A. Masclee[1], S. Sanduleanu[1], Dept of Gastroenterology and Hepatology[1], Dept of Pathology[2], Dept of Methodology and Statistics[3], Maastricht University Medical Centre, The Netherlands

10.00 Performance of an integrated risk profile for selection of high risk individuals for colorectal cancer (p. 131)

S.T. van Turenhout[1], I. Stegeman[2,3], F.A. Oort[1], B.S. Ferket[3], G.A. Meijer[4], R.A. Kraaijenhagen[3], C.J.J. Mulder[1], Gastroenterology and Hepatology, VU university medical centre, Amsterdam[1], Clinical Epidemiology and Biostatistics, AMC, Amsterdam[2], NDDO Institute for Prevention and Early Diagnostics (NIPED), Amsterdam[3], Pathology, VU university medical centre, Amsterdam, The Netherlands[4]

10.10 Is the performance of a faecal occult blood test really different in a referred population compared with a screening population? (p. 132)

S.T. van Turenhout[1], L.G.M. van Rossum[2], F.A. Oort[1], R.J.F. Laheij[2], A.F. van Rijn[3], G.A. Meijer[4], J.B.M.J. Jansen[2], E. Dekker[3] and C.J.J. Mulder[1], [1]Gastroenterology and Hepatology, VU University Medical Centre Amsterdam; [2]Gastroenterology and Hepatology, Radboud University Nijmegen Medical Centre; [3]Gastroenterology and Hepatology, Academic Medical Centre, Amsterdam; [4]Pathology, VU University Medical Centre Amsterdam, The Netherlands

10.20 Extended endoscopic mucosal resection is a safe and effective alternative for transanal endoscopic microsurgery concerning the treatment of large rectal adenomas (p. 133)

R.M. Barendse[1], F.J.C. van den Broek[1], W.A. Bemelman[2], P. Fockens[1], E. Dekker[1], Depts of [1]Gastroenterology and Hepatology and [2]Surgery, Academic Medical Centre, Amsterdam, The Netherlands

10.30 Koffiepauze

Nederlandse Vereniging voor Gastroenterologie — Parkzaal

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

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

11.00 Clinical trial: Low-volume PEG-solution plus ascorbic acid versus high-volume PEG-solution as bowel preparation for colonoscopy (p. 134)

S. Corporaal[1], J.H. Kleibeuker[1], J.J. Koornstra[1], [1]Dept of Gastroenterology and Hepatology, University Medical Centre Groningen, The Netherlands

11.10 Is coeliac disease overrepresentated in patients with constipation? * (p. 135)

R.A.A. Pelleboer[1], R.L.H. Janssen[1], J.M. Deckers-Kocken[2], E. Wouters[2], A.C. Nissen[3], W.E.A. Bolz[4], W.E. Tjon A Ten[5], C. van der Feen[6], K.J. Oosterhuis[7], M.H. Rövekamp[8], R.H.J. Houwen[6], [1]Dept of Pediatrics, Catharina Hospital Eindhoven, [2]Flevo Hospital Almere, [3]St Elisabeth Hospital Tilburg, [4]Elkerliek Hospital Helmond, [5]Máxima Medical Centre Veldhoven, [6]University Medical Centre Wilhelmina Childrens Hospital Utrecht, [7]St Jansdal Hospital Harderwijk, [8] Gelre Hospital Apeldoorn, The Netherlands

11.20 The significance of intraepithelial lymphocytosis without villous atrophy for diagnosing celiac disease (p. 136)

L. van den Heuvel, E.J. van der Wouden, J. Vecht, F. Moll, H. Engel and M.A.C. Meijssen, Isala Klinieken, Zwolle., The Netherlands

11.30 Effectiveness of cladribine treatment in refractory coeliac disease type II (p. 137 + p. 138)

G.J. Tack[1], W.H.M. Verbeek[1], A. Al-Toma[2], D.J. Kuik[3], M.W.J. Schreurs[4], O.Visser[5], C.J.J. Mulder[1], Depts of [1]Gastroenterology and Hepatology, [2]Dept of Gastroenterology and Hepatology, St.Antonius Hospital, Nieuwegein, [3]Epidemiology and Biostatistics, [5]Haematology and [4]Pathology, VU University Medical Centre Amsterdam, The Netherlands.

11.40 Universal duodenal microbiota with IS-pro in individuals undergoing routine gastroscopy (p. 139)

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

11.50 Bovine antibody-based oral immunotherapy for reduction of intragastric *Helicobacter pylori* colonization: A randomized placebo-controlled clinical trial (p. 140)

C.M. den Hoed[1], A.C. de Vries[2], P.B.F. Mensink[1], C.M. Dierikx[3], L. Capelle[1], H. van Dekken[1], E.J. Kuipers[1],[1]Dept of Gastroenterology and Hepatology, Erasmus Medical Centre, [2]Gastroenterology and Hepatology, St. Fansiscus Medical Centre, Rotterdam, [3]University Wageningen, Lelystad, The Netherlands

12.00 Prevalence of premalignant changes in the stomach of patients undergoing routine colonoscopy; a cross-sectional cohort study (p. 141)

C.M. den Hoed[1], L.G. Capelle[1], B.C. van Eijck[1], P.D. Siersema[1], E.J. Kuipers[1, 2], Depts of Gastro-enterology and Hepatology[1], and Internal Medicine[2], Erasmus Medical Centre, Rotterdam, The Netherlands

12.10 Esophaguscarcinoma: Staging with EUS-FNA and PET-CT and survival with or without neo-adjuvant chemoradiation followed by surgery in a medium volume Centre. (p. 142)

A.M. Zonneveld, A.C. Poen, Dept of Gastroenterology, Isala klinieken Zwolle, The Netherlands

12.20 Prevalence of gastrointestinal symptoms in the community: results of a survey among 50,000 persons (p. 143)

M.G.H. van Oijen[1], M.M. Tielemans[1], L.G.M. van Rossum[1], T. Eikendal[1], J. Jaspers Focks[2], R.J.F. Laheij[1], J.B.M.J. Jansen[1], Dept of [1]Gastroenterology & Hepatology, and [2]Cardiology, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands

12.30 Subgroup analyses of the Dutch Dyspepsia Study: over-the-counter versus prescribed NSAIDs and plain versus buffered aspirin (p. 144 + p. 145)

M.M. Tielemans[1], J. Jaspers Focks[2], L.G.M. van Rossum[1], T. Eikendal[1], M.A. Brouwer[2], R.J.F. Laheij[1], J.B.M.J. Jansen[1], M.G.H. van Oijen[1], Dept of [1]Gastroenterology & Hepatology, and [2]Cardiology, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands

12.40 Health-related quality of life change in patients with new onset dyspepsia treated with stepwise acid suppression strategies (p. 146)

C.J. van Marrewijk[1], M.G.H. van Oijen[1], G.A.J. Fransen[2], S. Mujakovic[3], J.W. Muris[2], N.J. de Wit[3], M.E. Numans[3], A.J. Knottnerus[2], D.E. Grobbee[3], R.J.F. Laheij[1], J.B.M.J. Jansen[1],[1]Radboud University Nijmegen Medical Centre, Nijmegen, [2]Maastricht University, Maastricht, [3]Utrecht University Medical Centre, Utrecht, The Netherlands

12.50 The MDM2 promoter SNP285C/SNP309G haplotype is associated with susceptibility for oesophageal squamous cell carcinoma and related to poor overall survival after surgical resection (p.147)

J.J. Boonstra[1], R. van Marion[1], L.B. Koppert[2], E. Steyerberg[3], H.W. Tilanus[2], W.N.M. Dinjens[1], [1]Dept of Pathology, Joseph Nefkens Insitute, Erasmus MC, Rotterdam, [2]Dept of Surgery, Erasmus MC, Rotterdam, [3]Dept of Public Health, Erasmus MC, Rotterdam, The Netherlands

13.00 Lunchbuffet in expositiehal

Vereniging Maag Darm Lever Verpleegkundigen **Auditorium**

09.30	Ontvangst met koffie en infomarkt
10.00	Opening door de voorzitter
10.05	De zieke obesitas patiënt; pathofysiologie en complicaties *Prof. dr. E. Mathus-Vliegen, maag-darm-leverarts AMC* *bijzonder hoogleraar klinische voeding*
10.50	Koffie en infomarkt (*V&VN, HAN, Obesitasvereniging, Coeliakie vereniging, en MDL-verpleegkundigen)*
11.20	Chirurgische benadering: bariatrische chirurgie *Dr. M.A.J.M. Hunfeld, bariatrisch chirurg, Rode Kruis ziekenhuis, Beverwijk*
11.45	Zin en onzin van diëten bij de obesitas patiënt. *Diëtist*
12.05	Angst voor ziekenhuisopname, waarom dan wel? *Obesitas Vereniging*
12.20	V&VN voor de leden: informeren en stemmen.
12.45	Lunch

Middagprogramma (gezamenlijk programma met SEVA in de Diezezaal)

14.00	Colonvoorbereiding
14.25	Coeliakie; pathofysiologie *Prof. dr. C.J.J. Mulder maag-darm-leverarts, VUmc, Amsterdam*
14.55	Coeliakie; dieetrichtlijnen *Mw. Ir. N. Wierdsma, diëtist-onderzoeker, VUmc, Amsterdam*
15.15	Diverticulitis – de radiologische benadering
15.45	Einde programma

Vrijdag 9 oktober 2009

Sectie Endoscopie Verpleegkundigen en Assistenten **Diezezaal**

Ochtendprogramma:

10.30 Opening door de voorzitter

10.35 Percutane endoscopische colonostomy, het medisch technische aspect
Mw. Dr. T.E.H. Römkes, MDL-arts, UMC St Radboud, Nijmegen

11.00 Percutane endoscopische colonostomy, de nazorg
Specialistisch verpleegkundige, UMC St. Radboud, Nijmegen

11.25 Endomicroscopie
Mw. Dr. S. Sanduleanu, MDL-arts, MUMC, Maastricht

11.50 SFERD
Afgevaardigde van de werkgroep

12.15 Ledenvergadering

13.00 Lunchbuffet in de Kempenhal

Middagprogramma (gezamenlijk programma met de VMDLV)

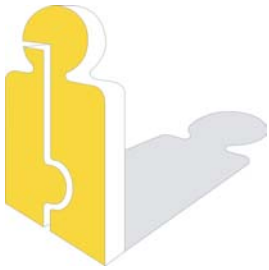
14.00 Colonvoorbereiding
Mw. M. van Waveren en mw. P. Peterson, verpleegkundigen Bethesda Ziekenhuis, Hoogeveen

14.25 Coeliakie; Pathofysiologie
Prof. dr. C.J.J. Mulder, MDL-arts VUmc, Amsterdam

14.55 Coeliakie; voedingsverhaal
Mw. Ir. N. Wierdsma, diëtist-onderzoeker, VUmc, Amsterdam

15.15 Diverticulitis; de radiologische benadering
Naam van spreker volgt nog

Abstracts




Nederlandse
Vereniging voor
Hepatologie


NVGIC
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Chirurgie

Taurine levels are decreased in critically ill patients despite adequate nutrition

S.M.P. Lemmens[1], M.A.R. Vermeulen[1], M. Visser[1], G.C. Ligthart-Melis[2], H.M. Oudemans -van Straaten[3], P.A.M. van Leeuwen[1], Depts of [1]Surgery and [2]Nutrition and Dietetics, VU University Medical Centre, Amsterdam, [3]Intensive Care, Onze Lieve Vrouwe Gasthuis, Amsterdam, The Netherlands

Rationale: Adequate nutritional support is vital for critically ill patients and has been subject of extensive study in recent years. Within the intensive care population there is high prevalence of disease-related malnutrition, associated with increased infectious morbidity and mortality and prolonged hospital stay. Although studies on nutrition in the ICU have demonstrated numerous clinical benefits, actual amino acid deficiencies have never been investigated in presumably optimally fed patients. Aim was to evaluate whether there are detectable amino acid deficiencies in patients given adequate nutrition, and if there are correlations between these and clinical outcome parameters.
Methods: In a prospective cohort of patients (N=39) with septic or cardiogenic shock we measured plasma amino acid concentrations on day 1, 2 and 5 of ICU admission. Patients received protein enriched enteral nutrition. We investigated the change in plasma amino acid concentrations. Correlations were studied by using Spearman test. Statistical significance was defined as 2-tailed $p < 0.05$. Results: Within the first 24 hours at ICU, median amino acid plasma levels increased. In contrast, taurine levels significantly decreased >50%, from 47.6 to 20.0 umol/L (p=0,000). From day 2-5 amino acid levels increased, whereas taurine stayed at the same level. Plasma taurine levels (at admission and throughout hospital stay) correlated with mechanical ventilation (p=0,015 / p=0,017 / p=0,011) and length of stay at ICU (p=0,064 / p=0,085 / p=0,002).
Conclusion: When on adequate nutritional support, amino acid levels raised, independent of severity of disease. However, plasma taurine levels declined. Low taurine levels were associated with a longer period of mechanical ventilation and a longer stay at the ICU. Taurine could be an essential candidate to enrich daily nutritional support for the critically ill patients, although more extensive research on this topic is required.

Arginine/ADMA is a predictor for cardiac output in septic shock patients

M.A.R. Vermeulen[1], M. Visser[1], M.C. Richir[1], S.M.P. Lemmens[1], G.C. Ligthart-melis[2], H.M. Oudemans-van Straaten[3], P.A.M. van Leeuwen[1], Depts of [1]Surgery and [2]Nutrition and Dietetics, VU Medical Centre, Amsterdam, [3]Intensive Care, Onze Lieve Vrouwe Gasthuis, Amsterdam, The Netherlands

Rationale: Arginine, the sole nitric oxide (NO) precursor and a semi-essential amino acid, is thought to become essential in septic patients. Controversially, some studies suggest that supplementation of arginine in sepsis may increase mortality, possibly mediated by effects of NO on vasodilatation and oxidative stress. Accumulation of the endogenous inhibitor of nitric oxide synthase (NOS) asymmetric dimethyl arginine (ADMA), is associated with ICU mortality. NOS and ADMA may antagonistically regulate production of NO in the systemic circulation. In humans, systemic infusion of ADMA results in immediate decrease of cardiac output. In septic patients, organ oxygenation is at risk and cardiac output is of vital importance. Therefore we investigated the relation of arginine and ADMA with cardiac output, and outcome of septic patients at ICU admission. Methods: In a prospective cohort of 24 patients with septic shock we measured arginine and ADMA concentrations as well as cardiac output at ICU admission. Results are expressed in median (±IQR). Correlations were studied by using non-parametric tests. Statistical significance was defined as 2-tailed $P < 0.05$. Results: Arginine levels tended to correlate positively with cardiac output (p=0.095). Arginine/ADMA ratio showed a positive correlation with cardiac output (p=0.031). Arginine levels tended to be higher in survivors (34.1 mol/L; IQR 28.1-52.8) than in non-survivors (22.1 mol/L; IQR 16.4-41.7) (p=0.110), whereas ADMA levels were lower instead (resp. 0.359 mol/L; IQR 0.3000-0.4076 and 0.495 mol/L; IQR 0.361-0.758 trend: p=0.062). Arginine/ADMA was significantly higher in survivors (resp. 102.5; IQR 95.6-140.5 and 61.0; IQR 33.3-81.4 p=0.003).
Conclusion: These results show that a higher arginine/ADMA ratio in patients with septic shock is associated with higher cardiac output and survival. This ratio appeared more sensitive than arginine and ADMA concentrations alone, probably because it reflects the balance between vasodilation and vasoconstriction, which likely depends on the degree of oxidant stress.

Parenteral lipids impair pneumococcal killing by human neutrophils in a structure-dependent manner

M.W. Versleijen[1], H.M. Roelofs[1], R.H. te Morsche[1], E. Simonetti[2], P.W. Hermans[2], G.J. Wanten[1], Depts of [1]Gastroenterology and Hepatology and [2]Laboratory of Pediatric Infectious Diseases, Radboud University Nijmegen Medical Center, The Netherlands

Lipid induced modulation of phagocyte function seems to contribute to the increased susceptibility to infections in patients on parenteral nutrition. The role of various available structurally different lipid emulsions, however, remains unclear. In the present study, we therefore assessed phagocyte function, as the capacity of neutrophils to kill Streptococcus Pneumonia, under the influence of these lipids. Neutrophils from 7 volunteers were incubated for 1 hour in emulsions (5mmol/l) derived from soybean- (LCT), fish- (VLCT), olive- (LCT-MUFA), mixed soybean/coconut oils (LCT/MCTs) or structured lipids (SL). After opsonisation of the pneumococci (strain OREP4), using human immunoglobulins, the bacteria were incubated with the neutrophils, in the presence of complement. Next, pneumococcal killing was evaluated and expressed as the percentage of survival relative to the initial bacterial count (in neutrophil-free samples). Neutrophils that were not exposed to lipids showed a killing capacity of 70±5% (mean±SEM). This basal capacity decreased after exposure to LCT (63±5% killing, p=0.06), and even more after exposure to LCT-MUFA, VLCT, SL and LCT/MCT 65±5% (p=0.02), 64±3% (p=0.03), 60±7% (p=0.02) and 44±6% (p=0.004), respectively. Conclusion: These data show that parenteral lipids impair pneumococcal killing of neutrophils in a structure-dependent manner. LCT/MCT is by far the most potent in this respect.

Quantification of intestinal absorption capacity in patients with chronic Graft-versus-Host Disease of the digestive tract

B.S. van der Meij[1], O.J. Visser[2], S. Hesselink[1], J.A.E. Langius[1], P.A.M. van Leeuwen3, A.A. van Bodegraven[4], N.J. Wierdsma[1], Depts of [1]Nutrition and Dietetics, [2]Haematology, [3]Surgery and [4]Gastroenterology and Hepatology, VU University Medical Center, Amsterdam, The Netherlands

Graft versus HostDisease (GvHD) is a common complication of allogeneic stem cell-transplantation. If GvHD involves the digestive tract (DT), symptoms includediarrhoea and weight loss. It is expected that intestinal malabsorption due toGvHD-DT causes significant energy and nutrient loss. Our objective was to quantify intestinal absorption capacity in patients with chronic GvHD-DT. Six patients (5 male, 1 female) with chronicGvHD-DT were studied at median 205 [151 – 619] days following allogeneic stem cell transplantation. Four patients experienced moderate chronic GvHD-DT and 2 patients experienced severe chronic GvHD-DT. During 3 days, faeces were collected. At the same time, energy and nutrient intake were recorded. Daily faecal energy and macronutrient loss were determined by bomb calorimetry and laboratory analyses. Intestinal absorption capacity was calculated as the differencebetween intake and faecal losses, expressed as percentage of intake. Malabsorption was defined as an intestinal absorption capacity of < 85%. Data are presented as median [range]. Results of faecal analyses showed an energy loss of 751 [573– 1454] kcal/24 h. Faecal production amounted 593 [435 – 1177] g/day, with a relatively high amount of water (dry faecal weight: 13 [9 – 24] %). Energy, fat, protein and carbohydrate absorption were respectively 77 [45-81], 69[58-81], 69 [0-90] and 80 [52-89]. All patients showed a malabsorption ofenergy and fat. Five patients also showed a protein malabsorption and 3 patients showed a carbohydrate malabsorption.
In conclusion, patients with GvHD-DT experience a substantial, and clinically significant reduced absorption capacity, indicating the need for specific nutritional intervention.

Preoperative chemotherapy and/or radiation in rectal cancer patients reduces hepatic insulin sensitivity

M.F.M. van Stijn[1], J.J. Atema[1], M.R. Soeters[2], M.J.M. Serlie[2], M.T. Ackermans[2], P.A.M. van Leeuwen[3], A.P.J. Houdijk[1], [1]Dept of Surgery, Medical Center Alkmaar, [2]Department of Endocrinology and Metabolism, Academic Medical Center, Amsterdam, [3]Dept of Surgery, VU University Medical Center Amsterdam, The Netherlands

Many patients with rectal cancer undergo chemo- and/or radiotherapy prior to surgery, to reduce local recurrence and improve outcome. However, these therapies may have negative impact on the preoperative metabolic state, which may result in delayed recovery. In a pilot study we assessed glucose metabolism in terms of insulin sensitivity in eight rectal cancer patients, after finishing their chemo- and/or radiotherapy, with a two-step hyperinsulinemic euglycemic clamp in the week prior to surgery. First a primed continuous infusion of [6,6-^{2}H2]glucose isotope (prime, 11 µmol/kg; continuous 0.11 µmol/kg/min) was given. Thereafter a continuous insulin infusion at a rate of 10 mU/m^2/min was started to assess hepatic insulin sensitivity (step 1; two hours); Then the insulin infusion rate was increased to a continuous rate of 40 mU/m^2/min to assess peripheral insulin sensitivity (step 2; two hours). During both steps glucose 20%, enriched 1% with [6,6-^{2}H2]glucose isotope, was added to maintain plasma glucose level of 5.0 mmol/L. At the closing stages of both steps five blood samples were withdrawn at five minutes intervals for determination of [glucose] and isotope enrichments to enable calculations on endogenous glucose production (EGP ~ hepatic insulin sensitivity) and peripheral glucose uptake (~ peripheral insulin sensitivity). The mean age was 62.7 years (range 48.9-74.6), and 50% was female. The mean body mass index was 25.5 kg/m^2 (23.3-28.1), fat free mass (FFM) was 71.5% (52.4-87.3). The EGP in the basal state was 11.8 $\pm$ 0.5 (µmol/kg/min; mean $\pm$ SEM), during step 1 6.2 $\pm$ 0.8, and during step 2 1.2 $\pm$ 0.4. Corrected for FFM the EGP in the basal state was 16.8 $\pm$ 1.0 (µmol/kg FFM/min; mean $\pm$ SEM), during step 1 8.6 $\pm$ 1.0, and during step 2 1.6 $\pm$ 0.5. The peripheral glucose uptake during step 1 was 12.3 $\pm$ 0.9 (µmol/kg/min) and during step 2 it was 30.1 $\pm$ 4.2. Corrected for FFM the peripheral glucose uptake during step 1 was 17.8 $\pm$ 1.9 (µmol/kg FFM/min) and during step 2 it was 44.1 $\pm$ 7.2.
Conclusions: The hepatic insulin sensitivity is markedly decreased prior to surgery. Even at an insulin infusion rate of 40 mU/m^2/min the EGP could not be depressed. Compared with available data on insulin sensitivity in elderly this is not just an age related decrease. Future studies are needed to reveal the separate effects of cancer, chemotherapy and radiation on insulin sensitivity in order to design strategies to improve preoperative glucose metabolism.

Timing of enteral nutrition in patients with predicted severe acute pancreatitis: an early start is associated with a reduction in bacteremia

O.J. Bakker[1], H.C. van Santvoort[1], M.G. Besselink[1], K. Fischer[2], T.L. Bollen[3], M.A. Boermeester[4], H.G. Gooszen[1], [1]Dept of Surgery, University Medical Center Utrecht, [2]Julius Center for Health Sciences and Primary Care, Univerity Medical Center Utrecht, [3]Dept of Radiology, St. Antonius Hospital, Nieuwegein, [4]Dept of Surgery, Amsterdam Medical Center, Amsterdam, The Netherlands

Introduction**:** Enteral nutrition (EN) has replaced parenteral nutrition in the management of patients with acute pancreatitis. The optimal time to start EN after admission is unknown. International guidelines recommend starting EN after a few days after admission whereas recent insights suggest that an early start of EN might be effective in reducing infectious complications. The aim of this study was to investigate if an early start of EN is associated with fewer infectious complications in patients with predicted severe acute pancreatitis. Methods**:** During 2003-2007, all patients with predicted severe acute pancreatitis (Acute Physiology and Chronic Health Evaluation [APACHE-II] score ≥8, or Imrie/modified Glasgow score ≥3, or C-reactive protein [CRP] >150 mg/L) were prospectively included in 15 hospitals in the Dutch 'probiotics in acute pancreatitis trial' (PROPATRIA). All patients received EN via a nasojejunal feeding tube. The time between admission and start of EN, however, varied between patients (at the discretion of the treating physician).Two groups were retrospectively defined: 1) the 'early EN group' (start of EN within 48 hours after admission) and 2) the 'standard EN group' (start after 48 hours after admission). Groups were compared for the total number of infectious complications: pneumonia, bacteremia and infected necrosis. Multivariate logistic regression was used to adjust for differences at baseline ($p<0.2$) and predicted disease severity (APACHE-II score). Results**:** The early (n=184) and standard (n=112) EN groups were highly comparable at baseline for APACHE-II score, C-reactive protein, Imrie-score, computed tomography severity index and the presence of (multi)organ failure. Infectious complications occurred in 49 patients (27%) in the early EN group versus in 38 patients (34%) in the standard EN group (adjusted odds ratio [OR] 0.659, 95%-confidence interval [CI] 0.33-1.33, p=.244). Early EN was associated with a reduction of bacteremia (14% versus 27%; adjusted OR 0.389, 95%-CI 0.17-0.88, p=.024). No reduction of infected necrosis (11% versus 13%, p=.853) or pneumonia (16% versus 14%, p=.861) was observed.
Conclusion**:** An early start of enteral nutrition may prevent bacteremia and hence improve outcome in patients with predicted severe acute pancreatitis. To this end, the Dutch Pancreatitis Study Group has recently started a nationwide randomized controlled trial comparing an early start of EN with standard therapy in predicted severe acute pancreatitis.

The necessity and timing of pancreatic duct visualization in the treatment of pancreatic fluid collections associated with acute pancreatitis

E.M.V. de Cuba, R.P. Voermans, E.A. Rauws & P. Fockens, Dept. of Gastroenterology & Hepatology, Academic Medical Center, Amsterdam, The Netherlands

Pancreatic fluid collections (PFCs) communicating with the pancreatic duct (PD) tend to recur more often than non-communicating collections. Therefore an ERCP is often performed in combination with transluminal drainage. It is still controversial if an early diagnosis and subsequent treatment of the disrupted PD is of benefit to all patients with PFCs complicating acute pancreatitis. Aim was to evaluate if performing an ERCP in combination with PFC drainage would reduce recurrence of PFCs in this group. We have performed a retrospective study on our prospectively collected cohort of patients evaluating all consecutive patients who underwent endoscopic transluminal drainage of PFCs complicating acute pancreatitis from April 2001 until January 2009. Our primary endpoint was recurrence of PFCs. Secondary endpoints were the number of endoscopic and surgical procedures and the mean duration of hospital stays per subject. We identified a total of 155 subjects from our database with PFCs complicating acute pancreatitis. 115 out of 155 subjects (74%) did not have their PD visualized during treatment. In 15 subjects the PFC recurred (13%). Forty subjects out of 155 (26%) had their PD visualized at one point during treatment. Of these 40, 31 subjects (77.5%) had their PD visualized via ERCP. All other subjects underwent either an MRCP, MRI or CT (22.5%). Of these 40 subjects, 19 (47.5%) had recurrent PFCs. The non-visualized group showed significantly less recurrences. ($P<0.05$) The 40 subjects with known anatomy were divided into an early and a late visualization group. Of the 13 subjects in the early group 4 subjects (30.1%) had recurrent PFCs vs. 15 out of 27 subjects (67.5%) in the late group. The early group underwent a mean of 3.8 endoscopic procedures vs. 3.9 in the late group. There were 0.5 vs. 0.7 surgical procedures performed per subject in each group. There was a mean duration of hospital stays of 9.2 days vs. 19.5 days. In conclusion, uncomplicated PFCs have an acceptable recurrence rate without the need to visualize the PD anatomy during treatment of the PFC. In complicated cases, visualization seems of additional value. However, knowing the additional risk of pancreatitis with ERCP we tend to advise the use of secretin enhanced MRCP for the visualization of the PD in this group of patients. Further research is needed to assess whether or not the diagnosis and subsequent treatment of PD alterations dictates the outcome of treatment of all PFCs.

Tropical Calcific pancreatitis is more severe than Western Idiopathic pancreatitis: a comparison between 2 cohorts from India and The Netherlands

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Introduction: Chronic pancreatitis (CP) is an inflammatory disorder leading to irreversible changes of the pancreas. In the western world it is most often considered to be idiopathic or caused by alcohol abuse, or genetic mutations. In the tropics there appears to be another CP type: tropical calcific pancreatitis (TCP). Though TCP superficially resembles idiopathic CP of the Western world, it is unknown whether both CP types are indeed similar. The goal of our study was to compare the clinical profile of CP in 2 large cohorts from India and The Netherlands. Study design: Observational cohort study. Material en method: The study population consisted of 354 (223 male) Dutch CP patients and 1033 (733 male) Indian CP patients of existing databases. Results: ICP was found in 83 (23%) Dutch and 671 (65%) Indian patients (p<0,0001), 246 (24%) of Northern and 323 (31%) of Southern India (p=0,02). Mean age of onset was 41,2 yrs (SD 16,6 yrs) in Dutch and 32,1 yrs (SD 14,9 yrs) in Indian patients (p<0,0001) without difference between South en North India (p=0,28). Diabetes was seen in 21/80 Dutch and in 253/671Indian ICP patients (p=0,05, OR 1,70, 95% CI 1,01-2,86). Patients of Southern India had significant more often diabetes than patients from the North (157/323 vs 73/246, p<0.0001, OR 2,24, 95% CI 1,58-3,18). Pancreatic calcifications were seen in 34/79 Dutch patients compared to 588/671 Indian patients (p<0,001, OR 9,376, 95% CI 5,68-15,48). Southern Indian patients had significant more calcifications than patients in the North (307/323 vs 191/246, p<0,0001, OR 5,25, 95% CI 3,08-9,92). The prevalence of pancreas carcinoma was similar between Dutch (1/80) and Indian (26/645) patients (p=0,31, OR 0,31, 95% CI 0,04-2,35). Pancreatic carcinoma was more often diagnosed in patients from southern India North (22/301 versus 3/243, p=0,01, OR 5,92, 95% CI 1,75-20,01).
Conclusions: The proportion of CP patients without a specific etiological factor is higher in India than in The Netherlands. The phenotype of ICP, especially in Southern India, is more severe than in The Netherlands.

Risk factors for abdominal arterial atherosclerosis

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Atherosclerotic disease of the abdominal arteries could lead to chronic gastrointestinal ischemia (CGI). Currently, little is known concerning the risk factors for atherosclerosis of abdominal arteries. The aim of this study was to investigate the prevalence of risk factors for atherosclerosis in patients with CGI due to atherosclerotic narrowing (>70%) of abdominal arteries.A prospective cohort study was performed in patients with unexpla d chronic abdominal symptoms referred for evaluation of suspected CGI. Other causes of abdominal complaints were previously excluded by appropriate diagnostic evaluation. A standard work-up was conducted including full medical and family history, physical examination, laboratory evaluation for atherosclerotic risk factors, CTA or MRA for imaging the abdominal vascular bed and gastrointestinal tonometry.From June 2006 until January 2009, we evaluated 195 patients. Twenty eight patients had celiac artery compression syndrome and 32 had non-occlusive CGI and were therefore excluded from further evaluation. Atherosclerotic occlusive CGI (ath-CGI) was diagnosed in 78 patients: 51 F, mean age 63 (17-86) years. Single- and multi-vessel disease was present in 42 and 36 patients, respectively. The remaining 57 patients did not have CGI (non-CGI group); they were comparable by age, mean BMI and gender with ath-CGI patients and were used as control group. Marked differences between patients with ath-CGI and the non-CGI group were: coronary vascular disease (CVD) and peripheral vascular disease were seen in 36% vs 23% and 33% vs 23% in ath-CGI vs non-CGI patients resp. Family history of CVD was present in 46% vs 30% in ath-CGI vs non-CGI patients. These differences did not reach statistical significance, likely due to insufficient power. No differences were apparent in cere-brovascular disease, DM, smoking and total homo-cyste. Mean ± SD total cholesterol was unexpectedly lower in ath-CGI vs. non-CGI patients (4.3 ± 1.1 mmol/l vs 4.9 ± 1.3mmol/l).
Conclusions: The prevalence of CVD, peripheral vascular disease and family history of CVD were observed higher in ath-CGI than in non-CGI patients. Despite low number of patients with this rare disease we did observe an increase in conventional risk factors for atherosclerotic disease. Higher cholesterol levels in non-CGI patients compared to ath-CGI patients is a new and remarkable finding. Further research is needed to confirm and evaluate these differences.

