Programma najaarsvergadering 4 en 5 oktober 2007

NEDERLANDSE VERENIGING VOOR GASTROENTEROLOGIE

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

NEDERLANDSE VERENIGING VOOR HEPATOLOGIE

NEDERLANDSE VERENIGING VOOR GASTROINTESTINALE CHIRURGIE

NEDERLANDS GENOOTSCHAP VAN MAAG-DARM-LEVERARTSEN

NH KONINGSHOF VELDHOVEN

INHOUDSOPGAVE pag.

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

Tijdstippen diverse ledenvergaderingen donderdag:
Assistentenvereniging Touché (mdl-artsen i.o.) 4 oktober, 12.30 uur - Zaal 82/83
Nederlandse Vereniging voor Hepatologie 4 oktober, 14.00 uur - Parkzaal
Nederlandse Vereniging voor Gastroenterologie 4 oktober, 21.30 uur - Brabantzaal

INHOUDSOPGAVE pag.

VRIJDAG 5 OKTOBER 2007

Ochtendprogramma

Middagprogramma

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

Tijdstippen diverse ledenvergaderingen vrijdag:

Sectie Endoscopie Verpleegkundigen en Assistenten 5 oktober, 11.45 uur - Diezezaal
Nederlands Genootschap van Maag-Darm-Leverartsen 5 oktober, 12.00 uur - Zaal 80-82

VOORWOORD

Hierbij treft u het volledige programma aan van de najaarsvergadering die gehouden wordt op 4 en 5 oktober a.s. in Congrescentrum Koningshof te Veldhoven.

Het programma zal donderdag 4 oktober om 10.30 uur van start gaan met een aantal projectpresentaties van de MLDS, gevolgd door voordrachten (basaal) van de Nederlandse Vereniging voor Hepatologie. In de middag zijn er behalve de minibattle van de NVGIC - 'Endoscopische versus operatieve behandeling van gastroesophageale reflux' - twee symposia: 'Neurogene Ziekten' en 'Inherited Liver Diseases'. Daarnaast zijn er de gebruikelijke sessies met vrije voordachten van de Nederlandse Vereniging voor Gastroenterologie en de Nederlandse Vereniging voor Hepatologie.
Om 17.00 uur vindt in de Brabantzaal de uitreiking van de AstraZeneca Gastrointestinale Research Award plaats gevolgd door de erevoordracht. Aansluitend is er de officiële uitreiking van de Dicke-medaille aan prof. dr. S.W. Schalm. Alle leden worden hierbij van harte uitgenodigd aanwezig te zijn!
Tijdens de avondsessie vindt de Presidential Selection plaats, gevolgd door de Nycomed Lecture (voorheen Altana Lecture) met als gastspreker prof. G. Falk uit Cleveland.

Op vrijdag 5 oktober staan er twee symposia op het programma, nl.: 'Hepatitis B en C-richtlijn' en 'Maagcarcinoom'. Daarnaast zijn er sessies met vrije voordrachten van de Sectie Gastrointestinale Endoscopie, de Nederlandse Vereniging van Gastroenterologie, de Nederlandse Vereniging voor Hepatologie en de Sectie Experimentele Gastroenterologie.
De Netherlands Society of Parenteral and Enteral Nutriton en de Nederlandse Vereniging voor Gastrointestinale Chirurgie organiseren een bijeenkomst over de Consensus / Richtlijn CBO Perioperatieve Voeding. Om 13.30 uur is er in de Parkzaal de Tytgat Lecture door prof. Dominique-Charles Valla uit Clichy, gevolgd door de International Teaching Session van de Sectie Experimentele Gastroenterologie. In respectievelijk de Diezezaal en het Auditorium worden tot slot door de Sectie Endoscopie Assistenten en Verpleegkundigen en de Vereniging van Maag Darm Lever Verpleegkundigen eigen programma's met lezingen verzorgd.