Serum sodium alone is the best predictor of waiting list mortality in patients awaiting liver transplantation

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Waiting list mortality in patients awaiting liver transplantation (OLT) remains high. In December 2006 the Model for End-stage Liver Disease (MELD) was introduced for prioritization of patients awaiting OLT. Although waiting time has decreased since the implementation of the MELD, waiting list mortality still remains high. Aim of this study was to improve liver allocation by assessing the predictive value for waiting list and overall mortality of several other "allocation models", compared to the currently utilized MELD model. In this single center study all patients listed for OLT in our center between Dec 15th 2006 and Feb 31st 2009 were included. For all patients MELD score and serum sodium levels at the time of listing were gathered. Patients were followed till June 6th 2009. Kaplan Meier curves were used to compare survival between groups. Using receiver operating characteristic (ROC)-curves the predictive value of the MELD was compared to the integrated MELD score (iMELD), MELD score comb d with serum sodium (MELDNa), MELD with added serum sodium (MELD-Na), MELD to sodium index (MESO), and serum sodium alone. The test with the greatest area under the curve (AUC) was considered best. A total of 142 patients were included in the study and 72 of these received OLT. In total 32 patients died, of which 19 died on the waiting list and 13 after OLT. Three patients were removed from the waiting list for other reasons. Analysis of the predictive value of above mentioned models for overall and waiting list mortality using ROC-curves showed an AUC of 0.661 and 0.687 for MELD, 0.698 and 0.700 for iMELD, 0.700 and 0.718 for MELDNa, 0.674 and 0.703 for MELD-Na, 0.674 and 0.700 for MESO index, and 0.725 and 0.753 serum sodium respectively. Further analysis showed that of the 142 patients listed, 36 had a hyponatremia at the time of listing (serum sodium ≤ 135 mmol/L). Analysis showed a strong correlation between serum sodium and waiting list and overall mortality ($P < 0.001$; $P < 0.001$). Survival was significantly worse in the hyponatremia group for both overall and waiting list survival ($P < 0.00001$; $P < 0.00001$).
Conclusion: There is a strong correlation between serum sodium and overall and waiting list mortality for patients awaiting OLT. The predictive value of serum sodium alone is superior to the currently used allocation model. Therefore serum sodium alone should be considered seriously as a model for liver allocation in the future.

Long-term results of liver transplantation with a national protocol for controlled cardiac death donors

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Within a national protocol for multi-organ donation after controlled cardiac death (DCD) we studied the outcomes of orthotopic liver transplantation (OLT) with DCD (n=55, 10.4%) and donation after brain death (DBD) (n=471) grafts. The 1- and 3-year patient survival rates for OLT after DCD were 84.6% and 80.4% respectively, and 86.3% and 80.8% afterDBD (p=0.763). Graft survival rates at 1 and 3 years after DCD-OLT were: 64.0% and 67.9%, and for DBD-OLT 80.5% and 74.7% respectively (p=0.212). Non-anastomotic biliary strictures (NAS) developed in 21.8% after DCD-OLT and in 8.2% after DBD-OLT (p=0.003). Primary nonfunction/ dysfunction and vascular complication rates were not different between OLT with DCD versus DBD grafts. Re-transplantation rate after DCD-OLT and DBD-OLT was 18.2% and 10.3% respectively (p=0.081), and retransplantation for NAS was 10.9% and 2.5% respectively (p=0.001). Independent risk factors for graft loss within one year after DBD-OLT were transplant center, warm ischemia time and severe head trauma as cause of donor death. Independent risk factors for graft loss after DCD-OLT was transplant center, first warm ischemia time, and cold ischemia time. A DCD liver graft was an independent risk factor for NAS.
In conclusion, a restrictive national protocol for DCD-OLT canb result in patient- and graft-survival rates similar to DBD-OLT, despite a higher rate of NAS and more retrans-plantation for NAS.

Trends in liver transplantation for primary biliary cirrhosis in The Netherlands 1988-2008

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Background and aims: A decrease in the need for liver transplantations (LTX) in Primary Biliary Cirrhosis (PBC), possibly related to treatment with ursodeoxycholic acid, has been reported in the USA. The aim of this study was to assess LTX requirements in PBC over the past 20 years in the Netherlands. Patients and methods: Analysis of PBC transplant data of the European Liver Transplantation registry during the period 1988-2008. The indication for LTX was categorized as liver failure, hepatocellular carcinoma (HCC) or poor quality of life (QOL; severe fatigue or pruritus). Data were analysed for two decades: 1988-1998 (1st) and 1998-2008 (2nd). The severity of disease was quantified using MELD scores. To fit a line which shows the trend over time we applied a linear regression model. Results: A total of 110 patients (87% women) was placed on the waiting list. 105 patients were transplanted (1st: 61, 2nd: 44), 5 (4.5%) died while listed. The annual number of LTX for PBC slightly decreased during the 20 year period (Figure). At the time of LTX the mean age was 53.6 yrs. (1st: 53.4, 2nd: 53.8), and the mean MELD score 13.9 (1st:14.5, 2nd:13.0). The median interval from diagnosis to LTX was 90.5 months (1st:86.5, 2nd: 93.5). 69% of patients was treated with ursodeoxycholic acid (1st 38%, 2nd 82%).
Conclusions: The absolute number of LTX for PBC showed a tendency to decrease. The reason for this trend remains speculative. During the last decade, the MELD score at the time of LTX slightly decreased.

Analysis of incidence and risk factors for chronic renal failure in long term liver transplant recipients

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The 10-year survival rate after orthotopic liver transplantation (OLT) has increased from 18 % to 60 % in the past two decades. As a consequence, more patients are at risk for complications related to the continuous use of immunosuppression, such as chronic renal failure (CRF). The aim of this study was two-fold: to asses the incidence of CRF and to identify the risk factors for CFR in a cohort of long term OLT recipients. We retrospectively reviewed the clinical and laboratory data of all patients who received a liver allograft between October 1986 and April 2008. The primary exclusion criteria were: less that one year survival post transplantation; having undergone a combined kidney-liver transplantation. Secondary exclusion criteria was the lack of, at least, one year follow-up data. In total 391 patients were analyzed for the development of CRF (defined as a calculated glomerular filtration rate of 59 mL/min or lower for more than 3 months). The median duration of follow-up was 6.4 years (mean, 7.2 ± 4.8). CRF developed in 143 patients (36.6 percent), the median duration to CRF was 0.5 years (mean, 1.5 ± 2.4). Of these patients, 11 (13 percent) required renal replacement therapy. The cumulative incidence of CRF was 35.7 percent after 5 years and 48.5 percent after 13 years. Multivariate analysis indicated that an increased risk of CRF was associated with male gender (HR 2.7; 95% CI: 1.9-3.8; p<0.001), age (HR 1.06; 95% CI: 1.04-1.08; p<0.001), body mass index (HR 0.95; 95% CI: 0.90-0.99; p=0.016), and the use of cyclosporine compared to tacrolimus (HR 1.7; 95% CI: 1.2-2.5; p=0.002).
Conclusions: This study shows that one out of every three liver allograft recipients develops chronic renal failure, with a five-year risk of 35.7 percent. In patients developing CRF, 13 percent will require renal replacement therapy. Male gender, higher age, lower BMI, and the use of cyclosporine were significant risk factors for the development of CRF.

The long-term effect of ursodeoxycholic acid on liver biochemistries in primary biliary cirrhosis

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Background and aims: Ursodeoxycholic acid (UDCA) has an established effect on liver biochemistries in Primary Biliary Cirrhosis (PBC). Few studies have evaluated long-term laboratory treatment effects and data beyond 6 years are not available. The aim of this study was to assess long-term treatment effects of UDCA on liver biochemistries and to identify potential biochemical patterns predicting imminent liver failure necessitating transplantation or liver related death. Patients and methods: Prospective multicenter cohort study of patients with PBC treated with UDCA 15 mg/kg/day. Follow-up data were collected at yearly intervals, including serum bilirubin, alkaline phosphatase (ALP), transaminases, albumin, IgG, IgM and cholesterol levels. Data were analyzed with a repeated measurement model. An event-related analysis was performed separately. Results: 375 patients were included, median follow-up was 9.7 years. The total number of study visits was 4776. Following 1 year treatment with UDCA 36-100% of the total biochemical improvement was achieved, the maximum response was observed after 2 years. After initial improvements, bilirubin and AST increased and albumin levels significantly decreased after 6-10 years. However, these secondary changes were of very limited magnitude. The beneficial effects on ALT and ALP were maintained while IgM continued to decrease (Figure). Bilirubin levels moved from a linear to an exponential phase 2-4 years before liver related events.
Conclusion: In the majority of patients with PBC the biochemical response to UDCA is maintained up to 15 years. The long-term evolution of bilirubin, albumin and ALT differs from that of AF, AST and IgM. Serum bilirubin levels start to increase progressively 2-4 years prior to major liver related events.

Malnutrition is an independent risk factor for complications in patients with liver cirrhosis

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Protein energy malnutrition (PEM) frequently occurs in cirrhosis. We determined nutritional status in 99 cirrhotics with complementary methods (adjusted BMI, mid-arm muscle circumference, hand-grip strength (HGS) according to Jamar and Citec; combined parameters: Body Cell Mass and Subjective global assessment (SGA)) and evaluated subsequent complications. Jamar HGS (most reliable for assessing PEM) was used to define well- and malnourished groups. 15 pts were excluded from analysis because of baseline hepatocellular carcinoma (HCC: n=5) or Interferon-based therapy during follow up (n=10). In the remaining 84 pts, underlying causes were viral hepatitis in 31%, alcohol in 26% and other in 43%. Baseline Child-Pugh (CP) class was A, B or C in 58%, 35% and 7% respectively. Energy and protein intake decreased significantly with increasing CP class, with shift from protein to carbohydrates. Various parameters indicated malnutrition in 41-70% of all cases. According to Jamar HGS, 67% (n=56) were malnourished (CP class A 58%, B 75%, C 100%) and 33% (n=28) well nourished at baseline. Follow up was 12±6 and 14±3 months respectively (P=0.04). Malnutrition was associated with older age and higher CP class but not with underlying disease or co-morbidity. During follow-up, 34 patients had a complication. Complications occurred in 18% and 48% in the well- and malnourished patients resp. (P=0.007): ascites 18 vs 27%: hepatic encephalopathy 0 vs 29%: variceal bleed 0 vs 11%: hepatorenal syndrome 0 vs 13%: spontaneous bacterial peritonitis 0 vs 14%: other bacterial infections 4 vs 18% and HCC 4 vs 5%. In univariate analysis, malnutrition (OR 4.3; 95%CI 1.4-12.9) and CP score (OR 2.0; 95%CI 1.5-2.8), but not underlying disease were significantly different between both groups. In multivariate analysis, malnutrition was an independent predictor of complications, after correcting for co-morbidity, sex and CP score (adjusted OR 4.230; 95%CI 1.090-16.422; P=0.037). Mortality (4 vs 18% P=0.1) and cumulative survival (P=0.056 Log Rank test) tended to be worse in the malnourished group.
Conclusion: Malnutrition is an independent predictor of complications in cirrhosis.
Considering its frequent occurrence, efforts should be intensified to improve nutritional status in these patients.

Prognosis of neonatal cholestasis due to alpha-1-antitrypsin deficiency *

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Objective: Alpha-1 antitrypsin (A1AT) deficiency is the most common genetic cause of liver disease in early childhood. Several studies, mostly from transplantation centers, have reported a poor outcome of patients with neonatal cholestasis due to A1AT deficiency. However a selection bias may have compromised these results. Therefore we retrospectively studied the natural course of liver disease in a cohort of patients with neonatal cholestasis due to A1AT deficiency. Methods: Infants with a ZZ or SZ phenotype born in the Netherlands between January 1991 and December 2006 were identified from the databases of the 5 Dutch centers for A1AT phenotyping and/or genotyping. Clinical and biochemical parameters at presen-tation and during follow-up were recorded. Results: In this 16 year time frame 50 patients were identified. Jaundice was the presenting symptom in 26 patients, 9 had failure to thrive, which could be attributed to malabsorption due to cholestasis and 15 had a vitamin K deficiency bleeding. During follow-up 7 patients died or had to be transplanted. At the end of follow-up 6/43 (14%) had cirrhosis, 31/43 abnormal ASAT and/or ALAT (72%), and 6/43 (14%) no biochemical or clinical abnormalities. Cumulative survival without liver transplantation was 87% at 5 years and 73% at 10 years.
Conclusions: In our study, the natural outcome of patients with neonatal cholestasis due to A1AT deficiency is better than was suggested in studies originating from transplantation centers, but similar to earlier studies by Sveger et al.

Low risk of hepatocellular carcinoma in UDCA-treated patients with primary biliary cirrhosis. Renewed recommendations for surveillance

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Background and aims: The reported incidence of hepatocellular carcinoma (HCC) among patients with Primary Biliary Cirrhosis (PBC) varies from 0.7-3.6% while in cirrhotic patients the risk may be considerably higher. Ursodeoxycholic acid (UDCA) may protect against the development of HCC, while age, advanced histological stage and presence of portal hypertension are thought to be risk factors. We aimed to define the risk profile for the development of HCC in PBC patients in order to identify a subgroup of patients who could benefit from surveillance. Patients and methods: Prospective multicenter cohort study of patients with established PBC treated with UDCA 15 mg/kg/day. Age, sex, AMA, bilirubin, albumin, ALP, ALT, AST, cirrhosis, portal hypertension, Mayo Risk Score (MRS <4.5>), prognostic class (based on bilirubin and albumin levels) and response to UDCA (normalization of abnormal bilirubin and/or albumin levels) were analyzed as potential risk factors in univariate and multivariate Cox regression analysis. Incidences were compared using Kaplan Meier method and Log Rank test. Results: 375 patients were included, median follow-up was 9.7 years. HCC occurred in 9 patients, corresponding with an annual incidence of 0.2%. Factors significantly associated with the development of HCC were MRS and response to UDCA ($p<0.001$). The incidence of HCC was highest for non-responders to UDCA (figure), the number needed to screen for this subgroup was 11.

Plasma levels of Apolipoprotein A1 are decreased in patients with Budd-Chiari Syndrome

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In many patients with Budd-Chiari syndrome (BCS) an underlying risk factor for thrombosis is present. Moreover, the etiology of thrombosis in these patients is often found to be multifactorial. Still, in a considerable number of cases no known etiologic factor can be identified. Using a proteomics approach, we aimed to identify novel factors that might play a role in venous thrombosis as observed in BCS-patients. We investigated the protein composition of plasma clots of 9 patients with BCS and 9 healthy, age- and sex-matched controls using two-dimensional difference gel electrophoresis (2D-DIGE). The relative abundance of plasma clot-bound proteins was compared between patients and controls. A total of 26 protein spots were detected that significantly differed ($p<0.001$) in standardized abundance between BCS-patients and controls. The protein spot with the most significant decrease in standardized log abundance (–0.19 in patients vs. 0.20 in controls) was identified with mass spectrometry as apolipoprotein A1 (apo A1). Mean levels of apo A1 in plasma of these nine BCS-patients were also significantly lower than in controls (0.74 g/l vs. 1.45 g/l, $p=0.002$). This finding was subsequently validated in plasma samples from a large cohort of 101 BCS-patients and 101 matched healthy controls. Mean plasma level of apo A1 was 0.97 g/l in cases as compared to 1.29 g/l in controls ($p<0.001$). Correlation between plasma levels of apo A1 and different liver function tests in this cohort of BCS-patients, showed only minor correlations (all correlation coefficients <0.35). Moreover, in a subgroup of BCS-patients with normal albumin levels (>35 g/l, n=34), mean apo A1 levels in plasma were still significantly lower than in their matched controls (1.08 g/l vs. 1.31 g/l, $p=0.002$), suggesting that the decrease in plasma levels was not explained by liver dysfunction. Conclusions: This is the first study to show that the protein composition of plasma clots is significantly different between patients with BCS and healthy controls. Levels of apo A1, both in plasma and in plasma clots, were significantly lower in BCS-patients as compared to controls. Although the precise causative mechanism remains to be elucidated, decreased levels of apo A1 are potentially involved in the etiology of thrombosis in patients with BCS.

Is there a place for preoperative gastroscopy in morbidly obese patients undergoing gastric bypass surgery?

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Background: Obesity (Body Mass Index; BMI > 25) is a world wide rapidly increasing problem. Bariatric surgery offers the only long lasting treatment with excellent effects on co-morbidity for morbid obesity (BMI >40 or BMI >35 with co morbidity). Laparoscopic Roux-Y Gastric Bypass (LRYGB) is one of the used techniques. After LRYGB, the stomach remnant is endoscopically inaccessible, but there are no guidelines for preoperative endoscopic screening. Although the complication rate for routine gastroscopy is low, sedation in morbid obese patients with highly associated sleep apnea increases the risk. Objective: To quantify and qualify the yield of clinically relevant pathology in gastroscopic screening prior to LRYGB. Methods: From November 2007 until June 2009 140 patients were consecutively operated or planned for operation (male: female=37:103; median age of 44.9 years; average BMI of 45.2). Of these patients 102 were screened by gastroscopy in this hospital (99 successful, 1 failed, 1 refused and 1 report missing). Patients who had preoperative screening elsewhere were excluded. Results: 2 cases (2%) showed clinically relevant pathology: 2 ventricular ulcers (Forrest IIc and III). 55 patients had abnormal findings (55.6%) without clinical consequences. In 42 patients no abnormalities were found (42.4%). HP/CLO-tests were performed in 34 patients (34.3%) of which 16 were positive (47.0%), 14 negative (41.2) and 4 unknown (11.8%). During follow-up in none of the patients postoperative diagnostic evaluation of the stomach remnant was indicated (n=80).
Conclusions: The yield of clinically relevant pathology in preoperative gastroscopic screening for LRYGB patients in our institute is very low (2%). In order to reduce costs and procedure related morbidity we recommend that invasive preoperative screening for upper gastrointestinal pathology should only be performed based on clinical suspicions. The role of alternative diagnostic options should be investigated.

Liver Transplantation in Polycystic Liver Disease: excellent survival and improvement of quality of life

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Patients with end-stage isolated polycystic liver disease (PCLD) suffer from incapacitating symptoms due to huge liver volumes. Liver transplantation is the only curative option. We aimed to assess its feasibility in PCLD and compare results those obtained in autosomal dominant polycystic kidney disease (ADPKD). We extracted demographics and outcome of 535 patients, listed in European Liver Transplant Registry (ELTR) database, who underwent liver transplantation between 1985-2007 because of polycystic liver. 190 patients were subjected to combined liver-kidney transplantation and 42 patients were excluded because polycystic disease was not the main indication for liver transplantation. Additional data of the remaining patients was collected using standardized questionnaires submitted to 75 European liver transplantation centers. We performed a literature search to compare survival rate from the literature with our cohort. Patient and graft survival were analyzed by Kaplan-Meier survival analysis and compared with ADPKD patients using the Log-Rank test. We received responses on 194 patients (49 centers). 125 patients were diagnosed with ADPKD and PCLD was confirmed in 57 patients (25 centers). Main indications for liver transplantation were mechanical difficulties (60%), invalidation (24%), pain (19%) and untreatable complications (12%). Explantation of the polycystic liver was extremely difficult in 36.8%, especially in patients with a previous surgical intervention (9/21). Median Karnofsky score for patients who are alive after transplantation was 90%, indicating capable of normal activity with only few symptoms or signs of disease. After liver transplantation, the 1- and 5-year graft (94.3% and 87.5%) and patient (96.2% and 92.3%) survival rates for PCLD patients liver transplantation did not differ from ADPKD patients. Although not statistically significant, ADPKD patients receiving liver transplantation had better survival compared with ADPKD patients with combined liver-kidney transplantation ($p=0.098$). Upon comparison with data extracted from the literature, liver transplantation in ADPKD patients has a better survival rate compared to combined liver-kidney transplantation in those patients ($p<0.01$). Furthermore, ADPKD patient survival rates after combined liver-kidney transplantation were better in the cohort from ELTR database compared with literature ($p=0.024$). LTx in PCLD leads to long-term survival with normal activity of the patient.

Predictors of common bile duct stones during early endoscopic retrograde cholangiopancreaticography in acute biliary pancreatitis

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Accurate prediction of common bile duct stones (CBDS) in acute biliary pancreatitis (ABP) is warranted to select patients for therapeutic endoscopic retrograde cholangio-pancreaticography (ERCP). We evaluated common radiological and biochemical predictors for CBDS in patients with ABP undergoing early ERCP.
173 patients with ABP undergoing successful early ERCP (<72 hours after symptom onset) were prospectively included in 15 Dutch hospitals (2004-2007). Abdominal ultrasound (US) and/or computed tomography (CT) was performed on admission and complete liver biochemistry determined daily. Patients were stratified as predicted severe ABP (APACHE II-score >7 and/or Imrie-score >2 and/or CRP >150) or not before early ERCP. We used univariate logistic regression to assess associations between CBDS during ERCP (gold standard) and the following parameters: 1) clinical: age, sex, predicted severity, 2) radiological; dilated CBD, impacted stone in CBD, and 3) biochemical; bilirubine, gammaglutamyltransferase (γGT), alkaline phosphatase (AP), alanine aminotransferase (ALAT) and aspartate aminotransferase (ASAT).
From the 173 patients, 98 (57%) had predicted severe ABP, 21 (12%) exhibited dilated bile ducts and 15 (9%) had CBDS on US/CT. Early ERCP was performed on the day of admission in majority of patients (65%). CBDS were found during ERCP in 90/173 patients (52%). The only parameters significantly associated with CBDS were γGT (per 10 points increase: odds ratio 1.02, 95%-CI 1.01-1.03, P=0.003) and AP (per 10 points increase: odds ratio 1.03, 95%-CI 1.00-1.05, P=0.025). However, using the 67th percentile as cut-off, both parameters showed low discrimination (γGT and AP: sensitivity 0.42, specificity 0.75) and predictive value (γGT: positive predictive value 0.65, negative predictive value 0.54, AP: positive predictive value 0.65, negative predictive value 0.55). Results did not change when sludge and/ or stones in CBD were considered as outcome of ERCP.
Conclusions: common radiological and biochemical predictors for CBDS do not seem valuable in early in the course of ABP. Alternative tests such as MRCP or endoscopic ultrasound might be preferred to select patients for early ERCP. Cholestatic liver biochemistry and CBD dilatation in ABP may be caused by other factors than CBD stones.

Routine preoperative liver function test in patients with uncomplicated symptomatic gallstone disease

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Background: In most patients with uncomplicated gallstone disease, liver function tests (LFTs) are done before laparoscopic cholecystectomy (LC). This retrospective study evaluates the value of these tests.
Methods: Between 2002-2008, 1112 patients had an LC for symptomatic gallstone disease, 415 patients were excluded because of complicated gallstone disease. We studied pre-LC LFTs (AST, ALT, ALP, GGT, -bilirubins), ERCPs and post-LC complications. Results: Of the 697 included patients, 629 patients had pre-LC LFTs done (I) and 68 patients did not (II). Group I was divided into four groups: 360 patients with normal LFTs (IA1) and 269 patients with at least one LFT> normal (IA2), and in 531 patients (IB1) with all LFTs< 2x normal value and a group of 98 patients (IB2) with at least one LFT > 2x normal. There were significant more ERCPs performed in group IA2 than in group IA1 (P< 0.001) and in group IB2 than IB1 (P< 0.001), due to more pre-LC ERCPs. There were no differences between the groups in ERCPs positive for choledocholithiasis or post-LC complications.
Conclusions: In patients with uncomplicated gallstone disease routine pre-LC LFTs does not influence post-LC complications for patients undergoing LC. Routine determination of LFTs pre-LC increases the number of pre-LC ERCPs.

Surgical management of submucosal oesophageal cancer: limited or extended lymphadenectomy?

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Introduction: The prevalence of lymph node metastases in patients with submucosal tumour infiltration of the oesophagus has been reported 20-25%. Therefore, a radical oeso-phagectomy is considered the standard therapy for tumours that infiltrate into the submucosa (T1b). At present, it is unclear whether a radical oesophagectomy with extensive lymphadenectomy is needed or a limited surgical procedure suffices. The aim of this study was to compare outcome of patients that underwent oesophagectomy for oesophageal cancer with submucosal tumour infiltration through a transthoracic approach with extended lymphadenectomy, with patients in whom a limited transhiatal oesophagectomy was performed with only locoregional lymph node dissection. Methods: Data were collected from four large expert centres. In Los Angeles, USA (N=31) and Leuven, Belgium (N=108) patients with T1b-tumours had been operated via the transthoracic route with extended lymphadenectomy. In Amsterdam (N=43) and Rotterdam, The Netherlands (N=47), a transhiatal oesophagectomy had been performed in these patients. Only patients who had undergone oesophagectomy for cancer between 1990 and 2004 and who had not received (neo) adjuvant therapy were included in the study. Results: The two patient groups (transthoracic versus transhiatal oeso-phagectomy) were comparable with regards to age, BMI and ASA class. Operative time was longer in the patients who underwent a transthoracic oesophagectomy (390 minutes versus 250 minutes, $p<0.001$). Intraoperative complication rate, length of hospital stay, overall morbidity and in-hospital mortality rate were comparable between both groups. There was no difference in pathological outcome (infiltration depth, pN-stage, pM-stage, lymph node ratio) between both groups, despite a higher number of harvested lymph nodes (median 27 lymph nodes in the transthoracic group versus 8 lymph nodes in the transhiatal group, $p<0.001$). Finally, overall 5-year survival (67% transthoracic versus 73% transhiatal, $p=0.61$) as well as disease-free survival were comparable in both groups. For N1-patients in specific, overall 5-year survival was 45% in the transthoracic group versus 33% in the transhiatal group ($p=0.58$).
Conclusions: In this analysis more extensive surgery by means of a transthoracic oesophagectomy with extended lymphadenectomy for patients with oesophageal cancer limited to the submucosa did not lead to a higher chance for cure.

Chemoradiation for oesophageal cancer: Patient-Tail ored treatment to minimize toxicity and maximize efficacy

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The poor outcome associated with surgical resection alone for patients with locally advanced oesophageal cancer has initiated the use of comb d-modality treatment protocols that include concurrent chemoradiotherapy (CRT). This study aimed to evaluate the toxicity and efficacy of three different concurrent CRT-regimens in patients with oesophageal cancer. Between 1997 and 2007, 94 patients with oesophageal cancer were treated with CRT in our institute. Treatment consisted of radiotherapy to 50 Gy in 25 fractions with concurrent cisplatin and 5-fluorouracil (group A, n=65), radiotherapy to 50.4 Gy in 28 fractions with concurrent carboplatin and paclitaxel (group B, n=16) or radiotherapy to 66 Gy in 33 fractions with low-dose cisplatin (group C, n=13). Regimen A was the standard regimen, regimen B was given in case of diminished renal function or hearing loss, and regimen C for cervical oesophageal cancer. Toxicity was scored according to Common Terminology Criteria version 3.0. CRT was planned as neoadjuvant (n=58) or definitive (n=36) treatment. Grade 4 haematological toxicity occurred only in group A (n=5), and grade 3 haematological toxicity was seen in 13 patients. Grade 4 non-haematological toxicity did not occur, and grade 3 non-haematological toxicity was experienced by 6 patients in group A and 2 patients in group C. In total, 24 (25%) patients experienced grade 3 or 4 toxicity during treatment (25%, 38% and 15% in group A, B and C, respectively).During treatment, two patients in group A died. Overall, 81 (86%) patients completed the planned treatment (86%, 94% and 77% in groups A, B and C, respectively). Clinically complete or partial response was observed in 28 of 92 (30%) patients (21%, 50% and 54% in groups A, B and C, respectively). After clinical and radiological re-evaluation, treatment plan changed in 14 (15%) patients. Forty-five patients underwent surgery. Four patients did not undergo resection. Pathologic complete response (pCR) and downstaging were seen in 12 (27%) and 34 (76%) of the 45 operated patients. Median follow-up was 15 (range 1-108) months. Three-year survival was 61% for patients who underwent CRT followed by surgery (n=45), 72% for patients with pCR (n=12) and 24% for patients who received definitive CRT (n=49).
Conclusion: With strict selection, patient-tailored treatment and multidisciplinary re-evaluation, ifferent regimens of chemoradiation for oesophageal cancer resulted in acceptable rates of toxicity and efficacy.

Pathological assessment of tumour response after Neoadjuvant Chemoradiotherapy for Oesophageal Cancer

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Combined-modality treatment regimens that include chemoradiotherapy (CRT) are increasingly used for oesophageal cancer. The aim of this study was to measure residual tumour in the oesophagus of patients treated with neoadjuvant CRT, to correlate clinical with pathological response, and to correlate specific pathological parameters with survival. Between 1998 and 2007, 37 oesophageal cancer patients were operated after preoperative 5-fluorouracil/cisplatin and radiotherapy. Their surgical resection specimens were reviewed. Clinical response was evaluated according to Response Evaluation Criteria in Solid Tumours (RECIST). Residual tumour was assessed in terms of resection margin involvement, the Mandard tumour regression grade (TRG1: no residual cancer; TRG2: rare residual cancer cells; TRG3: fibrosis outgrowing residual cancer; TRG4: residual cancer outgrowing fobrosis; TRG5: absence of regressive change) and pTNM stage. A microscopically radical (R0) resection was obtained in all 37 patients. TRG1 was observed in 11 (30%) patients. TRG2 was present in 12 cases, TRG3 in eight, TRG4 in five, and TRG5 in one. Clinical response had an accuracy of only 14% to identify correct pathological response (according to TRG). Of the 11 patients with a TRG 1, one had a clinical complete response, three a partial response and seven stable disease. Downstaging was observed in 31 (84%) patients: downstaging of T alone occurred in 11 patients (30%), N alone in 2 (5%), and both descriptors in 18 (49%). With a median follow-up of 32 (range 3-108) months, 3-year survival was 54% for all patients. Median survival had not yet been reached for patients with TRG1 versus 24 months for TRG2-5 (log rank test, *P*=0.21), and the 3-year survival was 69% and 49%, respectively. Patients with pN0 tumours (n=26) had a 3-year survival of 66% versus 27% for those with pN1 tumours (n=11) (log rank test, *P*=0.01). Eighteen (49%) patients developed recurrent disease. Recurrence was only locoregional in two patients, only distant in 12 patients and both locoregional and distant in four patients. Nine relapses occurred in 11 (82%) patients with pN1 tumours, versus nine in 26 (35%) patients with pN0 tumours (*P*=0.009). Conclusion: Clinical response has a poor correlation with pathological response. A surgical resection should not be denied if a clinical complete response is detected. Pathologic complete regression of the primary tumour and pN0 status were both correlated with a higher overall survival.