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

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 voorjaarsvergadering 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 voorjaarscongres, 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. H.M. van Dullemen (MDL-arts, UMC Groningen);
Drs. A.D. Koch (MDL-arts i.o, Erasmus MC)
Dr. C.J.H.M. van Laarhoven (chirurg, Elisabeth Ziekenhuis Tilburg)
Dr. R.A. de Man (MDL-arts, Erasmus MC)
Prof. dr. C.J.J. Mulder (MDL-arts, VU medisch centrum)
Dr. A.M.P. de Schryver (MDL-arts i.o., UMC Utrecht)

Woensdag 3 oktober 2007 - *HPB-oncologie*

20.00 – 20.30	Indicaties voor HPB-chirurgie *Dr. E.A.J. Rauws MDL-arts, AMC*
20.30 – 21.00	Whipple chirurgie: "palliatieve oorlogschirurgie"? *Dr. H. van Goor, chirurg, UMCN*
21.00 – 21.30	Interventie endoscopie na lever-pancreas chirurgie *Dr. H.M. van Dullemen, MDL-arts, UMCG*
21.30 – 22.00	Centralisatie van carcinoom-operaties, tobben op de wachtlijst? *Prof. dr. J.W.W. Coebergh, Soc. Geneesk., IKZ, Eindhoven*

Donderdag 4 oktober 2007 - *Colon Oncologie*

08.00 – 08.30	Endoscopische follow-up na poliepen en of CRC *Dr. J.J. Koornstra, MDL-arts, UMCG*
08.30 – 09.00	Lynch syndroom *Dr. F.M. Nagengast, MDL-arts, UMCN*
09.00 – 09.30	T4-coloncarcinoom: palliatie of meer? *Prof. dr. R.P. Bleichrodt, chirurg, UMCN*
09.30 – 10.00	Metastasectomie voor coloncarcinoom *Dr. T.J.M. Ruers, chirurg, AVL, Amsterdam*
pauze	
10.30 – 10.45	Fasttrack CRC-chirurgie, aanzet tot discussie *Dr. C.H.C. Dejong, chirurg, AZM*
10.45 – 11.00	Laparoscopische CRC-chirurgie, aanzet tot discussie *Dr. W.J.H.J. Meijerink, chirurg, VUmc*
11.00 – 11.15	CRC chirurgie: waar staan we nu? *Dr. C.J.H.M. van Laarhoven, chirurg, St. Elisabeth Ziekenhuis, Tilburg*
11.15 – 11.45	Discussie Bleichrodt, Ruers, Dejong en Meijerink o.l.v. Van Laarhoven
11.45 – 12.15	Is CRC-palliatie al duurder dan adequate preventie? *Prof. dr. H.M. Pinedo, oncoloog, VUmc*

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 4 oktober 2007

DONDERDAG	BRABANTZAAL	BARONIEZAAL	PARKZAAL	AUDITORIUM	DIEZEZAAL
13.00	Vrije voordrachten Nederlandse Vereniging voor Gastrointestinale Chirurgie p. 12	**Symposium 'Neurogene ziekten'** verzorgd door de Sectie Neurogastro-enterologie en motiliteit p. 15	Start MLDS projecten en vrije voordrachten NVH om 10.30 13.00 Voordrachten NVH 14.00 Ledenvergadering NVH p . 10	Geen programma in deze zaal donderdagmiddag	Geen programma in deze zaal donderdagmiddag
15.00	Theepauze	Theepauze	Start symposium NVH		
15.30	**Minibattle NVGIC 'Endoscopische versus operatieve behandeling van gastroesofageale reflux'** p. 13	Vrije voordrachten Nederlandse Vereniging voor Gastroenterologie p. 15	**'Symposium Inherited Liver Diseases'** van de Nederlandse Vereniging voor Hepatologie p. 17		
17.00	**Uitreiking AZ Award 2007**				
17.15	**Uitreiking Dicke-medaille aan prof. dr. S.W. Schalm**	Geen programma in deze zaal	Geen programma in deze zaal		
17.30	Congresborrel expositiehal	Congresborrel expositiehal	Congresborrel expositiehal		
18.00	Diner in Genderzaal	Diner in Genderzaal	Diner Genderzaal		
20.00	President Select gevolgd door **Nycomed Lecture door prof. dr. G.W. Falk** (21.00) p. 20				
21.30	**Ledenvergadering NVGE**				
22.30	Congresborrel Brabantzaal				