Quality of life in long-term survivors after potentially curative treatment for oesophageal cancer

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Clinical outcome parameters are well-studied in the treatment of oesopageal cancer, whereas long-term quality of life (QoL) is not. The aim of this study was to assess various aspects of QoL at least one year after potentially curative treatment for oesophageal cancer. Between January 1995 and December 2007, 163 consecutive patients with cancer of the oesophagus underwent a potentially curative treatment. All patients with a minimal follow-up of one year and without tumour recurrence were eligible for this study. Questionnaires consisted of: (a) the European Organization for Research and Treatment of Cancer (EORTC) core questionnaire (QLQ-C30), (b) the EORTC oesophageal site-specific questionnaire (OES-18), and (c) additional questions about effects of treatment and about survivorship issues. Scores ranged from 0-100 (± S.D.). A higher score represented a higher ("better") level of functioning, or a higher ("worse") level of symptoms. One patient could not be contacted because of emigration. Response rate was 97% (35/36) for all other eligible patients. Twenty had received neoadjuvant therapy followed by surgery, nine had undergone surgery only, and six chemoradiation only. Median survival was 55 (16-162) months. Physical functioning (mean 83 ± 15) was unaffected in 10 (29%) patients, and social functioning (mean 80 ± 24) was diminished in 20 (57%) patients. Fatigue (mean 34 ± 27) was experienced by 26 (74%) patients. In the OES-18, early satiety was the most frequently reported complaint (n=28; 80%). Furthermore, 20 (57%) patients still experienced trouble with eating (in front of other people) (mean 37 ± 30). Dysphagia (mean 24 ± 33) was reported by 17 (49%) patients. When asked to rate their current overall QoL on a visual analogue scale, patients scored a mean of 76 (range 25-100), with 30 patients rating 60 or higher. Eleven (31%) patients still had additional expenses related to their disease and its treatment. Twenty-six (74%) patients were convinced that they had been cured. However, 19 (54%) patients worried that the disease might come back.

Conclusion: Patients who survive one year or more after potentially curative treatment for oesophageal cancer can lead satisfactory lives. Although some residual symptoms may persist, their reported general quality of life is similar to that of healthy individuals of the same age. The results of this study can be used when informing patients about the long-term effects of treatment.

Impact of delay in diagnostic work-up and treatment of patients with oesophageal cancer

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Introduction: Outcome of oesophageal cancer treatment is related to the stage of the disease. Therefore, the disease should preferably be detected and treated at an early stage. This may be prohibited by delays in referral, diagnostic work-up and operative waiting list. The aim of this study was to investigate the delays between onset of symptoms until surgery. Methods: For 577 patients undergoing oesophagectomy for cancer between 1991 and 2008, patients' short- and long-term outcome were analyzed according to the different time intervals. Results*:* Patients underwent endoscopy after a median time period of 3 months after onset of symptoms (patient's delay). Referral to the Erasmus MC occurred in 427 patients, in whom the diagnosis of oesophageal cancer had been established histologically. The remaining 150 patients were directly sent to the Erasmus MC by the GP, or underwent primary endoscopy in our hospital because of Barrett's oesophagus surveillance. All patients underwent (re-)endoscopy in the Erasmus MC to confirm the diagnosis, after a median time period of 6 days (range 0 – 36) after patient's first visit to the outpatient clinic. During the multidisciplinary oncology meeting a definitive treatment plan was made, after which the patients were put on the waiting list (median delay endoscopy – oncology meeting was 8 days, range 0 – 169). The waiting list for surgery caused another delay of 13 days (range 0 – 89). In total, patients' delay from establishing the diagnosis until surgery lasted a median time period of 27 days (range 1 – 217). An interval <50 days between establishing the diagnosis of oesophageal cancer (histologically on patient's first endoscopy) and surgery, was associated with lower overall morbidity (56.2% versus 67.3%, p=0.01), mortality (3.5% versus 7.6%, p=0.04) and re-operation rate (7.4% versus 13.5%, p=0.02). None of the other time intervals reflecting a specific delay within the Erasmus MC led to worse short-term outcome. There was no relationship between any time interval and overall survival.
Conclusion: The total length of time between establishing the diagnosis of oesophageal cancer and surgery influences patients' short-term but not long-term outcome after oesophagectomy for cancer. It is unclear whether this can be explained by a more time-consuming diagnostic work-up in patients with a poorer physical status or whether the delay itself prior to surgery causes a worse physical status in oesophageal cancer patients.

Tailored or routine addition of an antireflux fundoplication in laparoscopic hiatal hernia repair; a comparative cohort study

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The controversy regarding the tailored or routine addition of an antireflux fundoplication in the repair of para-oesophageal hiatal herniation is still persisting. We hypothesized that a fundoplication should only be selectively added in patients with preoperatively diagnosed gastro-oesophageal reflux disease.Between 2002 and 2008, 60 consecutive patients with para-oesophageal hiatal herniation were preoperatively evaluated by medical history, upper endoscopy, and oesophageal 24-hr pH monitoring. If two or three of these work-up components were indicative of gastro-oesophageal reflux disease, an antireflux procedure was added. Symptomatic outcome after surgery was determined by questionnaires, and objective outcome was assessed by endoscopy and pH monitoring.In 35 patients (25 females, mean age ± SD 58.2 ± 10.8 years) an antireflux fundoplication was added because of preoperatively established gastro-oesophageal reflux disease. In the remaining 25 patients (15 females, mean age ± SD 61.0 ± 9.2 years), gastro-oesophageal reflux disease was preoperatively absent and underwent hernia repair only. Questionnaires were postoperatively returned by 58 patients (96.7%), 45 (75%) had endoscopy, and 45 (75%) underwent pH monitoring after surgery. In patients with fundoplication, oesophagitis was present in six patients (22.2%) after surgery and abnormal oesophageal acid exposure persisted in 11 patients (40.7%). Seven patients (38.9%) with hernia repair only developed abnormal oesophageal acid exposure after surgery. In addition, oesophagitis was postoperatively generated in five patients (27.8%) in this group. New-onset daily heartburn and dysphagia was present in none of the patients in either group.
Conclusions: in this study, omission of an antireflux procedure during the repair of para-oesophageal hiatal herniation in patients without preoperatively diagnosed gastro-oesophageal reflux disease induced oesophagitis in 28% of patients, and abnormal oesophageal acid exposure in 39%. Therefore, routine addition of an antireflux fundoplication should be recommended in the laparoscopic repair of para-oesophageal hiatal herniation.

Early Total Parenteral Nutrition (TPN) after rectal surgery implies a shorter length of stay (LOS) than late TPN

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Major rectal surgery is associated with a high incidence of postoperative ileus (POI). This study describes administration of TPN and complications.In this analysis 238 patients undergoing surgery for primary or recurrent rectal cancer were included. Administration of parenteral nutrition was registered from January 2005 until December 2008. Postoperative ileus was registered for 76 patients operated in 2008. Furthermore an inventory of possible complications due to TPN, such as central l sepsis (CLS) and bacteraemia (n=104) were deducted from electronically microbial reports. Data are represented as mean ± (SEM), for statistics SPSS 16 was used. 37% of patients operated developed POI. Patients on TPN had a longer LOS ($p<0,05$). Early TPN (started from day 1 until day 3) (18 ± 3 d was associated with a shorter LOS compared to late TPN (27 ± 3 d, $P<0,05$). The number of days on TPN did not differ between early (10 ± 3 d) or late TPN (11 ± 2 d, $P>0,05$). Late TPN is associated with a higher incidence of CLS (32% ± 10) and bacteremia (36% ± 10) if compared to standard care (5% ± 2; 8% ± 3, $P<0,05$), while no differences were found between standard care and early TPN.
Conclusions: Early start of TPN after rectal surgery was associated with a shorter LOS than late TPN, while total days of TPN administration were similar for both TPN groups. Our results are confounded by patient selection because patients receiving TPN developed POI or were at high risk of malnutrition, and are therefore the poorer group with regards to clinical outcome. This is reflected in the result that patients on standard care had the shortest LOS. Late TPN was associated with more CLS and bacteremia than early TPN or standard care. Preoperative evaluation of patients benefiting of postoperative TPN might lead to a reduction in LOS in favor of an early start.

The Malone antegrade continence enema in children with defecation disorders, the Amsterdam experience *

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Introduction: The Malone Antegrade Continence Enema (MACE) procedure has been previously described as a safe and effective option for the treatment of children with chronic defecation disorders where maximal medical therapy and conventional treatment has failed. Aim: To evaluate outcomes, complications and Quality of Life of children with chronic defecation disorders with a MACE stoma. Methods: A retrospective analysis was performed in 23 patients (14 boys and 9 girls) with intractable constipation and/or fecal incontinence, who underwent a MACE stoma between July 2002 and May 2008. Preoperative and postoperative data were evaluated. A specific Quality of Life questionnaire was used to assess patient satisfaction. Results: A MACE was performed in 15 children with intractable constipation and fecal incontinence, in 5 children with spina bifida and in 3 children with Hirschsprung's disease. Median age at surgery was 7.3±4.5 (boys 6.5±4.7; girls 9.4±4.2) years. An increase in defecation frequency: pre 1.0 (range 0-4) versus 5.5 (range 0-28; $p<0.006$) post treatment/one week and a significant decrease in fecal incontinence frequency: 10 (range 0-140) pre versus 0 (range 0-14; $p<0.034$) post/week was found. Postoperatively, 11 patients still had abdominal pain. After the MACE-procedure fecal leakage occurred in 10 patients (43%). Stomal stenosis developed in 9 patients (39%). Wound infection was seen in 12 patients (52%). The questionnaire showed that 86% of the patients were satisfied with the results of the Malone-stoma (n=21). A total of 73% of these patients would recommend this procedure to other patients.
Conclusion: The MACE procedure is an effective treatment in children with intractable defecation disorders, however postoperative complications are not uncommon with a high number of patients experiencing fecal leakage, stomal stenosis and wound infection. Further research is needed to reduce the incidence of complications.

Endoscopic transcolonic specimen removal in laparoscopic ileocolic resection for Crohn's Disease: initial experience

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Ileocolic resection for Crohn's disease can be performed entirely laparoscopically, including devascularisation, transsection and reanastomosing. The only reason to perform a minilaparotomy is to remove the specimen. Aim of this prospective observational study was to assess feasibility of endoscopic transcolonic specimen removal obviating the need for a minilaparotomy. In a consecutive series of 10 patients scheduled for laparoscopic ileocolic resection, endoscopic specimen removal was attempted. Primary outcomes were feasibility, operating time, complication rate, length of stay and postoperative pain scores. To assess applicability, outcomes were compared to data of laparoscopic-assisted operated patients from earlier study. A 4-trocar approach was used. The right colon was mobilized and the mesentery was devascularised close to the bowel to minimize specimen diameter. Large bowel and ileum were transsected. After bowel division, the endoscopist introduced the colonoscope up to the area of bowel transsection. When the endoscope reached the cross stapled large bowel, terminal ileum and large bowel were opened to introduce a stapler. The small bowel was clamped to avoid spillage. With an endostapler, a side-to-side anastomosis was created. Next, the endoscope was advanced through the remaining anastomotic gap, grasping the specimen using an endoscopic snare. During endoscopic removal, the laparoscopist facilitated passage of the specimen through the anastomosis for transcolonic retrieval. After this the remaining anastomotic gap was sutured laparoscopically.Seven women and three men with a median age of 31 were included. Transcolonic removal was successful in 8 out of 10 patients. Median operating time was 208 minutes, median postoperative hospital stay 5 days. Postoperatively, two patients developed an intraabdominal abscess, which was dra d laparoscopically or percutaneously. Compared to conventional laparoscopy, operating time was longer, while hospital stay was similar.
Conclusion: Transcolonic removal of the specimen in ileocolic Crohn's disease is feasible in the absence of a large inflammatory mass and is associated with a fast postoperative recovery. It is as yet unknown whether the increased complexity of the technique and the time consuming logistics can be justified by the potential benefit for patients when compared to conventional laparoscopic techniques.

Impact of anorectal symptoms on quality of life in patients with faecal incontinence

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Faecal incontinence has a profound impact on quality of life (QoL). Better understanding of factors affecting QoL can guide treatment decisions. Although previous studies found a significant relation between severity of faecal incontinence as measured by the faecal incontinence severity index (FISI) and QoL, the association with a condition specific quality of life score (FIQL) was not very strong. The FISI only rates type and frequency of stool leakages. We hypothesise that a composite score of several anorectal symptoms is a better predictor. Aim of the study was to further explore the relationship of anorectal symptoms with quality of life in patients with faecal incontinence and to identify the most important predictors. Sixty-one consecutive patients with faecal incontinence (17 female; mean age 66 yrs, range 31-83 yrs) filled out a questionnaire to assess FIQL. Presumed aetiology of faecal incontinence was radiation toxicity in 35, previous pelvic or colorectal surgery in 8, a medical history in 9, an obstetric history in 3 and unknown in 6 patients. The validated FIQL consists of 29 items covering four aspects of QoL including lifestyle, coping/behaviour, depression/self perception and embarrassment. We used a 7-item score (EPICB-F) to rate frequency of bowel movements, rectal urgency, uncontrolled leakage of stool, loose or liquid stool, bloody stool, painful bowel movements and crampy pain in the lower abdomen. In addition, type and frequency of stool leakages were scored by the FISI. Twenty-six patients had mild (FISI<25), 29 moderate (25≤ FISI≤45) and 6 patients severe incontinence (FISI >45). Lifestyle (r=0.71 vs r= -0.35), coping (r= 0.71 vs r= -0.52), depression (r=0.56 vs r= -0.26) and embar-rassment (r= 0.55 vs r= -0.28) correlated more strongly with the EPICB-F score than with the FISI. Frequency of uncontrolled stool leakages, bloody stool, painful bowel move-ments and frequency of bowel movements were independent predictors ($p < 0.01$) for QoL and explained 26-51% of variation in individual FIQL scores.

Conclusion: Apart from frequency and type of stool leakages, the presence of bloody stool, painful bowel movements and an increased frequency of bowel movements are important independent predictors for quality of life in patients with faecal incontinence. Therefore, clinicians are encouraged to focus their attention on these complaints when managing patients with faecal incontinence.

The inter-relation between Minimal Distension Pressure, Rectal Capacity and First Sensation in rectal barostat measurements

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Introduction: The use of barostat methodology for assessing visceral perception is a widely accepted technique. Besides perception scores (pain, urge and discomfort), parameters like First Sensation (FS), compliance (C), minimal distension pressure (MDP) and Rectal Capacity (RC), are often used for classification of patients or for correcting the measurements for body posture and position. In literature, different barostat protocol designs are described with respect to these parameters. The aim of this study was to establish the effect of the barostat procedure itself on values of MDP and FS and to find possible associations between the measures for MDP with RC, C with RC, and FS with RC. This information may improve future barostat protocols and selection of correction factors, used during barostat measurements. Methods: 11 healthy volunteers participated in this study. The barostat protocol consisted of five parts, each with its own purpose (Priming, C, MDP, semi-random staircase and again MDP). FS was measured before and after the semi-random protocol and RC was calculated afterwards (volume at p=30mmHg). Results/discussion: No difference was found between the first and second measurement of MDP and FS (p=0.7 and 0.9 respectively). Although the study population should be expanded, this suggests that both MDP and FS are stable throughout the barostat procedure. FS correlated significantly with RC, and C correlated significantly with RC. We were not able to show a correlation between MDP and RC although expected, which could be due to a lack of statistical power. The associations between RC and FS and C, respectively, suggests that a large rectum is able to distend more, leading to a decreased visceral perception as compared to people with a small rectum.
Overall, we conclude that MDP and FS are not affected by a barostat procedure in healthy volunteers, and that FS is affected by RC, which implies that the determination of RC should be integrated into the barostat protocol.

Critical reappraisal of anorectal function tests in fecal incont nce: Only anal ultrasound is discriminatory

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Objective: Anorectal function tests are often performed in patients with fecal incontinence [FI]. The additional value of each individual test is not clear. We evaluated the results of anorectal function testing in patients with FI. Patients and methods: Between 2003 and May 2009, all referred patients with FI were prospectively evaluated according to protocol in our function laboratory and assessed by an extensive questionnaire regarding their perianal complaints. Anorectal manometry [ARM] (consisting maximal basal [MBP] and squeeze [MSP] pressure, sphincter length [SL]), rectal compliance measurement (consisting first sensation [FS], urge volume, maximum tolerable volume [MTV]) and anal endosonography [EUS] (consisting internal anal sphincter [IS], external anal sphincter [ES]) were performed. Patients with diarrhoea and IBD, pouches or rectal carcinoma were excluded. Results: In total 210 patients (196 women [93%]) were evaluated. Of these 129 (61.4%) patients had no sphincter defects, 46 (21.9%) isolated ES defects and 35 (16.7%) combined IS/ES defects. 13 of 14 males with FI had no sphincter defects and the left one had an anal injury possible due to sexual abuse in the past. Men had higher MSP and longer SL then women (P<0.05). Patients with anal sphincter defects had a significantly shorter SL and higher rectal sensitivity (i.e. lower volume en pressure thresholds for the desire to defecate) compared to patients without sphincter defects. 17 patients (8.1%) had a MTV between 65-100 ml, they did not differ from patients with MTV >100 ml regarding anal pressures and sphincter defects. 44 patients (21.0%) had MBP and MSP ≥ 40 mmHg, their MTV did not differ from patients with lower pressures.
Conclusion: In patients with fecal incontinence without IBD or pouches, only EUS in detecting sphincter defects is contributory in detecting the cause and possible subsequent (surgical) therapy. Anal pressures and rectal compliance do not differ in these subgroups.

Mortality of biliary atresia in children not undergoing liver transplantation *

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Orthotopic liver transplantation (OLT) is a life saving treatment for children with end stage liver disease due to biliary atresia (BA). Nevertheless, some BA patients die without undergoing OLT. We quantitated and characterized the mortality of non-transplanted BA patients before the age of 5 years, using a recently established national database (Netherlands Study group of Biliary Atresia Registry (NeSBAR) database, 1987-2006). To determine whether mortality had changed over time, we compared the cohort 1987-1996 (n = 98) with 1997-2006 (n = 99). Causes of mortality were obtained from patient charts. Clinical condition at the time of assessment for OLT was expressed in the Pediatric End-stage Liver Disease (PELD) score. Children with BA who were trans-planted before their 5th birthday served as controls. Mortality of non-transplanted BA children before the age of 5 years decreased from 27% (26/98) in 1987-1996 to 15% (15/99) in 1997-2006. In cohort 1987-1996, mortality was predominantly based on BA patients who had not been assessed or who had not been accepted for OLT (17/98 vs. 7/99 in cohort 1997-2006). Sepsis was the prevailing cause of death (12/41). In cohort 1997-2006, the PELD-score at time of assessment was significantly higher in non-trans-planted children (26.0 ± 5.1 vs 20.3 ± 6.6, respectively), indicating more advanced liver disease.
Conclusions: Our national data indicate that, between 1987 and 2006, liver transplantation has increasingly been considered as treatment option for BA, resulting in decreased non-transplant mortality in The Netherlands. Ongoing mortality of BA patients without OLT is mainly due to sepsis and seems attributable to assessment of BA patients for OLT in an already clinical advanced condition.

Concentration of Fecal Calprotectin in Children with Abdominal Pain Presenting in Primary Care – a pilot study *

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Paediatric Inflammatory Bowel Disease (IBD) is diagnosed by endoscopy under general anaesthesia, an invasive and very troublesome procedure for children. Faecal calprotectin is a promising non-invasive test to assist the physician in his decision to refer a child for endoscopy. However, all studies describing the concentration of faecal calprotectin are performed in secondary and tertiary care in children highly suspicious for IBD, and not where the test is needed most, namely primary care. The aim of our pilot study was to investigate the concentration of faecal calprotectin in children aged 4-17 years presenting with abdominal pain in primary care. In addition we evaluated whether the concentration is associated with alarm symptoms and assessed the prognosis of the concentration calprotectin.We performed a prospective cohort study between May 2004 and March 2006. All consecutive children aged 4-17 years consulting their general practitioner for a new episode of abdominal pain were eligible to participate. At baseline and at 12 months follow up a faeces sample was collected, a questionnaire concerning alarm symptoms (vomiting, diarrhoea, gastrointestinal blood loss and fever) was completed and height and weight were measured.In total 306 children were included. Of 269 children a faeces sample was available at baseline, 106 boys (39.4%) and 163 girls (60.6%). Median age was 7.9 years (IQR 5.7-10.5). Median concentration of faecal calprotectin was 27.8mg/g (IQR 19.8-49.4). If we applied a cut off value of 50 mg/g faeces, 65 children (24.2%) had a positive test result. Twenty-six children (9.7%) had a concentration above 100mg/g. None of the alarm symptoms were associated with a positive test result when we applied a cut off value of 50 mg/g faeces. If we applied a cut off value of 100 mg/g faeces gastrointestinal blood loss showed an OR of 5.4 (95%CI 0.9-31.3) for a positive test result. Results of the concentration faecal calprotectin after 12 months follow-up will be available by the end of June 2009.
Conclusions: The concentration faecal calprotectin is above the frequently used cut off value of 50 mg/g faeces in 24.2% of children presenting with abdominal pain in primary care. A positive test result seems to be associated with gastrointestinal blood loss.

Balancing liver homeostasis by modulating c-Myc activity

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A balance between removal of damaged cells by apoptosis and renewal of tissue through proliferation of healthy cells is fundamental in maintaining liver homeostasis. The c-Myc proto-oncogene is a key regulator of liver homeostasis and was shown to be deregulated in most liver cancers as well as in cirrhotic livers. When c-Myc is active, proliferative and apoptotic programs are activated simultaneously; what the net outcome is in terms of tissue gain or loss is dependent on the cellular context. Although Myc itself is difficult, if not impossible, to target, this leaves two options to influence the phenotypic outcome of deregulated c-Myc activity: 1) through modulation of cell cycle k tics 2) through modulation of the cellular apoptotic threshold. The Phosphatidyl Inositol 3-kinase (PI3K) pathway, downstream of the Insulin Receptor, could serve to interfere with c-Myc induced deregulation of liver homeostasis via both arms; PI3K signaling is known to negatively regulate apoptosis, while it relieves cell cycle suppression at the same time. To test this hypothesis, we have made use of our novel transgenic mouse model which expresses conditionally active c-Myc specifically in its hepatocytes (alb-MycER mice). When c-Myc is activated in this model, the hepatocytes rapidly start proliferating. When the alb-MycER mice are treated with an inhibitor of the insulin signaling pathway (LY294002), Myc-induced proliferation was drastically reduced, while Myc-induced apoptosis was slightly increased. We are currently exploring to what extent enhanced, rather than decreased, insulin signaling influences the outcome of c-Myc activation in liver, using a cross of the alb-MycER mouse model with a liver specific PTEN knockout mouse.
Our findings show that modulation of insulin signaling can alter the phenotypic outcome of c-Myc activation, and thus, that targeting the insulin signaling pathway could prove useful in rebalancing a defective liver homeostasis due to deregulated Myc activity, as seen in liver cancer and cirrhosis.

Early response assessment of neoadjuvant therapy with Positron Emission Tomography in patients with oesophageal cancer

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Background: In a proportion of patients with potentially curable oesophageal cancer, insufficient objective response on neoadjuvant chemoradiotherapy is achieved. These patients do not benefit from neoadjuvant therapy, but do suffer from toxic side effects and inevitable delay of appropriate surgical therapy. Metabolic imaging with Fluorodeoxy-glucose Positron Emission Tomography (FDG-PET) seems to be a promising modality to identify non-responders early during neoadjuvant chemoradiotherapy. Therefore, the aim of the present study was to determine whether FDG-PET is able to differentiate between re-sponding and non-responding oesophageal tumours early in the course of neoadjuvant chemoradiotherapy. Methods: Serial FDG-PET before and after 2 weeks of neoadjuvant therapy was be performed in the multimodality treatment arm (concurrent Carboplatin/ Paclitaxel and 41.4Gy radiotherapy in 23 fractions) of a multicentre randomized controlled trial including patients with potentially curable oesophageal carcinoma. FDG uptake was expressed as the Standardized Uptake Value and corrected for body weight and glucose level. Resection specimens were assessed for tumour response using the Mandard score. Responders were defined as score 1 or 2 (no or <10% viable tumour cells). ROC analysis was used to determine optimal cut-off values and consequently calculate diagnostic parameters. Results: A total of 100 patients were used for PET response analysis, of whom 64 patients were histopathological responders and 36 were non-responders. Median SUV decrease between PET before and after 14 days of therapy was 30.9% for histopathological responders and 1.7% for non-responders (p=0.001). With a 20% SUV decrease as cut-off value for detection of histopathological response, PET identified 58 patients as responder: 45 correctly and 13 incorrectly. A total of 42 patients were identified as non-responders by PET: 23 correctly and 19 incorrectly. Diagnostic parameters for detecting histopathological responders by using PET were: sensitivity 70%, specificity 64%, positive predictive value 78% and negative predictive value 55%.

Conclusion: SUV decrease as measured by PET before and after 14 days of chemo-radiotherapy is significantly associated with histopathological tumour response but showed a limited accuracy. The negative predictive value was too low to justify early discontinuation of neoadjuvant chemoradiotherapy in patients with oesophageal cancer based on response as measured by FDG PET.

Lanreotide reduces the volume of polycystic liver: a randomized, double-blind, placebo-controlled trial

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Therapy for polycystic liver is invasive, expensive and has disappointing long-term results. Treatment with somatostatin analogues slowed kidney growth in patients with polycystic kidney disease (PKD) and reduced liver and kidney volume in a PKD rodent model. We evaluated the effects of lanreotide, a somatostatin analogue, in patients with polycystic liver due to autosomal dominant (AD) PKD or AD polycystic liver disease (PCLD). We performed a randomized, double-blind, placebo-controlled trial in 2 tertiary referral centers. Patients with polycystic liver (n=54) were randomly assigned to groups given lanreotide (120 mg) or placebo, administered every 28 days for 24 weeks. The primary endpoint was the difference in total liver volume, measured by computerized tomography at Weeks 0 and 24. Analyses were performed on an intention-to-treat basis. Baseline characteristics were comparable for both groups, except that more patients with ADPKD were assigned to the placebo group (p=0.03). The mean liver volume decreased 2.9%, from 4606 mL (95% CI 547–8665) to 4471 mL (95% CI 542–8401), in patients given lanreotide. In the placebo group, the mean liver volume increased 1.6%, from 4689 mL (95% CI 613–8765) to 4895 mL (95% CI 739–9053) (p<0.01). Post-hoc stratification for patients with ADPKD or PCLD revealed similar changes in liver volume, with statistically significant differences in patients given lanreotide (P<0.01 for both diseases). In conclusion, in patients with polycystic liver, 6-months of treatment with lanreotide reduces liver volume.

Lectin complement pathway gene polymorphisms and life-threatening infections after orthotopic liver transplantation

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Background: Components of the lectin complement pathway are liver-derived and crucial effectors of the innate immune response to pathogens. Immunosuppressed orthotopic liver transplantation (OLT) recipients almost completely rely on their innate immunity. We examined the role of gene polymorphisms (SNPs) in the complete lectin complement activation pathway, which affect the functional activity of the respective proteins, in association with the risk of developing clinically significant infections after OLT. Methods: We analyzed 13 SNPs in the mannose-binding lectin gene (MBL2), the Ficolin-2 gene (FCN2) and the MBL-associated serine protease gene (MASP2) in 143 recipients and their donor liver, and in a confirmation cohort of 167 OLT patients. Multivariate Cox analysis was used to assess the contribution of these SNPs to infection risk in the first year after transplantation. Results: The intergenic haplotype with mutations in all three components of the lectin pathway, i.e., MBL2 (XA/O; O/O), FCN2+6359T and MASP2+371A, in the donor liver increased the cumulative risk of clinically significant infection from 18% up to 75% (X^2= 14.7, P=0.002). The confirmation study showed a similar association of donor haplotype and infection (X^2= 8.2, P=0.04). The intergenic haplotypes of the recipients did not contribute to the infection risk after transplantation, although genotypically MBL-sufficient recipients receiving a genotypically MBL-insufficient donor liver had a significantly higher infection risk (52% vs 26%, P<0.002). The multivariate Cox analysis including all patients revealed a stepwise increase in infection risk with the intergenic gene dose haplotype (up to an adjusted HR of 4.52; 95% CI 1.81 to 11.31; P=0.001), independent from gender and antibiotic prophylaxis treatment algorithm (both with adjusted HR > 2.2 and P<0.02). Moreover, within the group of patients receiving a liver with one or more lectin pathway gene mutations those with an infection had a significantly higher mortality than those without an infection (28% vs 4%, $P<0.9x10^{-8}$).
Conclusions: The intergenic donor liver haplotype of the lectin complement pathway is a major determinant of the risk of clinically significant infection and mortality after OLT. In addition, MBL-sufficient recipients receiving an MBL-insufficient donor liver are at high risk. Screening of the lectin complement pathway haplotype is advocated to improve postoperative infection prevention and patient survival in OLT.

Therapeutic erythrocytapheresis, a new treatment for naïve patients with hereditary hemochromatosis

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Background: Standard treatment of newly diagnosed hereditary hemochromatosis (HH) patients is phlebotomy (P) which consists of removal of 500 ml whole blood weekly to reduce the serum ferritin levels to 50µg/L. Depending on the initial ferritin levels this requires 20-100 P's over a period of 6-24 months. Therapeutic erythrocytapheresis (TE) provides a new therapeutic modality. With TE up to 4 times more erythrocytes can be removed per treatment, compared to the 250 ml per P, suggesting that TE is a more efficient therapy. Aim: To compare TE and P prospectively in reducing the number of treatments required to reach a serum ferritin level of ≤ 50µg/L and thereby the total duration of both treatments. Methods: A prospective, randomized, single blind, clinical trial involving naïve patients with HH (homozygote for C282Y) was conducted. We randomly assigned patients with HH to TE or P in a 1:1 ratio. Results: 40 patients were included. Both per protocol treated and analysed groups consisted of nineteen patients. The baseline anthropometrics and laboratory characteristics were similar among the treatment groups. Only the baseline serum ferritin levels were signifficantly lower in the TE group (mean 1104 µg/L; SD 677) compared to the P group (mean 1666 µg/L; SD 912). Univariate t-test showed that in the TE group the mean number of treatments required to reach a serum ferritin level of ≤ 50 µg/L was one third of the number of treatments needed in the P group (9 vs. 27; p ≤ 0,05). Multivariate logistic regression analysis shows a decline in the reduction factor of the number of treatments to 2,17(CI $_{95\%}$ 1.23 – 3.80) when adjusted for the baseline serum ferritin levels, and a decline to 2,60 (CI $_{95\%}$ 1.10 – 6.14) when also body weight was included in the model. Total treatment duration was significantly shorter in the TE group (34, vs. 20 weeks in the P group; p ≤ 0,002). A significant difference was also found in treatment intensity (1082 vs. 205, P ≤ 0,001) with substantially higher values in the P group. No significant differences in side effects were observed. Patients experienced TE as a more convenient therapy. Conclusion: TE reduces the number of treatments required to normalize serum ferritin levels in newly diagnosed HH patients with more than 50% when compared to P. TE accomplishes this in a shorter period of time although the interval between TE's was 1, 5 weeks greater when compared to P. Furthermore, TE was a well accepted therapy.

Safety and Antiviral Activity of SCH 900518 Administered as Monotherapy and in Combination with Peginterferon Alfa-2b to Naïve and Treatment-Experienced HCV-1 Infected Patients

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Background: SCH 900518, a novel HCV NS3 protease inhibitor, demonstrates potent antiviral activity (EC90 of 40 nM). This study explored the safety and antiviral activity of SCH 900518, administered as monotherapy and combination therapy with PegIntron (± ritonavir) to HCV genotype 1 infected patients. Methods: This was a two period study in HCV genotype 1 infected subjects (naïve and treatment-experienced). SCH 900518 was administered as oral suspension for 7 days (800 mg TID or 400 mg BID with ritonavir). After a 4 week washout, SCH 900518 was administered at the same dose in combination with PegIntron for 14 days. Safety, PK, and antiviral activity were assessed. After the study, all patients initiated SOC treatment. Results: Forty subjects completed the study (N=8 placebo). SCH 900518 (± ritonavir) alone or in combination with PegIntron was found to be well tolerated. Both dose regimens resulted in trough plasma concentrations of SCH 900518 above the EC90 as determined by the HCV replicon assay. There were no clinically significant changes from baseline in vital signs, laboratory values, or ECGs. The majority of AEs were mild or moderate. An SAE of fever occurred during follow-up (treatment with PegIntron and ribavirin only) and was unlikely related to SCH 900518. A rapid and continuous decline in plasma HCV RNA was observed in both treatment-experienced (mean Δ -4.42 & -4.01 $\log_{10}$ IU/ml) and naïve (mean Δ -4.49 & -4.18 $\log_{10}$ IU/ml) patients during 7 days of SCH 900518 monotherapy (± ritonavir). A high percentage of both treatment-experienced (50% & 50%) and naïve (75% & 63%) patients had plasma HCV RNA below the LLQ (<25 IU/mL) during combination therapy with PegIntron (± ritonavir) on Day 15.
Conclusions: SCH 900518 administered alone or in combination with PegIntron was safe and well tolerated. Robust reductions in plasma HCV RNA levels were achieved in both treatment-experienced and naïve HCV genotype 1-infected subjects.

SVR Results in Chronic Hepatitis C Genotype 1 Patients Dosed with SCH 900518 and Peginterferon Alfa-2b for 2 Weeks, Followed by Peginterferon Alfa-2b and Ribavirin for 24/48 Weeks: An Interim Analysis.

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Background: SCH 900518, a second generation hepatitis C virus (HCV) NS3 ser protease inhibitor, resulted in robust reductions of HCV RNA after 1 week of monotherapy and after 2 weeks of combination therapy with peginterferon alfa-2b (Peg-IFN) with or without ritonavir. At the end of this proof-of-concept (POC) study (i.e. after SCH 900518), all patients were offered standard of care (SOC) with Peg-IFN and ribavirin (RBV). Methods: Forty HCV genotype 1-infected patients (20 treatment-naïve and 20 treatment-experienced) completed the POC study of SCH 900518. These patients received SCH 900518 (n=32) or placebo (n=8) in combination with Peg-IFN for 2 consecutive weeks, immediately followed by SOC with once weekly 1.5 µg/kg Peg-IFN and daily weight-based RBV (800-1400 mg). Patients were treated for 24 or 48 weeks, provided standard stopping rules did not require premature discontinuation. HCV RNA measurements were centrally performed using Cobas® Ampliprep/Cobas® TaqMan® HCV Test (LLD 15 IU/ml). Patients with plasma viral load >1000 IU/mL at start of SOC were analyzed for known resistant mutations by sequence analysis. Results: All 40 patients began treatment with SOC (see table), 39 patients have completed follow-up and 1 patient (placebo) is still in follow-up. Premature discontinuation due to an increase of HCV RNA during SOC (>1 $\log_{10}$ from nadir) was seen in 10 patients who received SCH 900518 (treatment-naïve n=3 vs. treatment-experienced n=7) and in 1 patient who received placebo. Non-response at week 4, 12 or 24 was seen in 5 treatmentxperienced patients (SCH 900518 n=2, placebo n=3). Virological relapse after SOC was observed in 2 treatment-experienced patients (SCH 900518 n=1 and placebo n=1). In total 15 patients had HCV RNA >1000 IU/mL at start of SOC; 7 patients received SCH 900518 and 8 patients received placebo. In 5 of 7 SCH 900518 dosed patients at least one of the following variants, associated with protease inhibitor resistance, within the NS3 protease were detected: R155K (n=5), A156T/S (n=2), V36M/L (n=4).
Conclusion: This study demonstrates that administration of SCH 900518 for two weeks (with or without ritonavir) plus Peg-IFN followed by SOC for 24 weeks or 48 weeks resulted in 81% and 38% SVR in treatment-naïve and experienced patients, respectively. These results support further development of SCH 900518 in both treatment-naïve and treatmentexperienced patients.

Serotonergic indices and psychiatric symptoms in treatment naïve chronic hepatitis C patients

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Introduction: Chronic immune activation during chronic hepatitis C virus (HCV) infection may cause depressive symptoms via enhanced tryptophan degradation, limiting the rate of central serotonin (5HT) synthesis.Aim:To investigate whether indices of 5HT metabolism and inflammation correlate withdepressive symptoms in treatment-naïve HCV patients. Methods: Symptoms of sadness, inner tension, impaired concentration and hostile feelings were measured using the validated Montgomery-Asberg Depression Rating Scale and the Brief Anxiety Scale. We measured tryptophan (precursor of 5HT), tryptophan ratio to other amino acids (marker for availability of tryptophan), neopterin (marker of monocyte/ macrophage activity), tetrahydrobiopterin (BH4) (cofactor in 5HT-synthesis), biopterin (de-gradation product of BH4), 5HT, 5-hydroxyindolacetic acid (5HIAA; a 5HT metabolite) as well as kynuren (neurotoxic metabolite of tryptophan).
Results: We included 79 patients, of whom 14 reported sadness (18%), 46 patients (58%) reported inner tension, 23 patients (29%) reported impaired concentration and 46 patients (58%) reported irritability. There were no statistically significant differences in gender, genotype or ethnicity between patients with and without symptoms.Univariate logistic regression analysis showed a correlation between levels of 5HIAA and higher scores of reported inner tension (p=0.138), impaired concentration (p=0.055), irritability (p=0.199) and sadness (p=0.089). In addition, there was a correlation between the rate of BH4 and inner tension (p=0.153) and impaired concentration (p=0.072). Furthermore, we found a correlation between the tryptophan ratio and higher scores of impaired concentration (p=0.060), irritability (p=0.098) and sadness (p=0.034). Finally, neopterin levels were correlated with perceived inner tension (p=0.094). Multivariate logistic regression showed that the tryptophan ratio was significantly correlated with sadness (OR 0.19;95%CI 0.01-0.38,p=0.043) and that there was a trend towards a correlation between neopterin levels and inner tension (OR -0.22;95%CI -0.05-0.00, p=0.079). The other correlations were not statistically significant.
Conclusion:Availability of tryptophan in the brain and neopterin concentrations as an index for immune activation, are correlated with the presence of depressive symptoms reported by HCV patients, suggesting that chronic inflammation influences brain serotonergic function and contributes to depressive symptoms.

On-treatment prediction of susta d response in HBeAg-negative chronic hepatitis B patients treated with pegylated interferon alfa-2a

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Background: Since peginterferon (PEG-IFN) is often not well tolerated and expensive it is important to predict a sustained response (SR) as early as possible. Previously we were unable to find good baseline factors predicting SR to PEG-IFN therapy in HBeAg-negative disease. Objective: To study the potential role of on-treatment HBV DNA and ALT levels (weeks 4, 8, 12 and 24) in predicting SR in HBeAg-negative chronic hepatitis B patients treated with PEG-IFN alfa-2a ± ribavirin. Methods: 133 HBeAg-negative chronic hepatitis B patients, predominantly (80%) infected with HBV genotype D, treated with 48 weeks of 180 µg PEG-IFN alfa-2a ± ribavirin were included. SR was defined as the combined presence of HBV DNA <10,000 cp/mL and normal ALT at 24 weeks after treatment discontinuation. Discrimination was quantified by the area under the receiver-operating characteristic curve (AUC). A dynamic prediction model was developed using logistic regression analysis. Results: Overall, SR occurred in 24 (18%) of patients using intent-to-treat analysis (20% of patients in the PEG-IFN monotherapy group vs 16% in the PEG-IFN and ribavirin combination therapy group, p=0.49). The treatment groups were merged for the analysis of on-treatment prediction of SR. HBV DNA reductions from baseline were superior to absolute HBV DNA levels in the prediction of SR. The AUC was 0.634, 0.647, 0.686 and 0.702 for reductions in HBV DNA from baseline at weeks 4, 8, 12 and 24, respectively. Patients who did not have a 1 log reduction in HBV DNA from baseline at week 12, constituting 26% of patients, had a probability of 97% of not achieving SR. At week 24, all patients who did not have a 1 log reduction in HBV DNA from baseline (26% of patients) would eventually not achieve SR. Addition of ALT levels to the model with HBV DNA reductions from baseline did not improve the prediction of SR. Extension of the model with flares (ALT >5 times upper limit of normal) significantly improved the prediction of SR: OR 3.9 (95% CI 1.3-12; p=0.02) for patients with a flare compared to those without.
Conclusion: Patients without a 1 log reduction in HBV DNA from baseline at weeks 12 were very unlikely to achieve SR. On-treatment HBV DNA levels may therefore be used to identify HBeAg-negative chronic hepatitis B patients with a very low probability of response to PEG-IFN early during the treatment course, thereby avoiding unnecessary treatment.

Mutations in the precore and basal core promoter regions do not influence responsiveness to pegylated interferon alfa-2a treatment for HBeAg-negative chronic hepatitis B V

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Background Previous studies have suggested that the presence of core promoter mutations (CP, A1762T and/or G1764A or G1764T) in HBeAg-negative chronic hepatitis B patients is associated with poor response rates to interferon therapy. Objective To investigate the influence of PC and CP mutations on response to peginterferon (PEG-IFN) alfa-2a ± ribavirin in HBeAg-negative disease. Methods 133 HBeAg-negative chronic hepatitis B patients treated with 48 weeks of 180 µg PEG-IFN alfa-2a ± ribavirin were included. Follow-up lasted until week 72. Genotype, PC and CP mutations were assessed at baseline using INNO-LiPA assays. Samples with indeterminate results were sequenced. HBV DNA was quantified by the Taqman HBV assay (Roche). Results 80% of patients were genotype D-infected. A PC mutation was detectable in 85% of patients, more frequently in genotype D than A (95% vs 35%, p<0.001). A mutation at nucleotide 1762 (M1762) was detected in 53% of patients, always in conjunction with M1764 and more frequently in genotype A than D (76% vs 49%, p=0.03). M1764 was present in 77% of patients, in 69% combined with M1762 and associated with lower baseline HBV DNA (6.7 vs 7.2 log cp/mL, p=0.05). ALT levels and histology were comparable in patients with or without M1762, M1764 or PC mutation. Reduction in HBV DNA levels compared to baseline was greater in the PEG-IFN monotherapy group at the end of treatment (3.9 vs 2.6 log cp/mL, p<0.001), but similar for the two treatment regimens at the end of follow-up (1.5 vs 1.6 log cp/mL). On-treatment HBV DNA decline was smaller in the presence of M1762 (2.9 vs 3.7 log cp/mL, p=0.04) and/or M1764 (3.1 vs 3.9 log cp/mL, p=0.05). At week 72, HBV DNA decline compared to baseline was not significantly different in patients with or without M1762 (1.5 vs 1.6 log cp/mL) and/or M1764 (1.4 vs 2.2 log cp/ml, p=0.09) and the proportion of patients with HBV DNA <400 cp/mL was similar irrespective of the presence of M1764 (8% vs 7%). Multiple linear regression analysis identified treatment regimen (p<0.001), baseline ALT level (p=0.001) and M1764 (p=0.003) as independent predictors of HBV DNA decline at week 48 versus baseline. Baseline HBV DNA level (p<0.001) was the only predictor of HBV DNA decline at week 72 versus baseline.
Conclusion In contrast to previous reports we found that the presence of PC and CP mutations does not influence sustained response rates of PEG-IFN therapy in HBeAg-negative chronic hepatitis B.

Early ribavirin levels predict steady state concentration in hepatitis C patients

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Background: Ribavirin (RBV) is an essential component in the treatment of chronic heaptitis C (HCV) infection. Though RBV dosage is weight-based, data in literature suggest large interpatient variability in plasma RBV concentration. Recent studies indicate that higher RBV exposure results in higher sustained viral response (SVR) rates. Therapeutic drug monitoring (TDM) uses plasma drug concentrations to deliver effective treatment for a wide range of medicines. It is not known whether this concept is applicable to RBV. Aim: To investigate the inter- and intrapatient variability in plasma RBV concentration in our cohort of HCV patients and to explore the association between RBV dosing and plasma RBV steady state concentration (C_{ss}).Methods: We performed a prospective observational cohort-study in HCV patients who received pegylated interferon in combination with weight-based RBV. We studied plasma RBV concentrations at week 1, 2, 4, 8, 12, 16, 20 and 24 as determined by a validated high-performance liquid chromatography (HPLC) assay. Results: A total of 48 patients (36M,12F), mean age 50.1 years (range 26-68 years), of which 6 were HIV co-infected, were included from July 2007-Jan 2009. Median HCV viral load on baseline was $9.5*10^5$ IU/ml (range $4*10^3$-$3*10^7$ IU/ml) and 72% had HCV genotype 1 or 4. Median dosage of RBV was 14.9 mg/kg (range 8.6-29.0 mg/kg). We collected 161 samples. In contrast to what is stated in literature we found that C_{ss} was reached at week 8 instead of week 4 of HCV treatment (fig.1). The variation coefficient (VC) of plasma RBV C_{ss} between and within patients was respectively 37.8% and 12.6%. We did find a trend between week 1 plasma RBV levels and plasma RBV C_{ss} ($r=0.477$, $p=0.072$). In addition, a significant correlation between week 2 as well as week 4 and plasma RBV C_{ss} was found ($r=0.504$ and $r=0.671$, $p<0.05$, resp.). We did not find any correlation between dosage in mg/kg and C_{ss} ($r=0.237$, $p=0.151$).
Conclusion: RBV C_{ss} can be predicted by measurement of RBV levels as early as week 2 and perhaps even at week 1. The absence of a relation between dosage in mg/kg and C_{ss} and the large inter- but small intrapatient variability make TDM suitable for RBV.

Psychiatric side-effects and the fluctuation in serotonergic parameters during treatment of chronic hepatitis C-infection with peginterferon and ribavir

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Introduction Treatment of hepatitis C with PEG-Interferon (PEGIFN) is associated with development of psychopathology by influencing the serotonergic system and increased production of neurotoxic compounds. Previous studies found a decrease in tryptophan (TRP), precursor of serotonin (5-HT), and increase in neopterin (NEOP), inducing shortage of tetrahydrobiopterin (BH4), co-factor in synthesis of 5-HT. Increase of phenylalanine to tyrosine ratio (PHE/TYR) reflects decrease in BH4. PEGIFN also increases neurotoxic kynurenine (KYN) and Nitric Oxide (NO)-synthesis, the latter modulating 5-HT-function.Aim Explore relationships between indices for 5-HT-ergic function and psychological parameters during PEGIFN-treatment.Methods 80 patients participated in a double-blind randomized trial comparing escitalopram vs. placebo in prevention of psychopathology related to PEGIFN therapy. Symptoms of sadness, inner tension, impaired concentration and hostile feelings were measured using the Montgomery-Asberg Depression Rating Scale and Brief Anxiety Scale at baseline (t=0), week 4 (t=4), 12 (t=12) and 24 (t=24) together with TRP, TRP ratio (to other large neutral amino acids reflecting availability of TRP), NEOP, BH4, PHE/TYR, KYN and KYN to TRP ratio (KYN/TRP) and Citrulline to Arginine ratio (CITR/ARG, marker for NO-synthesis).Results TRP levels (µmol/L) decreased compared to t=0 (43.7±8.2,n=6) at t=4 (39.6±7.9,n=74), t=12 (38.4±8.1,n=70) and t=24 (37.1±7.9,n=69). NEOP levels (nmol/L) increased compared to t=0 (28.41±12.85,n=76) at t=4 (57.78±13.70,n=74), t=12 (60.27±13.72,n=74) and t=24 (61.14±19.31,n=69). KYN/TRP levels increased at t=4 (49.03±13.07,n=74), t=12 (54.23±16.80,n=70) and t=24 (54.65±13.51,n=69) compared to t=0 (39.86±12.90,n=76). PHE/TYR and CITR/ARG ratios increased at t=4, t=12 and t=24 compared to t=0. Non-parametric testing showed correlations between TRP levels with impaired concentration and hostile feelings at t=24. Changes in TRP were correlated at t=4 with changes in sadness and at t=24 with changes in hostile feelings. TRP ratio was correlated with sadness at t=4 and t=12, with inner tension at t=12 and with impaired concentration at t=24. PHE/TYR was correlated with inner tension at t=4. Changes in PHE/TYR were correlated with changes in irritability at t=24. Changes in BH4 ratio were correlated with changes in hostile feeling at t=24.
Conclusion: PEGIFN-induced psychiatric disturbance are related to changes in peripheral serotonergic indices.

Long-term follow-up of patients with portal vein thrombosis and myeloproliferative disease

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In patients with non-malignant non-cirrhotic portal vein thrombosis (PVT), myelo-proliferative disorders (MPD) are the most frequent underlying cause, occurring in approximately one third of the cases. The aim of this study was to describe the long-term outcome of this specific patient group. A retrospective study was performed including all patients referred to our hospital between January 1980 and December 2008 with non-malignant non-cirrhotic PVT and confirmed MPD. We included 47 patients (72% female) with a median age at diagnosis of PVT of 47 years (range 11-79). Thrombosis was either conf d to the portal vein (n=24) or extended into the splenic and/or superior mesenteric vein (n=23). In 34 patients (72%) PVT was the first manifestation of MPD. Type of MPD was def d as polycythemia vera (n=14), essential thrombocytosis (n=12), myelofibrosis (n=6) or unclassified MPD (n=15). The JAK2 V617F mutation was present in 28 of 30 tested patients. Additional prothrombotic factors were present in 15 cases (32%). Median follow-up time after diagnosis of PVT was 5.8 years (range 0.4-22). During follow-up 26 patients (55%) were treated with anticoagulation. Thirty-one cases (66%) developed esophageal varices, of whom 18 (38%) experienced at least one bleeding episode. The occurrence of variceal bleeding was not significantly related to long-term use of anticoagulation (p=0.26). In 12 patients (26%) at least one additional thrombotic event occurred, of whom 3 were using anticoagulants at the time of first new event. In 3 cases recurrent thrombosis developed after previous anticoagulation had been discontinued. Eighteen patients (38%) died during follow-up at a median age of 64.4 years (range 30-88). Overall survival rate was 97% and 88% at 1 and 5 years, respectively. In 11 cases (61%) death was directly related to a new thrombotic event (cerebral infarction (n=2) or mesenteric vein thrombosis (n=1)) or end-stage MPD (end-stage myelofibrosis (n=5) or acute myeloid leukemia (n=3)). One patient died due to variceal bleeding.
Conclusions: PVT is often the presenting symptom of an underlying MPD, highlighting the necessity for extensive screening. Treatment with anticoagulation was not associated with an increased risk of variceal bleeding during follow-up. Recurrent thrombosis is a frequent complication in patients with PVT and MPD. Mortality is primarily related to the underlying MPD and not to complications of portal hypertension.

Octreotide reduces liver volume in patients with a polycystic liver

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Patients with polycystic livers develop symptoms due to the enlarged liver volume. Treatment aims to reduce liver volume. So far, only surgical options have been shown to be effective, but are associated with considerable morbidity. There is a clear and unmet need for medical therapy for polycystic livers. Experimental evidence suggests that octreotide reduces liver volume in a rodent model for polycystic liver disease. Therefore, we aimed to evaluate treatment with octreotide in polycystic liver patients. Eight polycystic liver patients (1 male with PCLD, 7 female with all ADPKD; median age 48.1 years (IQR 40–68)) were treated with octreotide 100 mcg t.i.d. s.c.. We measured change in liver and kidney volume by computer tomography (CT) scans, prior and following treatment. Median and interquartile ranges (IQR) were calculated and statistical analysis was performed using the Wilcoxon signed rank test. Median liver volume at baseline was 4786 mL (IQR 2896–7895) and combined kidney volume 1352 mL (IQR 754–1880). The median duration of treatment was 135 days (IQR 90–180), 1 patient was treated for 70 days, 3 for 90 days and 4 for 180 days. The median change in liver volume was -3.0% (IQR -7.6–0.0, p=0.069), while kidney volume remained unchanged (-0.0%; IQR -6.9–3.7, p=0.674). In one patient, a 90-day treatment reduced liver volume by 9.4%, but the effect was negated at 3 months follow-up, when liver volume had increased to baseline. Liver enzymes remained unchanged. Side effects were common and most prevalent during the first 1-2 weeks and included diarrhea concomitant with pale stools (n=6), abdominal cramps (n=3), weight loss (n=3) and hair loss (n=3). Patients considered the t.i.d. treatment schedule as very intensive and difficult to continue.
In conclusion, octreotide t.i.d. reduces liver volume, but not kidney volume. Patient acceptance of this intensive treatment is low, and after terminating treatment, liver volume increases again.

Outcome of pregnancy in women with chronic portal vein thrombosis

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Little is known about the outcome of pregnancy in women with non-cirrhotic non-malignant portal vein thrombosis (PVT), although most patients are females of childbearing age. We therefore assessed the maternal and perinatal outcome of pregnancies in women with established PVT. A retrospective analysis was carried out of pregnancies in women with non-cirrhotic non-malignant chronic PVT, seen at our center between 1982 and 2008. Only pregnancies occurring after diagnosis of PVT were taken into account. A detailed history of obstetric events and bleeding episodes was recorded in all patients. We observed 16 pregnancies in 8 women with PVT. Median age at diagnosis of PVT was 18.7 years (range 0-29) with median time between PVT and first pregnancy of 4.8 years (range 1-34). In 7 cases an underlying cause of PVT was identified: essential thrombocytosis, protein S deficiency, factor V Leiden mutation, hyperhomocysteinemia, splenectomy, previous pregnancy and neonatal umbilical vein catheterization. Gastroesophageal varices were present in 5 cases (63%) before pregnancy. Three patients had a history of variceal bleeding, in all cases treated with sclerotherapy. In 2 of these patients repeated sclerotherapy of varices was performed during pregnancy. In total, 5 women were treated with anticoagulation during 7 pregnancies. The incidence of spontaneous abortion was 19% (3 of 16 pregnancies), all occurring before gestation week 12. Term delivery (≥37 weeks) occurred in 12 pregnancies and 1 pregnancy resulted in a preterm delivery (at week 34). Five deliveries (38%) were caesarean sections. Severe blood loss during labour (requiring blood transfusion) occurred in 3 pregnancies (2 women). Both women were not using anticoagulation. Median follow-up after last pregnancy was 5.4 years (range 0.5-20). Variceal bleeding or recurrent thromboses were not observed in any of the patients during and after pregnancy. All 13 infants were healthy and there was no maternal mortality.
Conclusions: This study shows that pregnancy in women with chronic PVT has an excellent maternal and perinatal outcome. Complications of portal hypertension and thrombosis are uncommon. Treatment with anticoagulation during pregnancy does not seem to increase the frequency or severity of bleeding complications. The presence of PVT should not be considered a contraindication for a successful pregnancy.

Results of patients with haemorrhoids treated with Doppler-guided haemorrhoidal artery ligation

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In 1995 Doppler-guided haemorrhoidal ligation (DG-HAL) was introduced, where by patients could be treated with relative low morbidity compared to the former treatment modalities. Nevertheless, the long term effects are still unknown. This study was designed to determ the effect of treating haemorrhoids with the DG-HAL procedure.
From June 2005 to March 2008, 244 consecutive haemorrhoidal patients underwent a HAL (DG-HAL system, AMI®) procedure. All patients were evaluated 6 weeks post-operatively with a proctologic examination and interview at which the postoperative grade and complaints were recorded. Further follow-up was performed by phone with a standardised questionnaire which was used to asses the final outcome. The average age was 49 years (range 26-81). The mean time of follow up was 18.4 months (range 1.4-37.2). 244 patients were treated with the DG-HAL. Sixty-seven percent had an improvement of symptoms after one treatment, 27% had no improvement on either symptoms or grading and 6% had a worsening regarding grading or symptoms. Fifty-three patients (22%) underwent a second procedure because of persisting symptoms. 13 patients (25%) underwent a second DG-HAL-procedure and 40 patients (75%) a RBL. In total, 69% of patients had a good response after one or two treatments using the DG-HAL technique. Multivariate logistic regression analysis revealed prolapse to be an independent risk factor for persistent symptoms and the need for a second procedure (OR 2.38 (95% CI 1.10-5.15, P 0.03). Patients with third and fourth degree haemorrhoids had a higher risk of developing recurrent disease and needing a second operation (odds ratio 4.94, 95% CI 0.67-36.42, P 0.11).
Conclusions: DG-HAL procedure seems an effective procedure for treating low-grade (1 and 2) haemorrhoids. After long-term follow-up, patient satisfaction and success rate decreased mainly due to recurrent or persisting prolapse. A resection procedure aimed at treating the prolaps should then be the treatment of choice.

Ex vivo comparison of current colotomy closure modalities for Natural Orifice Transluminal Endoscopic Surgery (NOTES)

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Secure transluminal closure is one of the most fundamental barrier to safe introduction of NOTES in humans. Various endoscopic colotomy closure modalities have been described in literature. Up till now, no complete and adequately powered comparison of different colotomy closure modalities has been reported. Aim of the present study was to evaluate the acute strength of various colotomy closure techniques in a previously described ex vivo experimental set-up by assessing air leak pressures.Colons were harvested from freshly slaughtered pigs. Standardized colotomies were created by a small (2mm) incision followed by dilation with an 18 mm balloon. After closure, each specimen was fixed on the benchtest pot with the mucosa facing down, creating an airtight space within the pot. A standardized water film was positioned on the specimen to visualize air-bubbles in case of leakage. Subsequently, pressure within this airtight space was gradually raised. By connecting the pressure gauge with two cameras, leak location and pressure could be determined in great detail. We started collecting gold standard values by means of testing 15 colotomies, closed with interrupted surgical suture with 3-0 polydioxane II. This resulted in a mean leak pressure of 86.9 mmHg (SD 7.5). Using a non-inferiority design a sample size of 12 specimens for each closure technique was determined. Five different NOTES closure techniques were included: Over-The-Scope-Clip (OTSC; Ovesco), Endoclips (Olympus), T-Tags (Ethicon), T-Tags (Ethicon), and two types of flexible stapler (PMI and Covidien). Mean colotomy leak pressures were: OTSC 90.3 mmHg (SD 19.1) and Endoclips 85.1 mmHg (SD 12.4), T-tags 53.9 (SD 8.06), PMI stapler 98.5 (SD 17.3), Covidien stapler 96.6 mmHg (SD14.7). Colotomy closure using OTSC ($p=0.018$), endoclips ($p= 0.048$), PMI stapler ($p<0.001$) and Covidien stapler ($p<0.001$) resulted in non-inferior leak pressures in com-parison with gold standard values. T-tag closure was inferior to gold standard values ($p=0.998$)
In conclusion OTSC, endoclips, both flexible staplers produced comparable closures in comparison with hand-sewn colotomy closure in this ex vivo model and thus are promising colotomy closure modalities in closing. These devices might also be promising in closing iatrogenic colonic perforations. In vivo survival experiments will need to be performed to further evaluate the most secure colonic closure techniques in real life.

Randomised, blinded comparison of transgastric, transcolonic and laparoscopic peritoneoscopy for the detection of peritoneal metastases in a human cadaver model

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NOTES peritoneoscopy could replace laparoscopic peritoneoscopy (LAP) for staging of gastrointestinal malignancies if this procedure is shown to be equally safe and accurate. In a previously performed study we showed that the transgastric peritoneoscopy (TGP) and the transcolonic peritoneoscopy (TCP) were inferior to LAP in detecting simulated metastases in a porcine model. In this study, however differences between pig anatomy and human abdominal anatomy may have influenced outcome.Aim was to compare TGP and TCP to LAP in a randomised, blinded, paired human cadaver model with simulated metastases. Experiments were performed in 6 fresh-frozen human cadavers. 2.5 mm color-coded beads were placed into the peritoneal cavity via an open approach to simulate metastases. Primary outcome was number of beads detected. Based on previous porcine experiments LAP was expected to result in a yield of 95%, using a non-inferiority design a sample size of 33 beads was determined. Randomisation was performed for number and location of beads. Randomisations for locations were based on clinically most important locations. 3-port LAP was performed by one of 2 surgeons blinded as to the location and number of beads. TGP and TCP were then performed in randomised order with a 2 channel therapeutic upper endoscope by one of 2 blinded endoscopists. A 30 min time limit per examination was used. A total of 33 beads were randomly divided over 6 cadavers: 7 beads were randomized for the peritoneum, 7 for the diaphragm, 17 on the surface of the liver and hepatoduodenal ligament and 2 beads for the miscellaneous sites. LAP found 32 beads (yield=97%, 90%-CI: 92-100%), TGP 25 beads (76%, 90%-CI: 63-89%; p= 0.09 vs. LAP), TCP 27 beads (82%, 90%-CI: 70-93%; p=0.025 vs. LAP). Majority of missed beads were located at the inferior liver surface, namely 6 out of 8 beads missed by TGP and 5 out of 6 beads missed by TCP. Conclusions: In this first prospective, blinded, comparative trial in a human cadaver model TCP was comparable to LAP in detecting simulated metastases. TGP, however, appeared to be inferior in comparison with LAP. Simulated metastases were mainly missed due to limited visualization of the inferior surface of the liver and future research should focus on improved access to the inferior liver surface.

Liver mobilization during liver resection induces immediate and profound hepatocellular damage in humans

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We recently observed in a non-standardized study that hepatocellular damage during liver surgery in man was principally caused by mobilization of the liver and not by transection of the liver or application of a Pringle maneuver. This study aimed at analyzing changes in hepatocellular damage during liver surgery in a standardized fashion in order to develop a model to study perioperative interventions aiming at a reduction of this damage. All consecutive patients undergoing liver surgery requiring full liver mobilization were included. Plasma samples and liver biopsies were obtained immediately after induction, prior to and directly after liver mobilization, and after liver transection. Liver fatty acid binding protein (L-FABP) and alanine aminotranferase (ALAT) were analyzed as markers of hepatocyte injury. Wilcoxon's signed rank test with Bonferroni correction was used to analyse differences. Nineteen patients were included (11M/8F, median age 64 years [30 – 79]) who underwent a right hemihepatectomy (n=11), central liver resection (n=4) or segmental resection (n=4). A Pringle manoeuvre was applied in 11 patients (58%) and median blood loss was 950 mL (100 – 3000). L-FABP levels increased significantly during liver mobilization (from 91.7 ng/mL [11.4 – 2212.5 ng/mL] to 1014.4 ng/ml [141.4 – 8986.1 ng/mL], $p<0.001$) and didn't increase significantly thereafter (1315.2 ng/mL [67.0 – 20099.2 ng/mL], $p=0.75$). L-FABP levels after ≥ 60 minutes mobilization time were significantly higher when compared to < 60 minutes mobilization (1679.7 ng/mL versus 645.9 ng/mL, $p=0.04$). ALAT levels increased significantly from 26 IU/L [13-147] before to 130 IU/L [74-813] after liver mobilization and to 275 IU/L [13-1352] after transection (all $p<0.05$).