Programma vrijdag 5 oktober 2007

VRIJDAG	BRABANTZAAL	BARONIEZAAL	PARKZAAL	AUDITORIUM	DIEZEZAAL
08.30 09.00	**Casuïstiek voor de clinicus** Vrije voordrachten Sectie Gastrointestinale Endoscopie p. 21	**Symposium Maag-carcinoom** p. 23	Vrije voordrachten (klinisch) Nederlandse Vereniging voor Hepatologie p. 26	09.45 Programma VMDLV p. 35	
10.00	Start symposium	Koffiepauze, expositie	Koffiepauze, expositie	Koffiepauze, expositie	Start programma SEVA
10.30	**Symposium Hepatitis B en C** *(richtlijn)* p. 22	Vrije voordrachten Nederlandse Vereniging voor Gastroenterologie p. 24	Vrije voordrachten Sectie Experimentele Gastroenterologie p. 28	Programma Vereniging voor Maag-Darm-Lever Verpleegkundigen p. 35	Programma Sectie Endoscopie Verpleeg-kundigen en Assistenten | p. 34
12.00	Lunchbuffet expositiehal	Lunchbuffet expositiehal	Lunchbuffet expositiehal	Lunchbuffet expositiehal	Lunchbuffet expositiehal
13.30	Vrije voordrachten Nederlandse Vereniging voor Gastroenterologie p. 30	**Consensus / Richtlijn CBO Perioperatieve Voeding** (organisatie: NESPEN-NVGIC) p. 32	**Tytgat Lecture** door prof. dr. D.C. Valla **International Teaching Session** (vanaf 14.00 uur) p. 33	Programma Vereniging voor Maag-Darm-Lever Verpleegkundigen p. 35	Programma Sectie Endoscopie Verpleeg-kundigen en Assistenten p. 34
15.00	Einde programma 15.20, thee	Einde programma, thee	Einde programma, thee	Einde programma, thee	Einde programma, thee

Voorzitters: K.N. Faber en L. van der Laan
Voordrachten in het Nederlands, spreektijd 7 minuten, discussietijd 3 minuten.

Presentaties MLDS-projecten

10.30 Does ursodeoxycholic acid protects against apoptotic liver injury? (p. 36)
T.E. Vrenken, L. Conde de la Rosa, M.H., Schoemaker, M. Buist-Homan, H. Moshage, Div. Gastroenterology and Hepatology, University Medical Center Groningen, Groningen, the Netherlands. (MLDS-project MWO 02-1)

10.40 Investigation of the applicability of antimicrobial peptides agains *Helicobacter pylori* (p.37)
J.G.M. Bolscher, P.A.M. van den Keijbus, K. Nazmi, A.J.M. Ligtenberg, M.M. Gerrits[1], E.C.I. Veerman, A.V. Nieuw Amerongen. Academic Centre Dentistry Amsterdam (ACTA), Dept of Oral Biochemistry, Amsterdam, The Neterlands, [1]Erasmus MC, Dept of Gastroenterology and Hepatology, Rotterdam, The Netherlands (MLDS-project WS 01-42)

10.50 Role of L-SIGN in pathogenesis, antigen presentation and cellular interactions. (p.38)
I.S. Ludwig[1,4,5], A.N. Lekkerkerker[1,6], E. Depla, F. Bosman S. Depraetere[2], R.J.P. Musters[3] , T.B.H. Geijtenbeek[1] Y. van Kooyk[1], [1]Molecular Cell Biology, VU University Medical Center Amsterdam, the Netherlands. [2]Innogenetics, Ghent, Belgium. [3]Laboratory of Physiology, VU University Medical Center Amsterdam, the Netherlands. [4]Maag Lever Darm Stichting (grant WS 