Conclusion: Liver mobilization during liver surgery induces profound hepatocyte injury with an 11-fold increase in L-FABP and 6-fold increase in ALAT level, dependent on its duration. Given the short half-live of L-FABP, hepatocyte damage predominantly occurred during mobilization of the liver and not during transection or application of the Pringle manoeuver. Liver mobilization offers a new model to study human hepatic damage. Futhermore, it might be the best time period to study perioperative interventions aiming at a reduction of hepatocellular injury. Validation studies are currently being performed.

Fasting protects against hepatic ischemia/reperfusion injury via upregulation of HO-1 and antioxidant defence

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Ischemia reperfusion (I/R) injury is an important factor determining patient outcome after major liver surgery and transplantation. Release of reactive oxygen species contributes to reperfusion injury of the liver after ischemia. We have shown that 72 hours of fasting protects against hepatic I/R injury. To elucidate the protective mechanisms, we investigated the effect of fasting on mRNA expression levels of hepatic HO-1 and antioxidant defence genes. Male C57BL/6 mice were fed ad libitum or fasted for 72 hours prior to surgery. The portal vein to the left and middle liver lobes (70%) was clamped for 75 minutes to induce I/R injury. Liver damage, neutrophil influx, mRNA levels of HO-1 and mitochondrial superoxide dismutase2, glutathione peroxidase1, and glutathione reductase were determined at 0, 6 and 24 hours after reperfusion. At 24 hours post-reperfusion, significantly lower ALAT levels ($P<0.01$), significantly less hemorrhagic necrosis ($P<0.001$) and a significantly reduced number of infiltrating neutrophils ($P<0.05$) was observed in livers of fasted animals. Hepatic HO-1 mRNA expression levels were upregulated at baseline, with values significantly higher than the ad libitum fed group. The peak expression level was found 6 hours post-reperfusion in the fasted group while the control group peaked at 24 hours after reperfusion. Hepatic mRNA expression levels of mitochondrial superoxide dismutase 2, glutathione peroxidase 1 and glutathione reductase were all significantly upregulated at baseline in livers of 72 hours fasted animals.
Conclusions: Short-term preoperative fasting protects against hepatic I/R injury. Fasting induces baseline upregulation of HO-1 and antioxidant mRNA expression levels. Maximum HO-1 levels were significantly higher and achieved earlier after I/R injury in the fasted group. This leads to improved antioxidant defence and reduced organ damage. In analogy to ischemic preconditioning we coin the term nutritional preconditioning for the beneficial effects induced by fasting.

Adjuvant radioimmunotherapy improves survival of rats after resection of colorectal liver metastases

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Half of the patients with colorectal cancer develop liver metastases somewhere in the course of their disease. Although partial hepatectomy can improve 5-year survival to about 30%, recurrent tumour growth in the liver develops frequently. The aim of the present study was to test the hypothesis that adjuvant RIT might be an effective way to prevent recurrent liver metastases after partial hepatectomy in an experimental model. Male Wag/Rij rats underwent a mini-laparotomy with intrahepatic injection of 0.3 x 10^6 CC531 tumour cells. The biodistribution of In^{111}-labelled MG1 after intravenous administration was determined at 1, 3 and 7 days p.i. The therapeutic efficacy of Lu^{177}-MG1 at the maximal tolerable dose was compared with that of Lu^{177}-UPC-10 (isotype-matched control antibody) and saline only. RIT was administered either at the day of the partial hepatectomy (day 14) or 7 days after surgery (day 21). Primary endpoint was survival. In^{111}-MG1 preferentially accumulated in CC531 liver tumours reaching a maximum 3 days post injection (8.7 ± 0.6 %ID/g). The tumour-to-blood ratio of In^{111}-MG1 was the highest at day 7: 19 ± 2. Both the administration Lu^{177}-MG1 and Lu^{177}-UPC-10 resulted in a transient decrease in body weight, compared to administration of the saline only. However, no other signs of clinical discomfort were registered. Two-month survival rate was 83% and 94% in the groups treated with Lu^{177}-MG1 on the day of surgery or 7 days later, respectively. Log rank test showed that the survival curves of the group that received Lu^{177}-UPC-10 and the group that received the saline only did not differ (P=0.638). Two-month survival rate in the group treated with ^{177}Lu-UPC-10 was 60%.
Conclusion: This study provides proof of principle that RIT can be an effective adjuvant treatment modality after surgical treatment of colorectal liver metastases.

Atherosclerosis: a new risk factor for anastomotic leakage?

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The search for risk factors for colorectal anastomotic leakage is important, considering its high incidence and significant morbidity and mortality. Atherosclerosis can reduce microcirculation, and therefore local oxygenation, but is also a systemic disease with an overall impaired quality of the cardiovascular system. We aimed to study the relation between atherosclerosis of the aorto-iliacal trajectory, quantified on an abdominal CT-scan, and leakage of anastomoses of the colon. In a retrospective study the abdominal pre-operative CT-scans of patients having undergone right- and left-sided anastomoses were used. The calcifications visible in the aorta, common iliac arteries, and internal iliac arteries were quantified using calcium-scoring software, much used for coronary calcifications. This software calculates the calcium load in different ways, including Agatston score and calcium mass. Postoperative anastomotic leakage was documented, together with risk factors for atherosclerosis and anastomotic leakage. 122 patients were included. Eleven (9%) developed anastomotic leakage (AL). The Agatston score was significantly higher in the common iliac arteries in patients having developed anastomotic leakage (mean (sd): 1103,3 (1056,6) AL vs. 301,9 (623,8) non-AL). The calcium mass (mg) was significantly higher in the abdominal aorta (755,2 (856,0) AL vs. 261,7 (540,1) non-AL) and in the common iliac arteries (514,8 (447,7) AL vs. 122,9 (257,2) non-AL) in patients having developed anastomotic leakage.
Conclusion: In this study, patients with anastomotic leakage after colonic anastomoses had a significantly higher calciumload in the aorto-iliacal trajectory in comparison to patients without postoperative leakage. A prospective study with a standardized CT-scanning protocol will be carried out to confirm these data. This retrospective study indicates that aorto-iliacal calcifications on the pre-operatively made abdominal CT-scan reflect an increased risk for anastomotic leakage.

Sentinel node procedure of the sigmoid using indocyanine green: feasibility study in a goat model

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Introduction: The sentinel lymph node (SLN) procedure in patients with colon cancer may alter the strategy of treatment of colon cancer. New techniques emerge that may provide the surgeon with a tool for accurate intraoperative detection of the sentinel lymph nodes. Methods: A sentinel lymph node procedure of the sigmoid was utilized in six goats. During laparoscopy, the near-infrared (NIR) dye Indocyanine green (ICG) was injected in the subserosa of the sigmoid via a percutaneously inserted long needle during four experiments and in the submucosa during colonoscopy in two experiments. After injection the near-infrared features of a newly developed laparoscope were used to detect the lymph vessels and SLNs. At procedure end, at two hours after injection, all goats were sacrificed and autopsy was performed. During post mortem laparotomy the sigmoid was removed and used for confirmation of ICG node uptake. Results: In all procedures the lymph vessels were easily detected by their bright fluorescent emission. In the first two experiments no lymph nodes were detected. In the subsequest four experiments, human serum albumin was added to the ICG solution before injection, to enable better lymph node entrapment. In all four experiments at least one bright fluorescent lymph node was found after tracking the lymph vessels by their fluorescent guidance. The mean time between injection and SLN identification was 10 min (range 8-12 min). In two cases the SLNs were located up to 5 mm into the fat tissue of the mesentery and were not seen by regular vision of the laparoscope. By switching on the near-infrared features of the scope a clear bright dot became visible, which increased in intensity after opening the mesentery. Ex vivo examination of the surgical specimens revealed in one case a second echelon SLN, which had not been recognized in vivo.
Conclusion: The sentinel node procedure of the sigmoid using near-infrared laparoscopy in the goat is a very promising technique. Achievements herein justify a clinical trial on the feasibility of ICG guided SNL detection in humans.

Isolated tumor deposits in colorectal cancer predict an adverse outcome

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The prognostic role of pericolic or perirectal isolated tumor deposits (ITDs) in node negative colorectal cancer (CRC) patients is unclear. Rules to define ITDs as regional lymph node metastases changed in subsequent editions of the TNM staging, but substantial evidence on which these changes are based is lacking.The aim of this study was to investigate the correlation between ITDs and disease recurrence in stage II and III CRC patients.The medical files of a total of 870 patients who underwent a resection for a colorectal adenocarcinoma between 1996 and 2005 were reviewed. Of all node negative patients with ITDs, number, size, shape and location pattern according to involvement of vascular structures and nerves were examined of all ITDs. The correlation between the different characteristics of ITDs and the development of disease recurrence was investigated. ITDs were found in 14.8% of all CRC patients. Increasing frequencies were seen in higher TNM stages. Disease recurrence was observed in 50.0% of stage II patients with ITDs (13 out of 26), compared to 24.4% of stage II patients without ITDs (66 out of 270), $p<0.01$). In a multivariate analysis, the presence of ITDs was maintained as an independent risk of recurrence when adjusted for other known risk factors, namely T-stage, differentiation grade and and lymphovascular invasion of the primary tumor ($p<0.05$, OR: 2.4; 95% CI: 1.0-5.9). Disease free survival of ITD positive stage II patients was comparable with that of stage III patients. Also within stage III, more recurrences were observed in ITD positive patients (28 out of 43) compared to ITD negative patients (66 out of 169), $p<0.01$. No correlation was found between size of ITDs and disease recurrence. More recurrences were seen in patients with irregular shaped ITDs as compared to patients with one or more smooth ITD's present ($p<0.05$).
Conclusion: Because of the high risk of disease recurrence, all node negative stage II patients with ITDs, regardless of size and shape of the ITDs, should be classified as stage III, for whom adjuvant chemotherapy should be considered.

Incisional Hernias in Old Stoma Wounds: a Cohort Study

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Incisional hernias are a frequent and well known problem occurring after midline laparotomies. Incisional hernias occurring after reversal of a stoma however, have just scarcely been researched in small or inadequately reported recent studies. Therefore, we set out to determine the true prevalence of and risk factors for incisional hernias in old stoma wounds by using a large cohort of patients. We included all adult patients with a stoma closed in a university tertiary care hospital during the the period January 2000 until August 2004. Main outcome was a hernia in the old stoma wound, defined as a defect within the musculature and fascia on ultrasound examination. Furthermore, risk factors for incisional herniation and diagnostic accurateness of clinical symptoms and palpation during Valsalva's manoevre were determined. Out of 150 alive patients, 111 (74.0%) could be included for analysis after follow-up at the outpatient clinic. After a median follow-up of 35 (range 5-77) months, hernia prevalence in the old stoma wounds was 32.4%. In patients with body mass index below 25 kg/m^2 incisional hernia rate wa 25.5%, above 30 kg/m^2 incisional hernia rate was 59.1%. Sensitivity was highest for palpation, yet only 58.3%. One out of six patients with physical complaints at the old stoma site, but no palpable defect, had an incisional hernia revealed on ultrasound examination. Morbid obesity was the only risk factor identified (odds ratio 5.53, 95% confidence interval 1.72-17.80). A stoma in situ for more than 6 months showed a trend towards lowering the risk for incisional herniation (odds ratio 0.42, 95% confidence interval 0.17-1.04).
Conclusions: Incisional hernias occur in one out of three old stoma wounds and BMI above 30 kg/m^2 is a risk factor.

Histological identification of epithelium in perianal fistulas

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Background: A procedure often performed following fistulotomy and advancement flap is curettage of the fistula tract after fistulotomy or after closing the internal opening. Epithelialization of the fistula tract might prevent closure of the fistula tract. The aim of this study was to assess the incidence and origin of epithelialization of the fistula tract in patients with perianal fistulas undergoing fistulotomy. Methods: Only patients with low perianal fistulas that were surgically treated by fistulotomy were included. Surgical biopsies were taken from the fistula tract from three different locations, respectively on the proximal side at the internal opening, in the middle of the fistula tract and near the distal end close to the external opening. Results: In the study period 18 patients with low perianal fistulas were included. In 15 of the 18 patients squamous epithelium was found at least in one of the biopsies taken from the fistula tract. Epithelium was predominantly found near the internal opening. There was no relation between the duration of fistula complaints and the amount of epithelialization (p=0.301). The amount of epithelium was not related to the presence of a history of fistula surgery (p=1.000).
Conclusion: The present study demonstrated epithelialization in the fistula tract in the majority of the patients surgically treated by fistulotomy for low perianal fistulas. The epithelium originated mainly from the internal opening. Curettage of perianal fistulas must therefore be considered an essential step in the surgical treatment of perianal fistula.

The anal fistula plug treatment compared to the mucosal advancement flap for cryptoglandular high transsphincteric perianal fistula: A double blinded multi-center randomized trial

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Surgical treatment of high transsphincteric perianal fistulas results in relatively low success rates compared to those of low perianal fistulas. Favorable results were initially reported using a new biologic anal fistula plug, a bioabsorbable xenograft made of lyophilized porcine intestinal submucosa for the treatment of high perianal fistula. Later publications reported less favorable closure rates (24-71%). The aim of this randomized prospective multicenter trial was to compare the anal fistula plug with the mucosal advancement flap for the surgical treatment of high transsphincteric perianal fistulas of cryptoglandular origin.Patients with high perianal fistula were randomized to either the anal fistula plug or the mucosal advancement flap repair. Patients were blinded for the type of treatment. Outcome parameters were closure rate, postoperative pain, continence and quality of life. At the final follow-up closure rate was determined by clinical examination by a surgeon blinded for the intervention. Postoperatively patients were asked to fill out visual analogue scales for pain-measurement. Continence was assessed by COREFO, Vaizey and the Wexner score. Quality of life was assessed by SF-36 and EQ5D questionnaires. The aim of this randomised prospective double blinded multicenter trial was to compare the anal fistula plug with the mucosal advancement flap for the surgical treatment of cryptoglandular high transsphincteric perianal fistulas.The median follow-up duration was 11 months (range 5-27). In the group that was treated with the anal fistula plug the recurrence rate was 71% (n=22). This was not significantly different (p=0.126) with the group that was treated with the mucosal advancement flap where in 52% the fistula recurred (n=15). There were no statistically significant differences in terms of postoperative pain scores after surgery. The continence was not significantly different pre- and postoperatively for COREFO, Vaizey, or the Wexner score in both groups. Soiling was not significantly different between groups pre- and postoperatively. There were no differences in the quality of life assessment.
Conclusions: Both the results of the anal fistula plug and advancement flap are disappointing in multicenter setting. There were no significant differences in recurrence, functional outcome and QOL between de plug and advancement flap. As the plug is simple to apply and minimally invasive it can be considered to use as initial treatment option for high transsphincteric fistulas.

Autofluorescence endoscopy improves the targeted detection of early Barrett's neoplasia but subsequent detailed inspection with Narrow-Band Imaging is of limited value. A randomized cross-over study comparing endoscopic tri-modal imaging with standard endoscopy (ISRCTN68328077)

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Introduction: Endoscopic tri-modal imaging (ETMI) incorporates high-resolution endoscopy (HRE), auto-fluorescence imaging (AFI) and narrow band imaging (NBI) in one single endoscopy system. In a recent feasibility study, we found that ETMI improved the detection of high-grade dysplasia (HGD) and early carcinoma (EC) in Barrett esophagus (BE) from 53% to 90%. The aim of the current study was to compare ETMI with standard endoscopy (SE) for the detection of HGD/EC using a randomized cross-over design. Methods: This study was performed in 5 tertiary referral centers for early BE neoplasia in the Netherlands, UK, and USA. Consecutive pts with BE>2 cm and referred for the work-up of inconspicuous HGD/EC were eligible. Pts underwent 2 consecutive endoscopies (SE and ETMI) within an interval of 6-12 weeks. Prior to the first procedure randomization to SE or ETMI was performed. Both procedures were performed by 2 different endoscopists experienced in early BE neoplasia. The endoscopist assigned to the second procedure was blinded for the results of the first procedure. During ETMI, inspection with HRE was followed by AFI. All detected lesions were inspected in detail with NBI and biopsied followed by 4q/2cm Bx. During SE, targeted Bx were performed from any visible lesion followed by 4q/2cm Bx. The combined histological outcome of both endoscopic procedures was considered as gold standard. The sample size of this study was calculated on 84 patients. Results: 107 eligible pts were entered in the study of which 23 pts were excluded: withdrawal of consent after 1st procedure (3), a clearly visible cancer requiring treatment without delay (16), BE<2cm (4). 84 pts (69 male; 67±10 yrs) completed the study and were analyzed. HGD/EC was detected in 54 pts (64%). The overall sensitivity of SE for HGD/EC was 74% compared to 83% for ETMI (p=0.405). The sensitivity for targeted detection of HGD/EC was 44% for SE and 67% for ETMI (p=0.012). In total 68 suspicious lesions were detected with SE of which 33 (49%) contained HGD/EC. ETMI detected 225 suspicious lesions of which 68 (30%) contained HGD/EC: 39 lesions were detected with HRE and 29 with AFI only. NBI reduced the FP-rate of ETMI from 70% to 47%, but NBI classified 12 lesions containing HGD/EC as not being suspicious (FN-rate 18%).
Conclusion ETMI statistically significant improved the targeted detection of HGD/EC compared to SE. This improved detection of ETMI was mainly due to the additional detection of 29 HGD/EC lesions by AFI which were not apparent with HRE. However, subsequent detailed inspection with NBI reduced the FP-rate of AFI only marginally at the expense of misclassifying 18% of HGD/EC lesions as not suspicious.

A randomized prospective trial in 74 patients comparing the ER-cap technique and multi-band mucosectomy technique for piecemeal endoscopic resection in Barrett esophagus

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Endoscopic resection (ER) is an important modality to treat high-grade dysplasia (HGD) or early cancer (EC) in Barrett esophagus (BE). The most widely used ER technique, the ER-cap technique, requires submucosal lifting and prelooping of a snare in a cap making it technically demanding and laborious for piecemeal ER, and a new snare is needed for every resection. The newer multi-band mucosectomy (MBM) technique does not require submucosal lifting or prelooping of a snare and one snare can be used for multiple resections. Aim was to prospectively compare ER-cap and MBM for piecemeal ER in BE. Patients scheduled for piecemeal ER of biopsy-proven HGD/EC in BE, without suspicion on submucosal invasion on endoscopy and EUS, were included. After delineation of the target area patients were randomized to ER-cap (16.1mm hard oblique, Olympus) or MBM (Duette, Cook Medical). Assessment criteria were: number of resections/ procedure; procedure time; complications; maximum diameter and thickness of specimens; costs of disposables. 74 pts (57M, median 70yrs, median BE 5cm) were randomized: 35 MBM vs 39 ER-cap. Procedure time (34 vs 50min, p=0.03) and costs (€240 vs €322, p=0.001) were significantly less with MBM vs ER-cap. MBM resulted in smaller specimens than ER-cap (17 vs 20mm, p<0.001). Maximum thickness of resected specimens and submucosa of specimens obtained with MBM vs ER-cap was 1.9 vs 2.0mm (p=ns) and 0.8 vs 1.0mm (p=ns), respectively. There were three severe complications: 3 perforations in the ER-cap group, all treated endoscopically.
Conclusions: This randomized trial shows that piecemeal ER with MBM is faster and cheaper than with ER-cap and may be associated with fewer complications. MBM results in statistically significantly smaller sized specimens, but the clinical relevance of this may be limited since the depth of resection did not differ. MBM may thus be preferable for piecemeal ER of flat-type HGD/EC with a low risk of submucosal invasion.

Do we still need endoscopic ultrasound (EUS) in the work-up of patients with early esophageal neoplasia for endoscopic treatment? A retrospective analysis of 131 cases

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Esophageal neoplasia confined to the mucosa has a minimal risk of lymph node metastasis (N+) and may be treated endoscopically, whereas submucosal invasion (SM+) increases the risk of N+ and warrants surgery. EUS is often used to stage early esophageal neoplasia during work-up for endoscopic therapy. Its value, however, has been questioned since current high-resolution endoscopy and diagnostic endoscopic resection (ER) enable accurate histological assessment of invasion depth and other risk factors for N+ (poor differentiation or lymph-vascular invasion). Aim of this study was to evaluate the clinical value of EUS in the work-up of early esophageal neoplasia next to endoscopic inspection (EGD) and diagnostic ER. A retrospective chart review was performed to identify all patients undergoing upper GI EUS from May ’01-June ’07 for esophageal high-grade dysplasia or early cancer referred for endoscopic therapy. 131 patients were included (98 M, mean age 71±14 yrs). EUS was unremarkable in 110, but diagnostic ER showed SM+ (n=15) or one or more other risk factors for N+ (n=11). In addition 2 patients did not have ER due to non-lifting (treated with radiotherapy), and endoscopic doubts on attainability of ER (surgery: T3N1M0). In 21 patients EUS was abnormal. In 8 of these 21 patients EGD had already raised suspicion that the lesion would not be eligible for endoscopic treatment and this suspicion was confirmed in 7 patients by ER (SM+ or N+ factors in the ER specimen in 5) or surgery (T2N0M0 and T2N1M0). In 13 of these 21 patients EUS showed signs of SM+ (n=8), N+ (n=2) or both (n=3) while EGD was unremarkable. FNA was performed in all 5 EUS-N+ patients showing benign cytology in 4 and a metastasis of an undiagnosed lung cancer in 1. All 13 patients had diagnostic ER, which did not show SM+ or N+ risk factors in 5 patients who subsequently underwent curative endoscopic treatment.
Conclusions: Despite normal EUS findings, ER revealed SM+ as well as other risk factors for N+ in 25% of patients. Furthermore, the additional value of EUS next to detailed EGD was limited: 38% of patients with suspicion on SM+ or N+ based solely on EUS findings, had no SM+ or other N+ risk factors in the diagnostic ER specimen and no esophageal cancer related lymph nodes were detected. The outcome of this study shows that EUS has virtually no clinical impact in the work-up of early esophageal neoplasia and strengthens the role of diagnostic ER as the final diagnostic step during work-up.

Risk of lymph node metastases in late early adenocarcinoma of the oesophagus and cardia diagnosed by endoscopic resection

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Most estimations of the risk of lymph node metastases (LNM) in adenocarcinoma of the oesophagus and cardia (EAC) with invasion in the muscularis mucosae (m3) and submucosa are based on surgical series. Estimated risks of LNM are reported to be 4-12% for m3, 0-22% for tumors invading the upper third of the submucosa (sm1) and 36-54% for tumors invading the middle and lower third of the submucosa (sm2/3). The aim of this study was to correlate m3 and submucosal infiltration depth of EAC in endoscopic resection (ER) specimens with LNM. Patients undergoing ER for EAC between January '00 and March '08 in 2 Dutch centres were included if the ER specimen showed m3 or submucosal cancer. Submucosal invasion depth was classified as sm1 (≤500 µm) or sm2/3 (>500 µm). For the purpose of this study, ER specimens were reviewed by an expert GI pathologist. Exclusion criteria were chemo/radiotherapy and irradical ER. Follow-up data of patients was retrieved until death or March 2009. The presence of LNM was evaluated in surgical resection specimens in the case of an esophagectomy, or during endoscopic follow-up in the case of endoscopic therapy. A total of 115 patients underwent ER for m3 or submucosal EAC of which 33 were excluded (7 chemo/ radiotherapy and 26 irradical ER). A total of 82 patients were included (67 male, median age 70 years, 75 located in the oesophagus). ER specimens showed 57 m3, 12 sm1 and 13 sm2/3 tumours. Five m3 tumours were poorly differentiated and 3 showed LVI. Sm1 tumours had a median infiltration depth of 200 µm (IQR 100-400), 3/12 were poorly differentiated and 1/12 showed LVI. Sm2 tumours had a median infiltration depth of 800 µm (IQR 800-1000), 5/13 were poorly differentiated and 1/13 showed LVI. Poorly differentiated tumours showed significantly more LVI (p=0.002) and infiltrated more often the submucosa (p=0.02). After initial ER, 7 patients underwent surgery and 75 were managed endoscopically. No LNM were found in a total of 158 lymph nodes in the esophagectomy specimens. None of the endoscopically treated patients was diagnosed with LNM during a median follow-up of 26 months (IQR 14-41). Seven patients developed a local recurrence: 5 patients were managed endoscopically, 1 was referred for surgery and 1 was managed conservative because of co-morbidity.
Conclusion: This study shows no LNM for m3 and submucosal EAC assessed in ER specimens and therefore suggests that the risk of nodal metastases may be lower than assumed by surgical series.

Comparative yield of endosonography and magnetic resonance imaging in individuals at high risk of pancreatic cancer

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In approximately 10% of all pancreatic cancer (PC) cases a hereditary factor plays a causative role. This provides the opportunity to identify a sub-population of individuals at high-risk of developing PC. A surveillance program could be of benefit for these individuals to prevent death by PC. Endosonography (EUS) has proved to be a potentially valuable tool for surveillance purposes. Data for MRI are lacking. We present preliminary results of a comparative study between baseline EUS and MRI investigations in high-risk individuals entering a yearly surveillance program. Asymptomatic high-risk individuals prospectively underwent EUS and MRI. Both investigations were carried out and scored according to predefined criteria. Fifty-four individuals underwent both baseline EUS and MRI. In 14 individuals (25%) focal lesions were detected by EUS and/or MRI; 10 with cystic lesions, two with a mass lesion and two with focal areas of hypoechogenicity. Cystic lesions were detected by EUS and/or MRI in 10 individuals. The total of cysts detected by EUS was 11 (median size 5 mm) and by MRI 18 (median size 4 mm). Communication between cysts and the pancreatic duct (PD) was more often reported by EUS (4 vs. 1). Both mass lesions were only detected by EUS, of which one latter proved to be a malignancy and in one no signs of malignancy were found. Both focal areas of hypoechogenicity were detected by EUS only. In one individual this 'lesion' had spontaneously disappeared at follow-up investigations after 3 months. In the second individual follow-up investigations are pending.
Conclusion: Based on these preliminary results, EUS and MRI seem complementary techniques to detect (pre)malignant lesions in individuals at high-risk for developing PC. All mass lesions were detected by EUS and missed by MRI. This included an adeno-carcinoma but also a falsely detected lesion. In at least one individual a focal area of hypoechogenicity resolved spontaneously. Cystic lesions were more often reported by MRI, however communication between cyst and PD was more often reported by EUS. The latter is valuable information since it differentiates a simple cyst from a side-branch IPMN.

Prevalence of features of chronic pancreatitis in a Dutch cohort of individuals at high-risk of developing pancreatic cancer

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Individuals at high-risk of pancreatic cancer (PC) are (1) mutation carriers of PC prone hereditary syndromes and (2) first-degree relatives of patients with PC who have familial PC. Previous studies revealed a high prevalence of chronic pancreatitis (CP)-like features in these high-risk individuals undergoing screening endosonography (EUS). The aim of this study was to determine the prevalence of CP features in a Dutch cohort of individuals at high-risk for developing PC entering a yearly surveillance program. Asymptomatic high-risk individuals prospectively underwent EUS. The operating endosonographer scored presence of nine validated features of CP; echogenic foci, strands, lobularity, cysts, stones, duct dilatation, duct irregularity, hyperechoic duct margins, and visible side branches. Since interpretation of EUS-images is known to be highly observer dependent, the videotaped examinations were re-evaluated and re-scored by four expert endosonographers. The interobserver agreement among the experts was assessed using interclass correlations (ICC) statistics. ICCs <0.2, 0.2-0.4, 0.4-0.6, 0.6-0.8 and 0.8-1 were considered as poor, fair, moderate, good and very good respectively.Eighteen individuals (M/F 7/11), age 41-63 years, median 55 years who had underwent baseline screening with EUS were included. Seven individuals were from familial PC kindreds and eleven were mutation carriers of PC prone hereditary syndromes. At initial screening, the number of features of CP scored per individual ranged from 0 to 4. The operating endosonographer scored three or more features in five individuals (28%) and four features were detected in four (22%) individuals. When re-evaluated by experts, three or more features were suggested in 19.5% of cases (range 11-28%). The maximum number of items scored per individual was four and found in 5,5% of cases (range 0-11%). The ICC for the number of features scored per individual was fair (0.3). The agreement for specific features of CP varied from poor to moderate.
Conclusion: Based on these preliminary results, features of CP were less commonly seen at baseline screening in this Dutch cohort of individuals at high-risk for developing PC compared to previous studies. Previous studies found three or more CP-like features in 78% of cases. In our series three or more features of CP were found at initial examination in 28% of cases and by re-evaluation of the examinations by experts in 19.5%. Further surveillance of these individuals will reveal if features of CP progress over time and may serve as a marker for early neoplastic changes.

Safety and efficacy of the Trans-Oral Endoscopic Restrictive System (TERIS) for the treatment of obesity

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Background and Aims: Surgical gastric bypass and adjustable banding procedures are effective in the therapy of morbid obesity. In order to obtain similar results in a less invasive manner an endoscopic implant procedure has been developed and studied in an animal model with encouraging results. We present the first results of this implant device (TERIS, Barosense,CA,USA) in humans. Aims of this study are to investigate safety and effectiveness. Methods: Inclusion criteria are a Body Mass Index (BMI) of 35.0-49.9 kg/m², age 18-50 and ASA I or II. Procedures are performed under general anesthesia. A 22 mm endogastric tube (EGT) is placed, through which a stapler and a 5 mm endoscope are advanced. With the stapler 5 plications are created in the cardia. Anchors are pulled through the plications and the restrictive device is attached to the anchors. Patients are followed for 6 months, after which the device is either removed or kept in place for 6 additional months. Primary endpoints are adverse events. Secondary endpoints are weight loss and improvement in co-morbid disease(s). Results: 13 patients (3 male, mean age 37.2 (SD 7.9)), median body weight of 122.6 kg (101.3-153.3) have been enrolled between 09/08 and 04/09. Median BMI was 42.1kg/m² (35.5-49.1). Median procedure time was 142 minutes (93-184). The device was placed in 12 of 13 pts. In one patient the procedure was abandoned after a gastric perforation occurred due to malfunctioning of the stapler. The perforation was treated laparoscopically and the patient was discharged 3 days after the procedure. In two patients a pneumoperitoneum developed which was desufflated with a percutaneous hollow needle in one and treated conservatively in the other. Both patients were admitted one additional day. After patient 7, the stapling device was redesigned and pressure controlled insufflation with CO2 was used instead of air. At one month patients obtained a median weight loss of 7.8 kg (4.1-14.1), representing a mean excess weight loss of 15.7%. Median BMI decreased from 43.6 to 41.3 (5.3%).
Conclusions: These preliminary results of a restrictive endoscopic device for the treatment of obesity showed successful placement in 12 out of 13 patients. Weight loss was excellent and seems to be comparable to LapBand results. Serious adverse events occurred in 3 of the first 7 patients, no further SAE`s occurred after redesigning the stapler and the use of CO2 insufflation. Further long-term studies should be pursued.

Polyp location is a risk factor for delayed type post-polypectomy hemorrhage: a multi-center case-control study

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Delayed type hemorrhage is an infrequent, but serious complication of colonoscopic polypectomy. Large polyp size is the only factor that has been unequivocally proven to increase the risk of late bleeding. The aim of this study was to determine whether polyp location is an independent risk factor for delayed type post-polypectomy hemorrhage.
A multi-center case-control study was conducted. Patients with delayed type post-polypectomy hemorrhage, defined as bleeding after one hour post-polypectomy, were identified from the complication registries of two university medical centers and two general hospitals. Non-bleeding polypectomies were randomly selected as controls from the same center in a ratio of 3:1 to case. The study period was January 2002 – March 2009. Forty-two cases and 126 controls were identified. The percentage of males was 57% in cases and 43% in controls (p=0.077). Mean age was 65±12 years in the cases and 61±12 years in controls (p=0.054). The odds ratio (OR) of delayed type post-polypectomy hemorrhage was 6.5 for polyps in the caecum, 1.5 for the ascending colon, 0.7 for the descending colon, 0.7 for the sigmoid and 0.2 for the rectum (p<0.001 for trend). No bleeding polyps were seen in the transverse colon. The OR of delayed type hemorrhage increased with polyp size (p<0.001 for trend); for polyps >6mm the OR was 13.0 (p<0.001). There was no correlation between polyp size and location (p=0.952 for trend). Polyp shape was not a risk factor: the OR was 1.1 for pedunculated polyps versus 0.9 for sessile polyps (p=0.467).
Conclusion: Polyp location is a risk factor for delayed type post-polypectomy hemorrhage. The caecum in particular is a high-risk location for polypectomy. Extra prudence is advised when removing polyps from this region.

Third eye retroscope randomized clinical evaluation ("TERRACE" study): Initial results

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Introduction: Colonoscopy is the gold standard for detection of polyps and cancers in the colon, but some lesions are missed. To improve the detection rate, the Third Eye® Retroscope® (Avantis Medical Systems, Inc., Sunnyvale, CA), was designed to provide an additional, retrograde view that complements the forward view of a standard colonoscope. Aims & Methods: This prospective study is designed to compare the diagnostic yield obtained by using the Third Eye Retroscope with a standard colonoscope (TER) vs. the diagnostic yield of a standard colonoscope alone (COLO) during same-day, back-to-back procedures. This report describes results for the initial 81 completed subjects in a study involving 16 investigators and 410 subjects at 8 centers in Europe and the U.S. Patients scheduled for screening, surveillance or diagnostic colonoscopy are randomized to COLO followed by TER (Group A) or TER followed by COLO (Group B). Reversing the order of procedures controls for any “second-pass” effect. Primary outcome measures are miss rates by each method for all polyps and for adenomas.
Results: The detection rate for all polyps by TER during the first pass in Group B (0.68 per subject) was 17% greater than the detection rate for all polyps by COLO during the first pass in Group A (0.58 per subject). In contrast, the detection rate for adenomas by COLO during the first pass in Group A (0.44 per subject) was 109% greater than that for adenomas by TER during the first pass in Group B (0.21 per subject). This may have resulted from the disproportionately high total number of adenomas per patient found with both passes in Group A (23/43=0.53) compared to Group B (13/38=0.34). For the 43 subjects in Group A, the second exam with TER yielded 7 additional all polyps and 4 additional adenomas. For the 38 subjects in Group B, the second exam with COLO yielded 6 additional all polyps and 5 additional adenomas. The differences were not statistically significant. The Relative Risk of missing a lesion using the standard colonoscope alone vs. using the colonoscope with the Third Eye was 1.03 for all polyps (p=0.99) and 0.71 for adenomas (p=0.85).
Conclusions: Initial results for this multi-centre study trend towards more total polyps being detected during the first pass with the TER compared to the first pass with the COLO, but at this early stage of study enrolment, not enough data have been collected to draw conclusions.

Is ileoanal pouch surveillance indicated after restorative proctocolectomy for neoplasia in ulcerative colitis?

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Introduction: Patients with ulcerative colitis (UC) have an increased risk of developing colorectal cancer, particularly when neoplasia is present. Restorative proctocolectomy (RPC) is recommended in these cases. A recent systematic review of observational studies suggested that UC patients with a proctocolectomy and ileoanal pouch reconstruction are at risk of developing neoplasia, either inside the ileoanal pouch or in the rectal cuff. The aim of the current prospective study was to assess the prevalence of neoplasia in UC patients who have undergone RPC. Methods: Patients with UC related neoplasia who underwent RPC from 1988-2008 were included and invited for surveillance endoscopy of their ileoanal pouch. The afferent and blind ileal loop, ileoanal pouch and rectal cuff were examined by standard endoscopy plus methylene blue dye-spraying. Mucosal abnormalities were sampled and 4 random biopsies were taken from the afferent and blind ileal loop, pouch and rectal cuff each. Results: 42 patients (23 male, mean 50 yrs) underwent surveillance pouch-endoscopy. The mean time between RPC and pouch surveillance was 8.6 (median 7.9, range 1-19) yrs. The RPC resection specimen contained indefinite for neoplasia in 12 (28.5%) cases, low grade neoplasia in 12 (28.5%), high grade neoplasia in 8 (19%) and carcinoma in 10 (24%). At surveillance endoscopy, 37 targeted biopsies and 672 random biopsies were taken. Dysplasia was detected in two patients. In one patient (male, 53 yrs) low grade neoplasia was detected by standard endoscopy in a visible lesion in the rectal cuff. This patient had indefinite for neoplasia in his RPC-specimen, there was no history of pouchitis, and his surveillance endoscopy was performed 4.7 years after the RPC. In the second patient (male, 53 yrs) low grade neoplasia was detected in a random biopsy taken of the pouch and a random biopsy of the blind ileal loop. The original RPC resection specimen of this patient contained multifocal high grade dysplasia, there was one episode of pouchitis and his surveillance endoscopy was performed 17 years after the RPC.
Conclusion: This prospective pouch-endoscopy study with random biopsies for surveillance after RPC detected neoplasia in 2 out of 48 patients (4.8%). Until the significance of neoplasia in the pouch is proven, we propose a 5-yearly surveillance endoscopy with targeted and random biopsies for all patients who underwent a proctocolectomy with RPC for dysplasia or cancer in longstanding UC.

Nurse endoscopists doing colonoscopy: a prospective study on performance in clinical practice of a general hospital

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Background: in 2005 we started the Nurse Endoscopist Project in our hospital, dealing with the education and training as well as the implementation of nurse endoscopists in clinical practice, but also addressing medico-legal aspects (wet BIG, WGBO) and the FWG function description nurse endoscopist. The first nurse endoscopist (MvdK) started in 2005, this resulted in a decrease of the average waiting time for colonoscopy from 7 to 4 weeks, a patient satisfaction survey carried out in 2006 was very positive (average score 8.8 on a scale from 1-10), in 2007 the second nurse endoscopist (AvN) started performing sigmoïdoscopy / colonoscopy. A financial analysis deducted by the hospital administration on 991 colonoscopies performed by nurse endoscopists from 01-06-2006 until 01-01-2008 revealed a positive result of € 218.000. Aim of the study: to evaluate the performance of two nurse endoscopists doing colonoscopy in routine clinical practice of a general hospital. Methods: from 01-01-2008 until 01-01-2009 two trained nurse endoscopists performed colonoscopies under supervision of an experienced gastro-enterologist working in the adjacent endoscopy suite. Any assistance by the gastro-enterologist and acute complications of the procedure such as bleeding or perforation were prospectively recorded. Results: the two nurse endoscopists performed together 995 colonoscopies, the ileum was intubated in 484 cases (49%), in 248 cases (25%) they did snare-polypectomy of one or more polyps. In 26 cases (3%) they asked for assistance with introducing the endoscope throughout the colon; the supervisor succeeded however in only 6 cases. Assistance with intubating the terminal ileum was asked for in 16 cases (2%), the gastroenterologist succeeded in only 3 cases. In 73 cases (7%) snare-polypectomy was performed by the gastroenterologist, in 57 cases (6%) the gastroenterologist was asked for help interpreting the endoscopic findings. No acute complications were observed.
Conclusions: trained nurse endoscopists are able to perform (therapeutic) colonoscopy, needing assistance of an experienced gastroenterologist in just a minority of cases. Implementation of nurse endoscopists in routine clinical practice creates the possibility of shortening the waiting time for colonoscopy and of reducing the workload of the gastro-enterologist.

Single nucleotide polymorphisms (SNPs) in C-type lectin genes, clustered in the IBD2 and IBD6 susceptibility loci, may play a role in the pathogenesis of Inflammatory Bowel Diseases

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In the last era it has become evident that the balance between microbes and host defence mechanisms at the mucosal frontier plays an important, yet unclarified role in the pathogenesis of inflammatory bowel disease (IBD). The importance of microorganisms in IBD is supported by the association of IBD with mutations in intracellular pathogen recognition receptors (PRRs) as CARD15/NOD2. The CARD15/NOD2 receptor belongs to a subgroup of the PRRs, knowing the C-type lectin like receptors (CLR's). Growing insight in the pathogenetic role of NOD2/CARD15 mutations in Crohn´s disease and the fact that the majority of the CLR encoding genes are located in IBD susceptibility loci, provided for strong arguments for further exploration of the role of CLRs in IBD. CLRs not only function as PRRs on dendritic cells and macrophages, but also mediate cell-cell interaction with other leukocytes and endothelial cells. CLRs recognize carbohydrates on pathogens and self-proteins; they take up antigen and deliver the antigen to the endosomal compartment, where the antigen can be processed for antigen presentation. Based on these features and their known function we selected 4 single nucleotide polymorphisms (SNP's) in different CLR's in this study to see whether there could be a role for these CLR's in IBD. Functional SNP's in the candidate CLR's DCSign, LLT1, Dendritic Cell Immuno Receptor (DCIR) and Macrophage Galactose-like Lectin (MGL) were investigated. Genotyping of all SNP's was performed in the AMC. In this study a total of 1348 patients were included of which 535 Crohn's Disease (CD) patients, 371 Ulcerative Colitis (UC) patients and 442 healthy controls (HC). No association was found between our IBD patient cohort and the candidate SNP's for DCSign (CD/HC $p<0.22$ and UC/HC $p< 0.36$), DCIR (CD/HC $p<0.22$ and UC/HC $p< 0.41$) and MGL (CD/HC $p< 0.37$ and UC/HC $p< 0.25$). However, an association between LLT1 and our Crohn's patient's population was found ($p < 0.034$). Our Ulcerative Colitis (UC) cohort was not associated with the variation in LLT1 ($p <0. 33$). LLT1 is a ligand for the recently discovered CD161. CD161 is a new surface marker for human IL-17 producing Th17 cells. The Th17 phenotype has recently been linked to CD by the fact that IL-22, IL-17 and IL-23 receptor levels are increased in CD. The signal transduction pathways involving LLT1 and CD161 are not completely clarified and currently under investigation in our laboratory.

Affinity capturing of autoantibodies using synthetic ganglioside epitopes for the treatment of the Guillain-Barré Syndrome

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Guillain-Barré Syndrome (GBS) is a post-infectious autoimmune disease of the peripheral nerves. Campylobacter jejuni, a food born pathogen normally causing uncomplicated enteritis, is the most frequently documented triggering agent of GBS. Antibodies formed against sialylated lipooligosaccharide (LOS) structures on the bacterial surface that are exposed during infection, cross react with similar ganglioside structures on neural tissue, inflicting immune activation and self-attack of neural cells resulting in cell damage and paralysis. Treatment of GBS patients consists of plasmapheresis, a relative crude method removing plasma from blood, and medications that suppress the immune system. Because of the non-specific nature of both these treatment modalities, a more specific therapy primarily targeting the pathogenic autoantibodies would be beneficial for the patient and potentially improve the course of the disease. For this purpose, gangliosides important in GBS pathology such as GD1a, GM1, GM2 and GM3 were enzymo-organically synthesized and equipped with hydrophobic tails to facilitate their directed coupling to solid phases. Molecules were tested in ELISA for their specificity and selectivity and subsequently coupled to a monolithic carrier and to sepharose beads for immuno-depletion purposes. Monolithic material containing synthetic GM2 could successfully deplete anti-GM2 IgG and IgM but not anti-GM1 antibodies from patient serum. When coupled to sepharose however, synthetic GM1 was able to bind and deplete anti-GM1 IgG antibodies.
Conclusions: Although exposure of the ganglioside epitope on the solid phase and composure of the hydrophobic tail contributed to efficacy and specificity of the procedure, synthetic gangliosides can be used for affinity capturing of pathogenic antibodies and future treatment of antibody mediated autoimmune disease.

Complement activation in human non-alcoholic fatty liver disease

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Activation of the innate immune system plays a major role in non-alcoholic fatty liver disease (NAFLD). The complement system is an important component of innate immunity which recognizes danger signals such as tissue injury. We aimed to determine if activation of the complement system occurs in NAFLD, to identify initiating pathways, and to assess the relation between complement activation, NAFLD severity, apoptosis, and inflammatory parameters. Liver biopsies of 43 obese subjects with various degrees of NAFLD were analyzed for deposition and activation of complement factors C1q, mannose-binding lectin (MBL), C4 (detection of C4d), C3 (detection of neo-epitopes on C3b, iC3b and C3c) and terminal complement complex (TCC) (detection of C9 neo-epitopes in membrane attack complex and fluid phase SC5b-9 complex). Furthermore, hepatic neutrophil infiltration, apoptosis, and pro-inflammatory cytokine expression were quantified. Complement activation was observed in the liver of 74% of the NAFLD patients as detected by deposition of activated C3 and C4d. C1q as well as MBL accumulation was found in the majority of activated C3-positive patients. Strikingly, 50% of activated C3-positive patients also displayed TCC deposition. Deposition of complement factors was predominantly seen around hepatocytes with macrovesicular steatosis. Subjects showing accumulation of activated C3 displayed increased numbers of apoptotic cells. Importantly, hepatic neutrophil infiltration as well as IL-8 and IL-6 expression was significantly higher in patients showing activated C3 deposition, whereas patients with TCC deposition additionally had increased IL-1β expression. Moreover, NASH was more prevalent in patients showing hepatic TCC and/or activated C3 deposition.
Conclusions: We show for the first time that there is activation of the complement system in NAFLD, which is associated with disease severity. This may have important implications for the pathogenesis and progression of NAFLD given the function of complement factors in clearance of apoptotic cells, hepatic fibrosis, and liver regeneration.

Baseline HBsAg levels predict HBsAg loss in HBeAg negative but not in HBeAg positive chronic hepatitis B patients treated with Peginterferon alfa-2a (Pegasys®) and Adefovir (Hepsera): an interim analysis.

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Background and aim: To establish markers of response before and on-treatment in chronic hepatitis B (CHB) patients treated with a combination of Peginterferon alfa-2a (Peg-IFN) and Adefovir (ADV) therapy for 48 weeks. Patients and Methods: 86 CHB patients (41 HBeAg positive and 45 HBeAg negative) with HBV DNA ≥ 20,000 IU/mL received at least one dose of combination therapy Peg-IFN and ADV by May 2009. Treatment duration was 48 weeks, with a follow up period of 24 weeks. After end of follow-up, a long-term follow-up period of 5 years started. Results: 64 CHB patients (28 HBeAg positive and 36 HBeAg negative) achieved end of treatment (ET), and 56 patients reached end of follow-up (EF) (26 HBeAg positive and 30 HBeAg negative). Eleven (20%) patients (7 HBeAg negative and 4 HBeAg positive) achieved HBsAg loss. One patient was HBsAg negative at ET, but positive again at EF. In HBeAg positive patients, median baseline log HBsAg levels (IU/mL) in patients attaining HBsAg loss were comparable with patients not attaining HBsAg loss (4.48 IU/mL (iqr 4.4-5.0 IU/mL) vs 4.83 IU/mL (iqr 4.1-4.8 IU/mL); p=0.4). In HBeAg negative patients, median baseline log HBsAg level (IU/mL) in patients achieving HBsAg loss were significantly lower compared to patients not attaining HBsAg loss (2.03 IU/mL (iqr 1.9-3.2 IU/mL) vs 3.65 IU/mL (iqr 3.5-3.8 IU/mL); p<0.0001). In HBeAg positive and HBeAg negative patients, baseline HBV DNA levels did not predict HBsAg loss (p=0.46 and p=0.26). If baseline HBsAg in HBeAg negative patients was below 675 IU/L, the positive predictive value (PPV) for achieving HBsAg clearance, using receiver operating curve (ROC) analysis, was 83%. Conclusion: This interim analysis shows that in HBeAg negative CHB patients baseline HBsAg level (≤ 675 IU/mL) predicts HBsAg clearance (PPV 83%).

Baseline HBsAg level and on-treatment HBsAg and HBV DNA decline predict sustained virological response in HBeAg negative chronic hepatitis B patients treated with Peginterferon alfa-2a (Pegasys®) and Adefovir (Hepsera); an interim analysis.

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Background and aim: To establish markers for sustained virological response (SVR) in chronic hepatitis B patients (CHB) treated with Peginterferon alfa-2a (Peg-IFN) and Adefovir (ADV) for 48 weeks.Patients and Methods: 45 HBeAg negative CHB patients with HBV DNA ≥ 20,000 IU/mL had received at least one dose of combination therapy Peg-IFN and ADV by May 2009. Treatment duration was 48 weeks, with a follow up period of 24 weeks. After end of follow-up, a long-term follow-up period of 5 years started.Results: 36 patients had achieved end of treatment (ET), and all patients attained a virological response (HBV DNA< 2,000 IU/mL). Thirty patients reached end of follow-up (EF), 14/30 (47%) patients developed SVR, (HBV DNA < 2,000 IU/mL at EF) and 16/30 (53%) patients relapsed (HBV DNA > 2,000 IU/mL at EF). In 7/14 (50%) patients with SVR, HBsAg was cleared during treatment or within 2 years after EF. Mean baseline log HBsAg level (IU/mL) of patients with SVR was 3.04 IU/L (± 0.8 IU/mL) and was significantly lower than mean baseline logHBsAg level in patients with a relapse (3.56 IU/mL (± 0.4 IU/mL) p=0.03). When baseline log HBsAg level was < 3.04 IU/mL, the positive predictive value (PPV) for SVR, using receiver operating curve (ROC) analysis, was 71%. There was no significant difference in genotype distribution between patients with SVR or relapse. Mean baseline log HBV DNA level in patients with SVR was comparable with baseline log HBV DNA level in patients with a relapse (5.68 IU/ml vs 5.18 IU/mL p=0.10) At week 12 of treatment, mean decline in log HBsAg level in patients with SVR was 0.32 IU/mL compared to 0.07 IU/mL in patients with a relapse. This was not significantly different (p=0.23). At week 12 of treatment, a decline in HBsAg level ³ 15% combined with an HBV DNA level < 1,000 IU/mL resulted in a PPV for SVR of 72%. At week 24 of treatment, mean log HBsAg level in patients with SVR was 2.43 IU/mL (± 1.2 IU/mL) compared to 3.48 IU/mL (± 0.6 IU/mL) in patients with a relapse (p=0.007). When at week 24 HBsAg level had decreased ≥ 25% and HBV DNA was undetectable (< 12 IU/mL) (in 10/30 (33%) patients), PPV for SVR was 100%. When at week 24 HBsAg level had decreased < 25% from baseline (in 5/30 (17%) patients), the negative predictive value for relapse was 100%. Conclusion: Baseline HBsAg level and on-treatment decline of HBsAg and HBV DNA are strong predict-tors for SVR in HBeAg negative CHB patients, treated with Peg-IFN and ADV.

On-treatment HBsAg and HBV DNA level predict failure for HBeAg seroconversion in HBeAg positive chronic hepatitis B patients treated with Peginterferon alfa-2a (Pegasys®) and Adefovir (Hepsera); an interim analysis

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Background and aim: To establish markers for HBeAg seroconversion in HBeAg positive chronic hepatitis B patients (CHB) treated with Peginterferon alfa-2a (Peg-IFN) and Adefovir (ADV) for 48 weeks.Patients and Methods: 38 HBeAg positive CHB patients with HBV DNA ≥ 20,000 IU/mL had received at least one dose Peg-IFN and ADV by May 2009. Treatment duration was 48 weeks, with a follow up period of 24 weeks. After end of follow-up, a long-term follow-up period of 5 years started.Results: 28 patients reached end of treatment (ET), and 10/28 (36%) patients had an HBeAg seroconversion. All patients had on-treatment HBeAg seroconversion. 9/10 (90%) patients who attained HBeAg seroconversion also achieved a sustained virological response (SVR) (HBV DNA < 2,000 IU/mL), and 18/18 (100%) patients with no HBeAg seroconversion relapsed during follow-up. In 4/10 (40%) patients with HBeAg seroconversion, also HBsAg was cleared. Genotype A was significantly associated with HBeAg seroconversion and HBsAg loss compared to genotype non-A (p=0.04 and p=0.02).Mean log HBsAg levels during treatment and follow-up are shown in the Table. Baseline HBsAg levels in patients achieving HBeAg seroconversion were not different from baseline levels in patients without HBeAg seroconversion (p=0.77). Mean decline in HBsAg level between baseline and week 12 and 24 was more pronounced in patients achieving HBeAg seroconversion (-0.99 IU/mL (± 0.97) and -2.04 IU/mL (± 1.55 respectively), but this was only significant as from week 24 of treatment (p=0.06 and p=0.013 respectively).When at week 24 of treatment, mean log HBsAg level was >10,000 IU/mL (in 11/28 (39%) patients), the negative predictive value (NPV) for HBeAg seroconversion was 82%, using receiver operating curve (ROC) analysis. When at week 24 also HBV DNA levels were > 1000 IU/mL (in 7/28 (25%) patients), NPV for HBeAg seroconversion was 100%.
Conclusion: Baseline HBsAg levels do not predict HBeAg seroconversion. HBsAg decline is more pronounced in patients with HBeAg seroconversion. HBsAg level and HBV DNA at week 24 is a strong predictor for treatment failure in HBeAg positive CHB patients treated with Peg-IFN and ADV.

Five year tenofovir therapy is associated with maintained virologic response, but significant decline in renal function in HIV/HBV coinfected patients

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We investigated the long-term efficacy and safety of tenofovir disoproxil fumarate (TDF) administered as a part of anti-retroviral therapy in a large cohort of HIV/HBV-coinfected patients. 102 HIV/HBV-coinfected patients who received TDF for at least six months were included in this multicenter cohort study. Virologic response (VR) was defined as undetectable HBV DNA with a sensitive real-time PCR assay. Screening for resistance was performed at baseline in lamivudine (LAM)-experienced patients or in case of virologic breakthrough by direct sequencing. The glomerular filtration rate (eGFR) in mL/min/1.73 m² was calculated using the Modification in Diet in Renal Disease (MDRD) equation, based on the serum creatinine, age, sex and race. Renal impairment was defined as eGFR less than 60 mL/min/1.73 m². Seventy-nine (77%) patients had detectable HBV DNA at baseline. Forty-eight (61%) of 79 patients were previously treated with LAM, and in 33 (42%) patients LAM-resistance could be detected at baseline. Median follow-up was 56 (range: 12-84) months. For HBeAg-positive patients (n=66), the cumulative probability of achieving VR at 1, 2, 3, 4 and 5 years of treatment was 41, 74, 82, 86, and 89%, respectively. There was no significant difference between patients with or without LAM-resistance at baseline (p = 0.31). HBeAg loss and HBsAg loss rates increased to 40% and 9% after 5 years of TDF therapy. For HBeAg-negative patients (n=13), the cumulative probability of achieving VR at 1, 2, and 4 years of treatment was 54, 72, and 100%, respectively. HBsAg loss occurred in 8%. Twenty-three (23%) subjects (all HBeAg-) had undetectable HBV DNA at baseline. Median follow-up was 53 (range: 8-83) months. During follow-up 22 (96%) subjects maintained virologic response, but none showed HBsAg loss. Overall, 4 of 102 patients experienced a virologic breakthrough, yet none of them demonstrated TDF-resistant mutations. The mean eGFR at baseline was 105±30 mL/min. The mean eGFR at the end of follow-up (94±26 mL/min) was significantly lower compared to baseline (p < 0.001). During follow-up nine (9%) patients developed renal impairment, wich persisted in three subjects for greater than 3 months. Three subjects stopped TDF due to renal dysfunction.
Conclusions: TDF is an effective anti-HBV agent through five years of therapy. Nevertheless, patients should be carefully monitored for development of renal impairment, as TDF therapy is associated with a significant decline in eGFR.

Intrahepatic Hepatitis B virus (HBV) covalenty closed circular DNA (cccDNA) is a predicttor of response in chronic HBV patients treated with a combination of peginterferon-alfa 2a and adefovir

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Background and aim: To determine whether baseline or end of treatment intrahepatic Hepatitis B (HBV) covalently closed circular DNA (cccDNA) level predict treatment response in chronic hepatitis B patients, treated with peginterferon alfa-2a (PEG-IFN) and adefovir (ADV). Material and Methods: In May 2009, 28 HBeAg-positive and 36 HBeAg negative CHB patients had been treated with PEG-IFN and ADV for 48 weeks. A liver biopsy was offered before treatment and at end-of-treatment (ET). Intrahepatic cccDNA and total HBV DNA copies were determined by real-time PCR (Lightcycler® 480). For quantitation of hepatocytes, a commercial Taqman® β-actin control kit was used. Plasma HBV DNA levels were determined using the Roche COBAS® TaqMan 48®. Results: 20 HBeAg positive and 30 HBeAg negative patients had baseline biopsies. In 18 HBeAg positive and 23 HBeAg negative patients, ET biopsy was performed. 14 HBeAg positive and 22 HBeAg negative patients had two biopsies. Nine patients are still on treatment. All patients who reached ET had a virological response (HBV DNA< 2,000 IU/mL). Ten HBeAg positive patients had an HBeAg seroconversion. In HBeAg negative patients, 13 patients attained sustained virological response (SVR) (HBV DNA <2,000 IU/mL at end of follow-up). Baseline mean intrahepatic cccDNA was 2.49 copies/ Hepatocyte in HBeAg positive and 0.47 copies/hepatocyte in HBeAg negative patients (p=<0.05). At baseline a strong correlation was seen between intrahepatic cccDNA level and plasma HBsAg level (R^2= 0.31; p<0.05), total intrahepatic HBV DNA (R^2= 0.48; p<0.05) and plasma HBV DNA levels (R^2= 0.42; p<0.05). At ET mean intrahepatic cccDNA level in HBeAg positive patients with HBeAg seroconversion was 0.12 copies/hepatocyte (± 0.12) compared to 0.40 copies/hepatocyte (± 0.37) in patients with no HBeAg seroconversion (p=0.03). When at ET in HBeAg positive patients intrahepatic cccDNA level was undetectable (<150 copies/biopsy), the positive predictive value (PPV) for SVR, using receiver operating curve (ROC) analysis was 67%. At ET mean intrahepatic cccDNA level in HBeAg negative patients with SVR was 0.10 copies/ hepatocyte (± 0.2) compared to 0.05 copies/hepatocyte (± 0.06) in patients with a relapse (p=0.42). When at ET intrahepatic cccDNA level was undetectable (<150 copies/biopsy), the PPV for SVR, using ROC analysis, was 73%.

Conclusions: In chronic hepatitis B patients treated with peg-IFN and ADV, undetectable cccDNA level at ET is a strong predictor of SVR.

Focal nodular hyperplasia and adenoma of the liver: contrast enhanced ultrasound performance.

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Background and aims: The purpose of this prospective single centre study was to assess the clinical value and impact of contrast-enhanced ultrasound (CEUS) imaging in the characterization of focal nodular hyperplasia (FNH) and hepatocellular adenoma in a tertiary referral centre. FNH and adenoma imaging have different typical findings, but smaller atypical nodules may still be difficult to differentiate. Currently, most liver lesions are regarded to be well recognized radiologically, and only a minority require biopsy.
Methods: Sixty-four consecutive patients with FNH or adenoma were assessed with CEUS, using 2nd generation contrast agent Sonovue (Bracco). The reference imaging included contrast-enhanced MRI (85%) and CT (15%). The final diagnosis was based on consensus interpreting all examinations, including histology (19%) and clinical follow-up. CEUS and MRI diagnosis was based on standard criteria (FNH: central scar, centrifugal arterial filling, adenoma: arterial filling, both lesions without wash-out during late phase).
Results: In these 64 patients the MRI and/or CT diagnosis was FNH in 35 pts, adenoma in 25 pts and not discernible (adenoma/FNH) in 4 patients. Average lesion diameter was 60.6 (20-120) mm. CEUS resulted in concordance with MRI in 56 out of 64 patients (87.5%) and falsely interpreted 8 patients (12.5%; 4 FNH as adenomas and 4 vice versa). CEUS correctly diagnosed 10 of the 12 biopsy proven lesions and MRI 8 of 12 lesions. Results against final diagnosis were for CEUS 54 out of 64 correct (84.4%) and for MRI 60 out of 64 (93.7%). If we regard both methods as complementary, the diagnosis was correct in 62/64 patients (96.8%)
Conclusion: CEUS has a comparable performance as MRI in the diagnosis of FNH and adenoma of the liver. Therefore, CEUS could be used as the first line imaging method. In patients, where CEUS findings are unclear, MRI is the method of choice. Only in patients with contradictory results from both imaging methods histological assessment is needed.

Prevalence of HCV among former and current drug users and marginally housed people: results of a multidisciplinary approach on screening and antiviral treatment.

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Background and Aims: Former and current drug users (DU) and the marginally housed are a specific social group who are usually characterised as difficult to treat. We estimated prevalence of HCV and HIV among this group and investigated social and behavioural characteristics. Feasibility of treatment of HCV was investigated in the setting of a multidisciplinary approach.Methods: The study population participated in a program of a large addiction treatment centre for homeless care in Rotterdam between May 2007 and May 2009. Well trained care givers offered information about HCV, screening for HCV and HIV and used extensive questionnaires on risk behaviour and social characteristics. The research physician treated patients at the opiate substitute services with standard of care antiviral treatment and monitored psychiatric side effects with questionnaires SF-36 and SCL-90. Results: Screening: 293 persons were tested on HCV, 274/293 on HIV and 256/293 responded to a standardised questionnaire. Results of screening: 111/293 (38%) were anti-HCV-positive of whom 81 were HCV-RNA positive (73%), 28/111 had cleared HCV (25%) and 2/111 unknown; anti-HIV-positive 7/274(3%). Genotype (GT) distribution: GT-1: 51% (41/81), GT-2: 5% (4/81), GT-3: 35% (28/81), GT-4: 9% (7/81), unidentified: 1% (1/81).Of the 256 HCV-tested persons who responded to the questionnaire, 82% reported heroin use in the past 6 months, 94% reported methadone use in the past 6 months, and. 15% had never injected drugs. Blood contact, sexual risk behaviour, sharing of toiletries and tools enabling drug use as well as prostitution did not show any significant relation with anti-HCV-positivity. 64 chronically infected persons were referred for treatment, of which 34 received at least 1 dose of standard of care (pegylated IFN and ribavirin). We are awaiting further results on treatment including results of the SF-36 and SCL-90 questionnaires.
Conclusions: HCV-infection was prevalent in 38% of (former) drug users and marginally housed persons in our region. Following our multidisciplinary design, this group proved to be well accessible for screening and treatment of HCV.15% of the anti-HCV-positive persons had never injected drugs, indicating other routes of infection unrecognized yet among this group.

Fatigue in Inflammatory Bowel Disease, results of a population based study in the Netherlands; the IBD-South Limburg cohort

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The importance of fatigue and it's impact on social functioning has been increasingly recognized and studied in several chronic diseases. However, little is known about fatigue in Inflammatory Bowel Disease (IBD). The aim of our study was to investigate the influence of IBD diagnosis, disease activity and haemoglobin level on fatigue scores in an unselected cohort of IBD patients in a regional population.Patients diagnosed between 1 January 1991 and 1 January 2003 were included. They completed a questionnaire including a disease activity score and the Multidimensional Fatigue Inventory (MFI-20). The MFI-20 measures the dimensions: general fatigue; physical fatigue; reduced activity; reduced motivation; and mental fatigue (high scores: worse). Haemoglobin levels were measured in the questionnaire period. Data were available in 304 Crohn's Disease [CD] and 368 Ulcerative Colitis [UC] patients. Mean MFI fatigue scores in all dimensions were higher than values found in healthy populations, indicating higher fatigue in IBD patients, regardless of diagnosis, disease activity and haemoglobin level. A general fatigue score above ten was found in 67% of CD and 63% of UC patients during quiescent disease. In CD, all MFI dimensions scored significantly worse in patients having active disease. For UC, this was only found for general fatigue, physical fatigue and reduced activity. The MFI in CD and UC patients with anaemia was significantly worse for general fatigue, physical fatigue and reduced activity. In a multiple regression analysis, in UC the haemoglobin level influenced the general fatigue score independently of disease activity, whereas disease activity significantly influenced the level of fatigue in both CD and UC.
Conclusions: Fatigue scores in IBD patients are high. CD patients suffered significantly more than UC patients in all measured fatigue dimensions. In UC, disease activity and anaemia are independent contributors, in CD disease activity mainly influenced the level of fatigue.

Factors determining the severity of fatigue in Crohn's disease patients

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Crohn's disease (CD) patients (pts) suffer from a disabling disease which negatively influences the quality of life. Fatigue is a common symptom in CD pts and contributes to the decreased quality of life. We performed a retrospective study to assess different determinants of CD influencing the severity of fatigue in CD pts. CD pts of our Inflammatory bowel disease clinic from December 2007 - December 2008 of whom the required data in the electronic medical records were accessible were included. The records were reviewed and demographic variables, medication used since the diagnosis of IBD, side-effects of the medication and clinical history was noted. Fatigue was assessed by the Checklist Individual Strength (CIS) (fatigue: CIS score ≥ 35; non-fatigue CIS score < 35), anxiety and depression by the Hospital Anxiety and Depression Scale (HADS) and disease activity by the Harvey-Bradshaw Index. For statistical analysis the Fisher's exact test was used. In total 300 CD pts were included, 192 females; mean age 40 years (range 17-75); mean duration of the disease 12 years (range 0-55). The mean CIS score was 39 (range 8-56). Overall, 68% of the patients (204 pts) experienced fatigue. There were no differences with respect to the mean age, age of diagnosis, the mean duration and the localisation of the disease between fatigue and non-fatigue patients. Significantly more females (142 pts, 74.3%) than males (62 pts, 57.4%, p=0.005) scored higher than 35 on the CIS. In the fatigue group there were significantly more patients with clinical depression (51 pts, 25%; 2 pts, 2.1% of non-fatigue patients, p=0.0001) and anxiety (62 pts, 30.4%; 7 pts, 7.3% of non-fatigue patients, p=0.0001). Furthermore, a higher percentage of fatigue patients than non-fatigue patients were not in remission according to the Harvey-Bradshaw Index (53.4%; 16.7% respectively, p=0.0001). Medical therapy and previous CD surgery did not influence the fatigue score. However, a significantly higher percentage of fatigue patients (136 pts, 64.2%; 76 pts, 35.8%; p=0.003) had corticosteroids treatment related side-effects.
Conclusions: Patients with Crohn's disease have a high prevalence of fatigue. The fatigue affects significantly more females, patients with active disease and patients with anxiety and depression. Although the medication does not seem to influence the fatigue, patients with a history of side-effects to corticosteroids experience fatigue more often than patients tolerating steroids.

Peri-conceptional use of medication for inflammatory bowel diseases in a referral center

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Inflammatory bowel diseases (IBD) affect mostly patients in reproductive age. The information on the pregnancy-related safety of the most therapeutics used in IBD is however limited and little is known about the actual use of medication by IBD patients with active reproductive wish.The aim of our study was to assess the type of medication used by IBD patients with active conception plans and changes of the medication in the peri-conceptional period. Between April 2007 and April 2009, pregnant IBD patients and IBD patients with active conception plans were recruited from the outpatient clinic of the gastroenterology Dept of academic hospital. The type of medication indicated for IBD and changes of the medication due to the active conception wish or pregnancy were noted.In total 61 patients (51 females; 41/20 Crohn`s disease/ulcerative colitis) were included. Thirteen (21%) had no medication, 44 used monotherapy (72%) and 4 patients (7%) used combination treatment (two on infliximab and azathioprine; one infliximab and prednisone; one azathioprine and mesalazine). From patients on monotherapy, 11 patients (19%) were on thiopurines; 11 (19%) patients received maintenance treatment with anti-tumor necrosis factor agents; 5 (9%) patients were using steroids (3 patients systemic steroids and 2 patients budesonide); 11 (19%) patients were on 5-amino-salicylates; 5 (9%) patients were using methotrexate and one patient was on study medication. From all patients included, 37 (61%) consulted the physician prior the conception. Because of the conception plans, 11 (30% of all consulting patients) patients changed their medication as advised by their gastroenterologists. Two patients stopped their medication themselves.
Conclusion: In a referral center, the majority of IBD patients with conception plans require medication for which limited information on the safety of the peri-conceptional use is available. The reproduction wish represents an important factor influencing the therapeutic strategy, as one third of these patients eventually change the medication due to their conception plans.

Bone Mineral Density in IBD: a 5- year follow-up study

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Introduction & aim: The inflammatory bowel diseases (IBD), Crohn`s disease (CD) and ulcerative colitis (UC) affect bone metabolism and are frequently associated with osteopenia and osteoporosis. The pathogenesis of low bone mineral density (BMD) in IBD is multifactorial and incompletely understood. We previously studied an interception cohort of 109 CD and 72 UC patients treated in our hospital. Morphometric vertebral deformities were found in 25% of these patients (1). The aim of this study was to evaluate the changes in BMD in this real life cohort after a 5-year follow-up period and to look for contributing environmental factors and medication. Materials & Methods: 101 patients (71 CD and 40 UC) who underwent dual- energy X-ray absorptiometry (DXA) of the hip and lateral single energy densitometry of the thoracic and lumbar spine in 2002/ 2003 were re-evaluated in 2008. Disease course with number of flares, calcium and bisphosphonates intake, general risk factors for osteoporosis and use of medication (anti-TNF, immunosuppressives, prednisone and budesonide) were noted. Results: The mean age of the CD patients in 2008 was 49 years and 56 years in UC patients. T-scores of the femoral neck were significantly higher in 2008 compared to 2002 ($p< 0.01$). Osteopenia was present in 37% of CD patients in 2008 and in 56% of patients in 2002. In UC patients osteopenia was present in 23% in 2008 and in 40% of patients in 2002. Multivariate analysis with number of flares, gender, age, smoking, prednisone, budesonide, immunosuppressives, anti-TNF, calcium, bisphosphonates, change in BMI and physical activity score included in the model showed in CD patients a negative association between increase of T-score in this five year period and number of flares ($p=0.02$, 95%CI{-0.318, 0.142}). Low body mass index was the only independent risk factor of having a T score <-1,0 in 2008 in both CD and UC patients ($p= <0,01$ 95% CI{0,658- 0,936}). Surprisingly prednisone and budesonide intake were no independent risk factors of having low BMD or change in BMD during this 5- year follow up study. Conclusion: In this 5 year follow-up study of an interception cohort of IBD patients BMD levels increased significantly probably due to improved disease control. We demonstrated an independent association between increase in T-score and number of flares in CD patients during the follow-up period. Low BMI was the strongest independent risk factor of having osteopenia or osteoporosis.

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6-Thioguan is an effective and tolerable rescue drug in the treatment of ulcerative colitis

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6-Mercaptopurine and its pro-drug azathioprine are of pivotal importance in IBD treatment. Unfortunately, a substantial number of patients with draws these conventional thiopurines due to intolerance or resistance. In Crohn's disease methotrexate seems a proper alternative, while in ulcerative colitis (UC) its use is controversial. Hence, 6-thioguanine (6-TG) may be an appropriate second-line agent in the treatment of UC. The aim of the present study was to determine the efficacy and tolerability of 6-TG in ulcerative colitis patients who were previously intolerant of or resistant to conventional thiopurines. A Dutch multi-centre cohort study of IBD patients using 6-TG was conducted. From a database, all UC patients who initiated 6-TG therapy between 2001 and 2007 were included in the analysis. Clinical efficacy and safety was assessed after a minimum of six months and compared with baseline. Remission was defined as 3 or less bowel movements per day without bloody stools. In addition, reports from colonoscopies were reviewed and scored for inflammation in an ordinal manner. Withdrawal rates and reasons were obtained. Findings from ultrasonography and liver biopsy reports were assessed. Fifty-three UC patients received 6-TG during the study period of whom three were lost to follow-up. Of the 50 patients left 27 were male. The mean daily 6-TG dose was 19.9 mg (SD 2.4) corresponding with a mean 6-thioguanine nucleotide concentration of 959 pmol/8x10*8 red blood cells (SD 203). The median treatment duration was 25 months (1.2-73.8). At baseline 42% of the patients was in remission. After a median follow-up of seven months, 60% of those in remission at baseline stayed in remission. Of those not in remission at baseline 36% went into remission. After a median treatment duration of 13 months an amelioration of endoscopically determined inflammation was reported (P=0.047). Eleven (22%) of the 50 patients eventually withdrew 6-TG therapy due to resistance in seven and adverse events in four. Ultrasonography (n=30) showed hepatosplenomegaly in one patient. Liver biopsies (n=18) revealed no case of nodular regenerative hyperplasia.
Conclusions: In UC patients who were intolerant of or resistant to conventional thiopurines, 6-TG seems an effective rescue drug which may induce mucosal repair. Moreover, 6-TG is tolerated by the majority of these patients and seems safe, as corroborated by ultrasonographies and liver biopsies.

Microsatellite status of colorectal cancer in patients with primary sclerosing cholangitis and concurrent Inflammatory Bowel Disease

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Proximally located (right-sided) colorectal cancer (CRC) is more frequently found in patients with primary sclerosing cholangitis (PSC) and concurrent inflammatory bowel disease (IBD) than in patients with IBD alone. Proximal tumors may develop through different molecular mechanisms compared to more distally located tumors and often display microsatellite instability (MSI), as is found in Lynch syndrome-related tumors.The aim was to compare microsatellite status of PSC-IBD-related CRC to other subtypes of colorectal tumors, such as IBD-CRC, sporadic CRC and Lynch syndrome-related CRC. A tissue micro-array was constructed with colonic samples from 7 groups of patients: (1) healthy subjects, (2) IBD-patients, (3) IBD-related CRC, (4) PSC-IBD-related CRC, (5) Lynch syndrome-related CRC, (6) sporadic left-sided CRC, and (7) sporadic right-sided CRC (7). Each group consisted of 8-20 patients. Immunohistochemistry was performed using monoclonal antibodies for MLH1, MSH2, MSH6, and PMS2. The staining pattern was scored as either positive or negative. Tumor DNA and respective normal tissue DNA were isolated from all samples to examine MSI status using the fluorescence-labelled microsatellite markers BAT25, BAT26, BAT40, D17S250, D5S346, and D2S123. Tumors were classified as MSI-High if more than 2 markers (at least with 1 BAT-marker included) showed instability, as MSI-Low if 1-2 markers showed instability, and as MSI-Stable if none of the markers was instable. Median age of all patients was 55 years (range 12-92 years), with 61% of cases being male. Of all cases in groups 2-4, ulcerative colitis was present in 53% of cases. In groups 3, 4 and 5, 29%, 60%, and 50% of CRCs, respectively, were proximally located, ($p=0.3$). In 55.4% of all tumors, CRC had metastasized to regional lymph nodes or distant sides. MSI-High was found in 0%, 0%, 12%, 0%, 100%, 0% and 35% of patients in groups 1-7, respectively ($p<0.001$). Negative expression of MLH1 and PMS2 was found in 62% of the MSI-High cases, 13% lacked PMS2 expression, and 25% missed MSH2 and MSH6 expression.
Conclusion: Microsatellite instability does not play a role in colorectal carcinogenesis in patients with PSC and IBD, despite the fact that a higher frequency of right-sided tumors is observed in these patients.

The outcome of longterm surveillance of families with dominant clustering of colorectal cancer

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Background: The most common inherited colorectal cancer (CRC) syndrome is the Lynch syndrome (LS) that is responsible for 2-4% of all cases of CRC. About 1-3% of all CRC's is caused by familial CRC type X or non-lynch syndrome (non-LS). The Lynch syndrome is caused by germline mutations in one of the mismatch repair (MMR) genes whereas the underlying gene defect of non-LS is still unknown. Because of evidence of an accelerated colorectal carcinogenesis in inherited CRC, an intensive colonoscopic surveillance program with intervals of 2 years have been recommended. The aims of the study were to evaluate the effectiveness of this program in LS and non-LS families. Patients and Methods: The database of the Dutch Hereditary CRC Registry was used. Lynch syndrome families with a known MMR mutation were selected for the study. Criteria for non-LS families included the presence of at least three relatives with CRC in two successive generations and the absence of microsatellite instability (MSI) in at least one colon tumour. The observation time was from 1-1-1995 until 1-6-2008. Endpoints of the study were CRC, death or the last colonoscopy. Kaplan-Meyer analysis was used to calculate the risk of CRC. Results: A total of 745 mutation carriers from 241 Lynch syndrome families were included. The mean follow up was 7.2 years. Thirty-three patients developed CRC under surveillance (83% Stage I and II). The cumulative risk of developing CRC was 6% at 10 yrs of follow-up. There was no difference between male and female mutation carriers and between carriers of mutations in the various genes. Forty-six families met the criteria for non-LS including 349 relatives. A total of seven CRC's (all Stage I and II) were detected by the program, four at first screening, three during follow-up.
Conclusions: With surveillance intervals of 2 years, the risk of developing CRC in LS families under surveillance is substantially lower than reported for screening intervals of 3 years. Because of the low CRC risk in non-LS families, a less intensive protocol is recommended that is colonoscopy at 3-6 years intervals.

First-degree relatives of hyperplastic polyposis patients have an increased colorectal cancer risk

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Introduction: Hyperplastic polyposis syndrome (HPS) is characterized by the presence of multiple colorectal hyperplastic polyps and is associated with an increased colorectal cancer (CRC) risk. First-degree relatives of HPS patients (FDRs) are also believed to have an increased CRC risk. CRC occurrence has been reported in FDRs of up to 50% of HPS cases. Thus an increased familial CRC risk seems likely but has not been adequately quantified. Reliable evidence concerning the magnitude of this excess risk is necessary to determine whether preventive measures, like screening colonoscopies, in FDRs are justified. Aims and methods: We analyzed the incidence rate of CRC in FDRs and compared this with the general population through person-year analysis with adjustment for demographics (age, sex, and calendar time). Family history concerning CRC and colorectal polyps was retrieved from all HPS patients undergoing endoscopic surveillance in 4 medical centers by examining data from the Depts of Clinical Genetics or by telephone interviews. Population-based incidence data from the Eindhoven Cancer Registry during the period 1970-2006 were used to compare CRC incidence in FDRs with the expected incidence in the general population. Results: In this study a total of 347 FDRs (142 male) from 57 pedigrees were included, contributing 11.053 person-years of follow-up. During the study period, a total of 27 CRC cases occurred among FDRs at a median age of 62 years (interquartile range: 57-78) compared to 5 expected CRC cases ($p<0.001$). The relative risk of CRC in FDRs compared to the general population was 5.4 (95%-CI: 3.7-7.8). No significant difference was seen between the relative risk for male and female FDRs regarding the CRC incidence. In 4 FDRs from 4 different pedigrees multiple histologically confirmed hyperplastic polyps were reported, satisfying the criteria for HPS. Based on the estimated HPS prevalence of 1:3000 in the general population the projected relative risk of HPS in FDRs would be 35 (95%-CI: 4-309). In most FDRs endoscopy was not performed (281/347: 81%) suggesting that the true prevalence of CRC and HPS in FDRs may be underestimated.
Conclusions: Our results showed that FDRs of HPS patients have an increased relative risk for both CRC and HPS. Hence, as long as no genetic substrate has been identified, screening colonoscopies for FDRs seems justified but needs to be prospectively evaluated.

Adenomatous and hyperplastic polyps: co-factors in colorectal carcinogenesis?

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It is generally accepted that the majority of colorectal cancers (CRC) originate from adeno-matous colorectal polyps, via the classic APC-pathway. However, increasing evidence shows that at least some of the hyperplastic polyps may also play a role in the development of CRC, via a serrated pathway. In a long-term, retrospective study, we have shown that patients with large, right-sided hyperplastic polyps have an increased risk for development of CRC. The precise underlying mechanism remains unclear. The aim of this prospective study was to investigate the relationship between serrated polyps (SPs) and synchronous advanced colorectal lesions. To this end, 2341 consecutive patients attending for routine colonoscopy at our endoscopy unit, between February 2008 and February 2009, were included. Clinical, endoscopical records and histopathology of removed polyps were obtained. During colonoscopy, size, location and morphology of the colorectal polyps were registered using a standardized reporting system (including digital photographic docu-mentation). SPs were categorized into i) high-risk SPs, defined as large (≥ 6mm), right-sided hyperplastic polyps / serrated adenomas or ii) low-risk SPs, including the remaining SPs. Advanced colorectal lesions were defined as presence of at least one of the following features: multiple (≥3), large (≥ 10mm), high-grade dysplastic adenomas or CRC. The prevalence of SPs was 13.5% (316) and the prevalence of high-risk SPs was 2.4% (57). Of the high-risk SPs, 44.8% displayed a flat morphology during endoscopy. In total, 323 patients (13.8%) had advanced colorectal lesions. Importantly, patients with high-risk SPs harbored more frequently synchronous advanced colorectal lesions, in comparison to patients with low-risk SPs or without SPs: 40.4% vs. 15.1% vs. 12.9%, respectively. Multiple logistic regression analysis showed that the presence of high-risk SPs was an independent risk factor for presence of synchronous advanced colorectal lesions (odds ratio 4.0, 95% CI 2.3 – 7.0, $p < 0.001$).
Conclusion: 1. Serrated polyps are common lesions in general population.
2. About 40% of the high-risk serrated polyps display a flat morphology, which makes them prone to under-detection. 3. Patients with high-risk serrated polyps are 4-times more likely to harbor syn-chronous advanced colorectal adenomas and/or CRCs. This association suggests parallel progression to CRC, via the classic APC-pathway and the serrated pathway.

Performance of an integrated risk profile for selection of high risk individuals for colorectal cancer

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Screening for colorectal cancer (CRC) can decrease cancer mortality and increase longevity. Population based screening with faecal occult blood (FOB) testing is the only strategy with documented effectiveness on mortality. Only a low number of participants with a positive faecal occult blood test (FOBT) show cancer or adenomatous lesions at colonoscopy. An alternative and probably more effective and efficient strategy could be to offer colonoscopy to people at increased risk of CRC, not just to those testing positive on FOBT. A multiple disease risk profiling program including CRC screening, the PreventionCompass (PC), is offered at the worksite and to collectively insured pensioners. We evaluated the positivity rate and the positive predictive value (PPV) of CRC screening based on a FOBT and risk factors, and compared this in the same population to that of FOB testing only. The aim of this study is to compare the positive predictive value (PPV) of a CRC risk profiling algorithm to that of FOB testing. Between August 2007 and May 2009 CRC risk profiling was offered to participants of the PC between 50 and 75 years of age. Their probability for advanced neoplasia was calculated based on a number of risk factors: first degree relative with CRC at any age, calcium intake, smoking, alcohol, BMI, physical activity, history of IBD, previous colonoscopies, use of aspirin or NSAID and an immunochemical faecal occult blood test (FIT). Individuals with FIT results ≥50 ng/ml or with a probability comparable to that of a 50 year old with a positive FIT were referred for colonoscopy. 1,699 participants completed the CRC risk profiling, of which 166 (10%) were referred for colonoscopy. Complete data were available for 129 referred subjects at time of analysis. 110 (85%) of this subgroup underwent colonoscopy. PPV for advanced neoplasia was 31% (n=34; PPV for CRC 5%, advanced adenoma 25%). The PPV for advanced neoplasia in FIT positive participants with none or low levels of risk factors (18%) was significantly lower (p=0.008), compared to FIT positive participants with high levels of risk factors (47%). The odds ratio for finding advanced neoplasia at colonoscopy in participants with of none or low levels of risks factors compared to high levels of risk factors was 0.242 (p= 0.011).
In conclusion, including an CRC risk profile in addition to FIT significantly increased PPV in a screening program.

Is the performance of a faecal occult blood test really different in a referred population compared with a screening population?

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The main advantage of studying the performance of immunochemical faecal occult blood tests (FIT) in patients referred for colonoscopy compared to average-risk subjects in population-based screening is, that colonoscopy reports are available for all patients. How-ever overestimation of the FIT performance might occur, due to differences in population characteristics and colorectal cancer (CRC) stage distribution. We propose that the differences in FIT results are mainly due to differences in tumour stage. Therefore we compared the differences in performance of the quantitative FIT, OC-Sensor®, in a referral population with a screening population according to tissue tumour stage (T-stage of the TNM classification). Between June 2006 and February 2007 a population-based screening study was performed in the Netherlands. Half the population was randomly assigned to perform a FIT, which was also used in a prospective study started in the same year in patients referred for elective colonoscopy. CRC patients were classified according to most advanced T-stage. In the screening group patients with a FIT value ≥50ng/ml were referred for colonoscopy. In the referral group every patient underwent colonoscopy, but patients with a value <50ng/ml were excluded for comparison. Differences in log (FIT values) per T-stage between screening and referral patients were calculated with the t-test. P-values were adjusted for gender and age with logistic regression analysis. In total 94 CRC patients were included: 28 in the screening group (64% male and mean age 63, SD 6.4) and 66 in the referral group (45% male, mean age 67, SD 9.2). In the screening group of the 28 CRC patients (average log(FIT value)), 13 were T1 (5.9), 8 T2 (6.7), 6 T3 (6.3) and 1 T4 (7.4) and in the referral group of the 66 CRC patients, 6 were T1 (5.8), 17 T2 (6.4), 36 T3 (6.6), 2 T4 (6.9) and for 5 unknown.The differences in log(FIT values) between screening and referral groups for T1 were 0.12 (p=0.83), for T2 0.31 (p=0.33) and for T3 and T4 -0.18 (p=0.50).
In conclusion, the results of this study confirm that differences in performance of the quantitative FIT, OC-Sensor, between a screening and referral population were mainly due to differences in tumour stage distribution.

Extended endoscopic mucosal resection is a safe and effective alternative for transanal endoscopic microsurgery concerning the treatment of large rectal adenomas

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Extended endoscopic mucosal resection (EMR) for large rectal adenomas has shown to be a safe and effective alternative for transanal endoscopic microsurgery (TEM). Extended EMR may be associated with lower morbidity and lower costs. However, prospective data of EMR for large rectal adenomas are limited. The aim of this prospective study was to evaluate the safety and effectiveness of EMR for large rectal adenomas. Consecutive patients with large (>2cm) non-pedunculated rectal adenomas undergoing EMR in a single academic centre were analyzed. Patients with endoscopic suspicion of invasive cancer were excluded. For EMR, submucosal injection was performed, followed by piecemeal snare polypectomy. Argon plasma coagulation (APC) was applied to the edges of the mucosal defect after EMR. Endoscopic findings, histopathology and complications were registered. Follow-up endoscopy was performed after 3, 6 and 12 and 24 months. From Jul 2006-Sep 2008, 23 patients (14 male; mean age 68 yrs) with rectal adenomas were treated by EMR. Mean adenoma size was 4.7 cm (range 2-10) with a mean distance of 4.7 cm (0-15) ab ano. Of all lesions, 18 (78%) were laterally spreading tumors (17 nodular; 1 flat) and 5 were sessile. The mean procedural time was 66 minutes (26-135). Hemorrhage occurred in five patients (22%), two of which using anticoagulants, after a mean of 5.4 days (0.8-11) post-EMR. Interventions consisted of transfusion (n=1), endoscopic clipping (n=1) and adrenaline injection (n=1). No perforations occurred. Three EMR procedures (13%) failed due to non-lifting on submucosal injection; these patients were excluded from further analysis. Resection specimen histology revealed intramucosal cancer in 3 patients (15%), high grade dysplasia in 11 (55%); no invasive cancers were found. Mean follow-up was 12.6 months (3-31). At the first follow-up endoscopy, residual adenomatous tissue was found in 6 patients (30%), for which APC was applied. Hereafter, only one recurrence occurred.
Conclusion: So far, the overall success rate of extended EMR for large rectal adenomas is 95%, necessitating APC for residual disease in 6 patients (30%). Bleeding occurred in 22% of patients. These results are in concordance with previous series, demonstrating that EMR is a safe and effective alternative for TEM. A prospective comparison of extended EMR versus TEM seems imperative to asses which treatment is more cost-effective.

Clinical trial: Low-volume PEG-solution plus ascorbic acid versus high-volume PEG-solution as bowel preparation for colonoscopy

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Introduction: Thorough cleansing of the colon is essential for good judgment of colon mucosa during colonoscopy. Generally, high volumes of Polyethylene glycol (PEG)-based solutions are administered, which are highly effective for bowel cleansing, but often poorly tolerated. Aim: To compare a relatively new 2 liter PEG-based solution combined with ascorbic acid (PEG + Asc) with a standard 4 liter PEG-based solution (PEG). Methods: In a single center, single blind, randomized, prospective study, 350 patients undergoing colonoscopy received 2 liters of PEG + Asc or 4 liters of PEG. For colonoscopies scheduled in the morning, the total dose of PEG + Asc was taken the evening before the procedure, for afternoon colonoscopies; the dose was given as a split dose. The 4 L PEG preparation was given as a split dose. Efficacy of preparation was scored on a 5-point scale in three different colon segments. An overall grading was derived from the individual segment scores. Patients' experiences were evaluated using a questionnaire. Results: From 307 patients (149 PEG + Asc, 158 PEG), results were available. Successful colon cleansing was achieved in 90.6 % in the PEG + Asc group compared to 96 % in the PEG group (not significant). In patients prepared with PEG + Asc, the bowel cleansing was worse when patients underwent colonoscopy in the morning, compared to afternoon procedures. Side-effects and patients' experiences were similar in the PEG + Asc and PEG group.
Conclusions: Low-volume PEG + ascorbic acid is as effective and well tolerated as high-volume PEG. The cleansing results were worse if patients received the full dose the evening before the procedure compared to the split dose. Our data support the administration of PEG + Asc as a split dose before the procedure.

Is coeliac disease overrepresentated in patients with constipation? *

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Background and aim: As coeliac disease (CD) is sometimes seen in patients with constipation it has been suggested that serological screening might be warranted in this patient group, especially when the usual treatment of constipation fails. However it is not known whether CD is indeed overrepresented in patients with constipation, which is a frequent condition, affecting 5-10% of the general population. Aim of the study was therefore to find the incidence of coeliac disease in children with constipation who were referred to the paediatrician by a primary care physician. At the same time patients were screened for hypothyroidism and hypercalcemia, as experts have suggested that these conditions too might have a causative relation with constipation. Methods: Between October 2006 and October 2008 prospectively 370 consecutive patients with constipation (clinically scored with the Rome III criteria, age between 1 and 18 years of age, gluten ingestion of at least 3 months) were included and screened for total serum IgA, IgA-human tissue transglutaminase (Celikey tTG Elisa kit, Pharmacia and Upjohn Diagnostics, Freiburg, Germany), serum calcium, fT4 (free thyroxine) and TSH (thyroid stimulating hormone). All patients with an abnormal IgA-tTG, or a low serum IgA, underwent a small intestinal biopsy. Results: Seven of the 370 patients with constipation had biopsy proven coeliac disease. This is significantly higher ($P<0.001$) than the 1:198 incidence of CD in The Netherlands, as recently determined in a survey of 6127 school children. An additional 2 patients had Hashimoto disease. There were no patients with hypercalcemia. Conclusion: Coeliac disease is significantly overrepresented in patients with constipation. All patients with constipation referred from a primary care physician to a paediatrician who fulfil the Rome III criteria should therefore be screened for coeliac disease.

The significance of intraepithelial lymphocytosis without villous atrophy for diagnosing celiac disease

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Histopathological abnormalities in celiac disease (CD) are classified according to the modified Marsh classification. Although higher Marsh classification is considered diagnostic for celiac disease, the clinical significance of Marsh I is largely unknown. Furthermore, absence of HLA-DQ2 and/or -DQ8 genotype virtually excludes celiac disease, although the presence of this genotype does not prove the diagnosis considering the high prevalence of this genotype in the general population. Objectives of this study were to evaluate the prevalence of the HLA-DQ2 and/or -DQ8 genotype in patients with Marsh I and to determine whether the risk of developing CD in patients with Marsh I is increased compared to the general population.The Dutch national pathology database (PALGA) was searched for patients from the study hospital from whom small intestinal biopsy specimens were taken showing Marsh I between January 2001 and February 2009. After giving informed consent patients were included. Blood was drawn for HLA-DQ2 and HLA-DQ8 genotyping, measuring of total IgA, IgA anti-endomysium antibodies, IgA anti-tissue transglutaminase antibodies and IgG Helicobacter pylori (H.pylori) antibodies. Data considering the general Dutch population were retrieved from national and regional blood banks.Fiftytwo persons were included with 143 follow-up years in total. The prevalence of the HLA-DQ2 genotype in this population was 38,5% and the prevalence of HLA-DQ8 genotype was 23,1%.This was not statistically different compared to the general Dutch population.
In conclusion, the prevalence of the HLA-DQ2 and/or DQ8 genotype does not significantly differ between compared populations. This suggests that a gluten free diet should no longer be prescribed to patients with Marsh I.

Effectiveness of cladribine treatment in refractory coeliac disease type II

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Background: Approximately 2-5% of adult-onset coeliac disease patients fails to respond to a gluten free diet and develops refractory coeliac disease (RCD). In contrast to RCDI, RCDII seems to be unresponsive to common immunosuppressive treatment. Transition into Enteropathy Associated T cell Lymphoma (EATL) occurs in 50-60% of these patients, which has a very poor prognosis. Therefore, it is of utmost importance to evaluate new treatment strategies for RCD II. Our previous report showed that cladribine (2-CDA) was well tolerated. This study reports on the effectiveness of 2-CDA therapy in more RCD II patients with extended follow up. Design and methods: A cohort study of patients who were prescribed 2-CDA, in a dose of 0,1mg/kg/day intravenously for 5 days, was performed between 2000 and 2009. Non-responders were intentionally treated with high dose of chemotherapy followed by autologous hematopoietic stem cell transplantation (aSCT) after 6 months. EATL development, survival rate, clinical course, Marsh classification and percentage of aberrant IEL were evaluated during follow-up. Results: Overall, 29 patients were included. Sixteen patients responded well to one or two course of 2-CDA. Out of the 13 non-responders, nine were actually transplanted. In two patients harvesting stem cells failed, two had an EATL and one died due to sepsis before first leukapheresis attempt. The median overall follow up time was almost 3 years (4-102 months). 2-CDA was well tolerated without serious adverse events. In total, EATL occurred in 17% (5/29) of the patients, all of which died within one year after diagnosis. Overall, 41% (12/29) died. The 2-, 3-, 4-year survival based on this treatment strategy was 83%, 75% and 57%, respectively. Clinical improvement was shown in 82% (23/29), complete histological remission (Marsh 0/I) in 69% (20/29) and a significant decrease in aberrant T cells in 31% of the patients during follow up. 69% of the patients achieved both a clinical and histological remission mainly in the first year of follow up. Conclusion: Treatment of RCD II patients with cladribine therapy and aSCT if unresponsive holds promise, showing a good clinical and histological remission of approximately 70%. aSCT seems to improve the overall survival rate. Although EATL could not be prevented in all cases, its incidence could be restricted to 17%.

Refractory Coeliac Disease type 2: does autologous stemcel transplantation improve clinical course?

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Background: Autologous hematopoietic stem cell transplantation (aSCT) is an increasingly accepted treatment for different refractory autoimmune diseases. Although it seems to be feasible and safe for refractory coeliac disease (RCD) type II based on short-term follow up, it has not yet been evaluated properly. RCD is seen in 2-5% of the adult-onset coeliac disease patients that fails to respond to a gluten free diet. In contrast to RCD type I, type II is characterised by immunophenotypically aberrant intraepithelial T cells which might be causative in 60-80% for transition into Enteropathy Associated T cell Lymphoma (EATL) having a very poor prognosis. For RCD II no standardised treatment approach is available yet. Methods: Between March 2004 and January 2009, 14 RCD II patients unresponsive to cladribine treatment were evaluated for aSCT preceded by conditioning with fludarabine and melphalan. Patients were monitored for survival rate, EATL development, and change in clinical and histological course during follow-up. Results: Nine patients underwent transplantation successfully, having a median follow up time of almost 3,5 years. In 5 patients aSCT could not be performed, two due to unsuccessful leukapheresis, two were diagnosed with EATL and one died due to sepsis. A statistically significance (p=0.001) survival advantage in the transplanted group compared to the non-transplanted group is found. All patients of the non-transplanted group died compared to three in the actually transplanted group. The median overall survival rate of the non-transplanted group is 4 months compared to almost 3,5 years in the transplanted group. EATL is shown in four patients of the non-transplanted and one of the transplanted group. Moreover, in the latter group EATL only occurred at 4 years after aSCT. Clinical remission was observed in the majority, complete histological remission (Marsh 0/I) in five and immunological remission in one of the transplanted patients during follow-up. Furthermore, long-term secondary malignancies and myelodysplastic disorders were not observed.
Conclusion: aSCT after conditioning with fludarabine and melphalan of patients with RCD II seems to be very promising, showing a tremendous survival improvement, less EATL development opposed to non-transplanted patients and in more than half of the cases improvement in clinical and histological course.

Universal duodenal microbiota with IS-pro in individuals undergoing routine gastroscopy

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Introduction: The intestinal microbiota received a lot of attention due to its putative role in the pathogenesis of several diseases including inflammatory bowel diseases and obesity. As yet, most research has focused on microbiota residing in colonic mucosal biopsy specimens and faecal samples, which has been shown to be host-specific. Much less is known about the bacterial composition in duodenal mucosal biopsy specimens. Since most intestinal bacteria are uncultivable, we developed IS-pro; a rapid, highly reproducible method for high-throughput bacterial profiling. Aim: To characterise the in-testinal microbiota adherent to duo-denal mucosal biopsy specimens in individuals undergoing routine gastroscopy. Methods Duodenal biopsy specimens were harvested from 21 consecutive individuals undergoing routine gastroscopy. In addition, four accompanying colonic mucosal biopsy specimens and 11 colonic mucosal biopsy
specimens from other individuals were harvested during routine colonoscopy. Samples were analysed with IS-pro, which is based on two features of the bacterial genome: species-specific length of the inter spacer (IS) region between the 16S and 23S rDNA and phylum-specific labelled primer sequences. With these specific labelled primers, species can be directly sorted into either Firmicutes/Actinobacteria or Bacteroidetes phylum. By colour and size sorting of amplified fragments specific bacterial profiles are created. Intra- and inter-individual variation of bacterial profiles was assessed with Pearson's correlation. Results: Duodenal and colonic specimens clustered in two distinct clusters. Colonic specimens were unique per individual with low homology between individuals (6- 59%). In contrast, duodenal specimens showed very high similarity up to 100% identity. Lowest similarity between duodenal specimens (64%) was higher than highest similarity in colonic cluster (59%). Matched duodenal and colonic microbiota were distinct with clustering based upon region of sampling instead of clustering per individual.
Conclusion Microbiota adherent to duodenal mucosa and to colonic mucosa were distinct. Where as colonic microbiota was found to be host-specific, duodenal microbiota was extremely homogenous, with inter individual profiles being almost identical. Findings of the present study provide a solid basis for the analysis of potential disease-specific differences in microbiota adherent to duodenal mucosa.

Bovine antibody-based oral immunotherapy for reduction of intragastric *Helicobacter pylori* colonization: A randomized placebo-controlled clinical trial

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For treatment of H. pylori (Hp) infections antibiotic-based regimens are mostly used. How-ever, antibiotic-based eradication fails in 15-40% of patients, due to antimicrobial resistance and poor patient compliance. Effective prevention and eradication of Hp by passive immunisation with orally administered bovine antibodies has been demonstrated in animal studies and may serve as an alternative therapy in humans. The aim of this study was to study efficacy and safety of orally administered antibodies for reduction of intragastric bacterial load and eradication of Hp in humans.Polyclonal antibodies (sIgA) were raised in milk of dairy cows by nasal and supra-mammary lymph node immunisations with a mix of clinical Hp isolates during lactation. The milk was processed into a whey protein concentrate (WPC). A prospective, double-blind, placebo-controlled randomized clinical trial was de-signed. Hp-infected subjects were randomized into a WPC-treated or placebo-treated group. Study medication was continued for 28 days; subjects were followed up for 56 days. Efficacy of treatment was evaluated as reduction in intragastric Hp colonization density, determined by urea breath test (UBT) and histology. A blinded pathologist assessed biopsies according to the updated Sydney classification system. Safety was evaluated with blood tests and quality of life questionnaires. All outcome measures were evaluated on day 0 and day 29; on day 56 UBT, blood tests and quality of life questionnaires were repeated. In total, 30 sub-jects were included; 27 completed the protocol, and the remainder either discontinued study medication within 2 weeks or was lost to follow-up. Within 27 evaluable subjects, there was no significant difference in UBT decrease between the WPC- and the placebo-group (mean decrease ± SEM 0.9 ± 4.3 vs. 3.0 ± 5.0, p=0.75). Hp density and polymorphonuclear neutrophil activity in antrum and corpus were not significantly reduced after treatment in both groups (all p>0.05). In one subject, Hp eradication was achieved after concomitant use of the WPC-product and a 1 day metronidazole course. No serious adverse effects occurred after treatment with the WPC-product. Bovine antibody-based oral immunotherapy appears safe, but does not significantly reduce intragastric Hp density in humans.
However, further studies are needed to determine whether WPC treatment has additional value to con-ventional antibiotic treatment for Hp.

Prevalence of premalignant changes in the stomach of patients undergoing routine colonoscopy; a cross-sectional cohort study

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Gastric cancer represents the fourth most common cancer and second leading cause of cancer-related mortality worldwide. The intestinal type of gastric cancer (GCA) is preceded by a cascade of premalignant gastric lesions; from Helicobacter pylori (Hp) positive gastritis through atrophic gastritis (AG), to intestinal metaplasia (IM), dysplasia (DYS) and GCA. The prevalence of these lesions is however unclear since most subjects with Hp infection and premalignant gastric lesions are asymptomatic.The aim of this study was to investigate the age-related prevalence of Hp infection and its related macroscopic and pathologic gastric changes in asymptomatic subjects without an indication for upper gastro-intestinal endoscopy. Patients undergoing routine colonoscopy were included in this study. All patients underwent upper GI endoscopy prior to colonoscopy and filled out the Gastrointestinal Symptom Rating Scale (GSRS). Biopsies taken from the antrum (n=2) and corpus (n=2) were reviewed by an experienced GI pathologist and scored for the presence of Hp, IM and AG and Dysplasia. 383 patients (F/M 192/191; mean age 53.1 yr; range 17-86 yrs) were included. Hp infection was demonstrated in 22% of patients, the percentage of Hp infection ranged from 10% in subjects under 40 to 27,7% in the oldest age-groups. Non-Caucasian subjects had a significantly higher rate of Hp infection 54.1% vs. 22% in Caucasians (p >0.01). AG and IM and DYS were found in respectively 8.9% of patients; 0.2% had AG, 7,2% IM and 1.4% had DYS. Subjects with Hp infection or premalignant gastric lesions were significantly older than subjects with normal gastric mucosa (p values <0.05). The more severe the gastric lesion found the more significant the age association. No association was demonstrated between gender, GI symptoms, as scored by GSRS, life-style and medication use between subjects with or without premalignant gastric lesions or Hp infection.
In conclusion although the incidence of GCA is declining, the prevalence of Hp and premalignant lesions is considerable even in asymptomatic patients. This emphasizes the need for a selective screening strategy.

Esophaguscarcinoma: Staging with EUS-FNA and PET-CT and survival with or without neo-adjuvant chemoradiation followed by surgery in a medium volume centre

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In the last decades there has been a marked increase in the incidence of esophageal cancer. Unfortunately, the survival of this disease remains poor with a 5-year survival of 20% even after curative resection. This has initiated new neo-adjuvant treatment strategies with chemoradiation (CRT), especially in high risk patients with locally advanced carcinoma. This implies adequate staging before starting therapy. We evaluated retrospectively all patients with esophageal cancer who were treated with curative intention, either with or without CRT followed by surgery. The accuracy of staging with EUS-FNA and PET-CT was evaluated with pathological staging of resected specimens as the gold standard. Furthermore, the survival with or without CRT followed by surgery was evaluated, CRT consisting of 6 cycles carboplatin and taxol and 28 fractions of radiotherapy (50,4 Gy). All patients (n=49) who were operated in our hospital because of esophageal cancer between January 2005 and December 2008 were included. Twenty one patients with locally advanced disease were treated with CRT and therefore excluded for the evaluation of staging. Accuracy of EUS-FNA overall was 77%, for T-stadium 82% and for N-stadium 90%. PET-CT did not add to the staging. In two of the 21 patients treated with CRT, the scheme was not completed due to adverse events. Seven of 21 patients had complete response, nine patients had partial response and five did not respond. At surgery, four patients were irresectable. In 8 patients resection was not complete. Postoperative complications consisted of anastomotic leakage (16%), spleen injury (9%) and pulmonary problems (24%). One patient (2%) died of sepsis due to leakage. Long term complications consisted of recurrence nerve injury (16%) and anastomotic stenosis (22%). Median follow up after diagnosis was 15 months (6-44) and for the CRT group 12 months. Relapse occurred in 60% of patients (median 13 months). In patients treated with CRT the relapse rate was 30% (two of these patients had complete response after CRT).
Conclusion: Staging with EUS seems superior to all other diagnostic tools. Our data concerning the staging are consistent with other results. CRT is well tolerated and might be able to reduce early relapse with a disease free survival of 70% after one year.

Prevalence of gastrointestinal symptoms in the community: results of a survey among 50,000 persons

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Several factors associated with gastrointestinal symptoms have changed within the community, which might have influenced symptom prevalence. The aim of this study is to investigate the actual prevalence of gastrointestinal symptoms in the general population.A total of 50.000 surveys were sent to a national representative part of adult Dutch inhabitants in December 2008. Questionnaires returned until April 1st, 2009 were included. Questions about demographics, gastrointestinal symptoms, medication use and co-morbidity were stated. Exclusion criteria were malignancy, inflammatory bowel disease, celiac disease and pregnancy. The prevalence of gastrointestinal symptoms was calculated and multivariate logistic regression analysis was performed to present adjusted odds ratios (OR) with 95% confidence intervals (CI) for factors associated with symptom presence. A total of 18,116 (response rate 36%) surveys were returned of which 775 were excluded leaving 17,341 surveys for analyses. The prevalence of gastrointestinal symptoms was 25.1% with a mean symptom duration of 11.9 years (SD 11.8). Most reported symptoms were bloating (39.7%), belching (26.3%) and flatulence (43.6%). Persons above 65 years of age (OR 0.77, 95%CI 0.69-0.85), male gender (OR 0.58, 95%CI 0.53-0.65) and coffee users (OR 0.84, 95%CI 0.72-0.98) reported less often gastrointestinal symptoms. Current smokers (OR 1.17, 95%CI 1.04-1.32) reported more often gastrointestinal symptoms, as did users of acid suppressive medication with corresponding odds ratios for proton pump inhibitor: 9.29 (95%CI 7.95-10.85); H&sub2;-receptor antagonist: 9.07 (95%CI 6.12-13.4); and antacid: 4.04 (95%CI 3.40-4.81).
Currently, the prevalence of gastrointestinal symptoms is 25.1 percent. Persons above 65 years of age, male gender and coffee users reported less often gastrointestinal symptoms, whereas current smokers and users of acid suppressive medication reported more often symptoms.

Gastrointestinal symptoms in non-steroidal anti-inflammatory drug (NSAID) users; a comparison between on prescription and over-the-counter (OTC) use

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Non-steroidal anti-inflammatory drugs (NSAIDs) belong to the most often prescribed drugs world-wide, and its use will only further increase due to aging populations and expanding over-the-counter (OTC) use. NSAID use can be complicated by gastrointestinal side effects. In several studies the gastrointestinal toxicity of NSAIDs was evaluated, however we are the first to describe the actual population prevalence of gastrointestinal symptoms in 'on prescription' and OTC users. A total of 50.000 surveys were sent to a national representative part of adult Dutch inhabitants in December 2008. Questionnaires returned until March 1st, 2009 were included. Questions about demographics, gastrointestinal symptoms, medication use and co-morbidity were stated. Exclusion criteria were malignancy, inflammatory bowel disease, celiac disease and pregnancy. Prevalence of gastrointestinal symptoms in persons using NSAIDs on prescription and OTC were analysed in a first random sample of 10,907 returned questionnaires. After exclusion, a total of 9,978 questionnaires remained, of which 3164 (32%) persons used NSAIDs. NSAID use was not specified by 72%, and 386 (12%) used on prescription and 517 (16%) used OTC medication. On prescription NSAID users experienced more gastrointestinal symptoms (37%) compared to OTC users (33%). This difference was not statistically significant (odds ratio 1.19, 95%CI 0.91-1.58), also after correction for possible confounding variables (odds ratio 1.14, 95%CI 0.77- 1,69). Of all persons at high risk for gastrointestinal complications (age ≥65 yrs or history of (complicated) peptic ulcer disease), only 51% of on prescription users and 17% of OTC users, concomitantly used adequate PPI gastroprotection. In conclusion, gastrointestinal symptoms are prevalent in one third of persons taking NSAIDs. Persons that used NSAIDs on prescription reported higher prevalence of gastrointestinal symptoms compared with OTC users. Adequate gastroprotection was often absent.

Gastrointestinal complaints in low-dose aspirin users in the community: a comparison between plain and buffered aspirin.

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Effervescent calcium carbasalate (Ascal®) is a buffered calcium-salt of acetylsalicylic acid (aspirin) causing less endoscopically visible local gastric damage than plain aspirin at high doses in healthy controls. Although prescribed to many cardiovascular patients, the benefit of low-dose buffered aspirin on gastrointestinal complaints remains unknown. The aim of this study was to investigate the prevalence of gastrointestinal symptoms in a population based cohort using low-dose plain or buffered aspirin.A total of 50.000 surveys were sent to a national representative part of adult Dutch inhabitants in December 2008. Questionnaires returned until April 1st, 2009 were included. Questions about demographics, gastrointestinal symptoms, medication use and co-morbidity were stated. Exclusion criteria were malignancy, inflammatory bowel disease, celiac disease and pregnancy. The prevalence of gastrointestinal symptoms in persons using acetylsalicylic acid (plain aspirin) or effervescent calcium carbasalate (buffered aspirin) were compared. Multivariate logistic regression analysis was performed.An amount of 18,116 (response rate 36%) surveys were returned of which 775 were excluded leaving 17,341 surveys for analyses. Of these, 908 persons (5.2%) used plain aspirin and 604 persons (3.5%) buffered aspirin. The prevalence of gastrointestinal symptoms is 26.0% and 25.8% in plain and buffered aspirin users respectively, with no significant difference between both variants (odds ratio 0.99; 95% CI 0.78-1.25; p=0.92). After correction for possible confounding variables this lack of difference remained (odds ratio 0.89; 95% CI 0.64-1.24;p=0.48).
In conclusion, the prevalence of dyspeptic complaints among low-dose aspirin users in the Dutch population is 26%. In this study, no significant benefit of buffered aspirin compared to plain aspirin was observed regarding gastrointestinal symptoms.

Health-related quality of life change in patients with new onset dyspepsia treated with stepwise acid suppression strategies

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Dyspepsia is a common problem affecting about 20-40% of the general Western population. Treatment that quickly increases health-related quality of life (HRQoL) besides symptom improvement is beneficial for both the individual and society. We aim to describe the impact of stepwise acid suppressive treatment on HRQoL in patients with new onset dyspepsia and identify predictors for HRQoL change over time.We conducted a multi-centre double-blinded trial that randomly assigned stepwise acid suppressive therapy with antacids, H&sub2;-receptor antagonists, and proton pump inhibitors (step-up) or these drugs in reverse order (step-down) to primary care patients with new onset dyspepsia. Each treatment step was 4 weeks. Treatment continued with the next step if symptoms persisted or relapsed within the next four weeks. Symptom relief and HRQoL (EuroQol-5D) were assessed at baseline, at 2 weeks, after each treatment step and at 6 months using questionnaires. Uni- and multivariate linear regression models were used to analyze treatment effect on HRQoL. A total of 664 patients (mean age 47 (SD: 15), 46% males) were randomly assigned to step-up (n=341) and step-down (n=323) treatment. In the step-up group 139 (41%) of the patients received only step1, 84 (25%) step 1 and 2, and 118 (35%) all 3 steps. For step-down the numbers were respectively 153 (47%), 57 (18%), and 113 (35%). Nineteen patients withdrew from the study (step-up n=9, step-down n=10). Treatment success was reported in 71% (n=645) of the patients after 6 months. Overall, 66% (n=316) of the patients reported HRQoL improvement after the follow-up period of 6 months. After 2 weeks, HRQoL was overall increased from EQ-VAS 54.3 to 67.6 ($p<0.0001$), and gradually increased further to 74.8 at 6 months ($p<0.0001$). HRQoL only differed between the treatment groups after step 1 (starting with antacids: 67.3, starting with proton pump inhibitors: 71.7, $p=0.02$). We found an inverse correlation between HRQoL and symptom severity score at 6 months (Pearson's correlation: $r=-0.61$, $p<0.0001$).
In conclusion, dyspepsia treatment improved HRQoL, but no differences were found between the step-up or step-down strategy after 6 months. Increase in HRQoL over time correlated strongly with symptom relief.

The MDM2 promoter SNP285C/SNP309G haplotype is associated with susceptibility for oesophageal squamous cell carcinoma and related to poor overall survival after surgical resection

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Introduction: A functional polymorphism within the MDM2 gene, SNP309T>G, has been linked to cancer susceptibility. In this study the association was investigated between three polymorphisms, SNP285G>C (novel), SNP309T>G (rs2279744) and SNP344T>A (rs1196333) in the promoter region (intron 1) of the MDM2 gene and susceptibility for oesophageal squamous cell carcinoma (OSCC) and overall survival after surgical resection. Methods: The three polymorphisms were genotyped by direct sequencing in a Caucasian cohort of 307 OSCC patients, who underwent surgical resection between 1988 and 2006 and in a Caucasian control cohort of 216 healthy blood donors. Associations between genotypes and overall survival were assessed using the Kaplan-Meier method. Cox proportional hazard models, adjusted for age, neoadjuvant treatment, radical resection (R0) and nodal status were developed. Results: No significant difference in allelic distribution was found for the SNP309 between OSCC patients and controls (P = .42). SNP285 was observed only in the heterozygous state and was found in complete linkage disequilibrium with the SNP309 variant G-allele. The SNP285C/SNP309G haplotype accounted for 14% and 8% of the SNP309G alleles among OSCC patients and controls, respectively (P=.078). The allelic distribution of the SNP344 T-variant allele (only present in the heterozygous state) was 1.4% in the OSCC cohort and differed from the control cohort 4.8% (P=.002). The median survival for all 307 OSCC patients was 18 months; the median follow-up time for surviving patients was 62 months. The SNP309 genotypes did not correlate with overall survival (log-rank P=.63; adjusted hazard ratio for death 0.96 95%CI:0.78-1.2). Patients harbouring the SNP285C/SNP309G haplotype had a poorer overall survival than patients with the SNP285G/SNP309G haplotype (log-rank P=.084; adjusted hazard ratio for death 1.6 95%CI:1.0-2.6).
Conclusions: In a Caucasian population, the MDM2 SNP309 is not associated with susceptibility for OSCC and not with overall survival after surgical resection. The MDM2 SNP285 and SNP344 do both correlate with susceptibility for OSCC. The prognosis of patients with the SNP285C/SNP309G haplotype is poorer compared to patients with the SNP285G/SNP309G haplotype.

Plattegrond

Alfabetische lijst van standhouders B = Beneluxhal K = Kempenhal	*Standnummer*
Abbott BV	K 3
Acertys BV	B 17
Alvleesklliervereniging	B 27
AstraZeneca BV	K 11
Boston Scientific Nederland BV	K 10
Bristol Myers Squibb	B 21
Brunschwig Chemie BV/Lans Medical	B 18
Cablon Medical BV	B 19
Campro Scientific GMBH	K 18
Cobra medical BV	B 13
Cook Medical	K 13
Crohn en Colitis Ulcerosa Vereniging Nederland	B 25
Datascope Patient monitoring (Mindray M.)	B 16
Endomed BV	B 9
Endotechniek	B 2
Erbe Benelux BV	K 19
Fa. Vygon Nederland BV	B 20
Ferring BV	B 1
FMH Endoscopy BV	K 5
Fresenius Kabi Nederland BV	K 12
Getinge BV	B 14
Gilead Sciences Netherlands BV	B 15
Hitachi Medical Systems	K 8
Jansen Medicars BV	B 5
Janssen-Cilag BV	B 6
KP Benelux BV	B 10a
Medical Measurements Systems BV	K 20
Medicor	K 4
Minntech BV	B 12
Nationaal Hepatitis Centrum	B 24
Nederlandse Coeliakie Vereniging	B 28
Norgine BV	B 3
Olympus Nederland BV	B 23
PENTAX Nederland BV	K 7
Pfizer BV	K 16
Rescope BV	B 10
Roche Nederland BV	B 7
RVC BV	B 4
Schering Plough BV	K 9
Shire Benelux	K 15
Solvay Pharma BV	B 22
Stichting Opsporing Erfelijke Tumoren	B 26
Stichting Vreemde Kronkels	B 29
Stöpler Instrumenten en Apparaten BV	K 14
TMI	B 11
Tramedico BV	K 1
Vifor Pharma Nederland BV	K 17
Wassenburg Medical BV	K 6
Zambon Nederland BV	B 8

Nederlandse Vereniging voor Gastroenterologie

Aanmeldingsformulier lidmaatschap *(doorhalen wat niet van toepassing is)*

naam en voorletters		m / v
voornaam		geb. datum:
titel		
specialisme / functie		
doctoraal examen	neen / ja d.d.	zo ja, studierichting:
arts examen	n.v.t. / ja d.d.	
assistent i.o. voor		einde opleiding:
inschrijving MSRC	neen / ja d.d.	BIG registratie nr.
huisadres		
postcode en plaats		
telefoonnummer		
werkinstelling		
afdeling		
adres		
postcode en plaats		
telefoonnummer		
e-mail adres		
Toezending verenigingspost aan huis- / werkadres		

Tevens wil ondergetekende zich aansluiten bij:

□ Sectie Gastrointestinale Endoscopie*
□ Netherlands Society of Parenteral and Enteral Nutrition*
□ Sectie Neurogastroenterologie en Motiliteit*
□ Sectie Experimentele Gastroenterologie*
□ Sectie Kindergastroenterologie*
□ Nederlandse Vereniging voor Gastrointestinale Chirurgie *(combinatielidmaatschap)*
contributiebedragen: graag aankruisen wat voor u van toepassing is
□ Specialisten € 90,00 (totaal € 125,00 incl. lidmaatschap NVGE € 35,00)
□ Assistenten i.o. € 25,00 (totaal € 60,00 incl. lidmaatschap NVGE € 35,00)

*Aanvullende lidmaatschappen van met * aangegeven secties zijn kosteloos*

□ Hierbij machtig ik de penningmeester van de Nederlandse Vereniging voor Gastroenterologie om de verschuldigde contributie tot wederopzegging automatisch van mijn bank-/girorekening af te laten schrijven. Betaling geschiedt nadat u door de eerstvolgende ledenvergadering als lid bent aangenomen. Indien u geen machtiging tot incasso geeft ontvangt u automatisch een factuur. Voor verzending van facturen worden vanaf volgend jaar administratiekosten in rekening gebracht.

Bank- / girorekening:

Datum en handtekening:

_____

Dit ondertekende formulier per post of fax (023 – 5513087) sturen naar: Secretariaat NVGE, Postbus 657, 2003 RR Haarlem

Aanvullende informatie: De contributie van de Nederlandse Vereniging voor Gastroenterologie bedraagt € 35,00 per jaar. Na toetreding als lid ontvangt u een factuur (conform de regels is volledige contributie verschuldigd in het jaar van toetreding). Het lidmaatschap loopt per kalenderjaar. Opzeggen dient daarom vóór 1 december te gebeuren.

NEDERLANDSE VERENIGING VOOR HEPATOLOGIE

Aanmeldingsformulier lidmaatschap

Nederlandse Vereniging voor Hepatologie

** Doorhalen wat niet van toepassing is.*

naam en voorletters		m / v
voornaam		geb. datum:
titel		
specialisme / functie		
doctoraal examen	neen / ja d.d.	zo ja, studierichting:
arts examen	n.v.t. / ja d.d.	
assistent i.o. voor		einde opleiding:
inschrijving MSRC	neen / ja d.d.	BIG registratie nr.
huisadres		
postcode en plaats		
telefoonnummer		
werkinstelling		
afdeling		
adres		
postcode en plaats		
telefoonnummer		
e-mail adres		
* Toezending verenigingspost aan huis- / werkadres		

□ Hierbij machtig ik de penningmeester van de Nederlandse Vereniging voor Hepatologie om de verschuldigde contriutie tot wederopzegging automatisch van mijn bank-/girorekening af te laten schrijven. Betaling geschiedt nadat u door de eerstvolgende ledenvergadering als lid bent aangenomen. Indien u geen machtiging tot incasso geeft ontvangt u automatisch een factuur. Voor verzending van facturen worden vanaf volgend jaar administratiekosten in rekening gebracht.

Bank- / girorekening: Datum en handtekening:

Dit ondertekende formulier per post of fax (023 – 5513087) sturen naar:
Secretariaat NVH, Postbus 657, 2003 RR Haarlem

Aanvullende informatie: De contributie van de Nederlandse Vereniging voor Hepatologie bedraagt € 35,00 per jaar.
Na toetreding als lid ontvangt u een factuur (conform de regels is volledige contributie verschuldigd in het jaar van toetreding). Het lidmaatschap loopt per kalenderjaar. Opzeggen dient daarom vóór 1 december te gebeuren.

SECTIE ENDOSCOPIE VERPLEEGKUNDIGEN EN ASSISTENTEN VAN DE NVGE

aanmeldingsformulier lidmaatschap

naam en voorletters			m / v
Evt. meisjesnaam			
voornaam			geb. datum:
titel			
specialisme / functie		BIG registratie nr.	
huisadres			
postcode en plaats			
telefoonnummer			
werkinstelling			
afdeling			
adres			
postcode en plaats			
telefoonnummer			
e-mail adres			

geeft zich hierbij op als lid van de Sectie Endoscopie Verpleegkundigen en Assistenten van de Nederlandse Vereniging voor Gastroenterologie tot schriftelijke wederopzegging.
Let wel, het lidmaatschap is persoonsgebonden en niet overdraagbaar. Verenigingspost zal uitsluitend naar uw huisadres worden gestuurd.

Datum:…… Handtekening:…….

** aangeven wat van toepassing is.*

☐ Hierbij machtig ik de penningmeester van de Sectie Endoscopie Verpleegkundigen en Assistenten om het bedrag van de jaarlijkse contributie ad € 20,00, tot wederopzegging automatisch van mijn bank-/girorekening af te laten schrijven. Betaling geschiedt pas nadat u door de eerstvolgende ledenvergadering als lid bent aangenomen.

Indien u geen machtiging tot incasso geeft ontvangt u automatisch een factuur.

(Post)bankrekeningnummer Handtekening

N.B. Het lidmaatschap loopt per kalenderjaar. Opzeggen dient dus vóór 1 januari te gebeuren.

Dit ondertekende formulier per post of fax sturen naar:
Centraal Secretariaat NVGE (ledenadministratie SEVA)
Postbus 657 2003 RR Haarlem fax: 023-5513087

VERENIGING MAAG DARM LEVER VERPLEEGKUNDIGEN

Aanmeldingsformulier lidmaatschap

naam en voorletters			m / v
Evt. meisjesnaam			
voornaam			geb. datum:
titel			
specialisme / functie		BIG registratie nr.	
huisadres			
postcode en plaats			
telefoonnummer			
werkinstelling			
afdeling			
adres			
postcode en plaats			
telefoonnummer			
e-mail adres			

Geeft zich op als lid van de Vereniging Maag Darm Lever Verpleegkundigen van de Nederlandse Vereniging voor Gastroenterologie tot schriftelijke wederopzegging. *Let wel, het lidmaatschap is persoonsgebonden en niet overdraagbaar. Verenigingspost zal uitsluitend naar uw huisadres worden gestuurd.*

Datum:…… Handtekening:…….

☐ Hierbij machtig ik de penningmeester van de Vereniging Maag Darm Lever Verpleegkundigen om de verschuldigde contributie, ad € 27,50 per jaar, tot wederopzegging automatisch van mijn bank-/girorekening af te laten schrijven. Betaling geschiedt pas nadat u door de eerstvolgende ledenvergadering als lid bent aangenomen.

Indien u geen machtiging tot incasso geeft ontvangt u automatisch een factuur.

(Post)bankrekeningnummer Handtekening

…….

N.B. Het lidmaatschap loopt per kalenderjaar. Opzeggen dient volgens de statuten vier weken voor het aflopen van het kalenderjaar **schriftelijk** te gebeuren.

Dit ondertekende formulier per post of fax sturen naar:
Centraal Secretariaat NVGE (ledenadministratie VMDLV)
Postbus 657, 2003 RR Haarlem, fax: 023-5513087

Notities:

Notities: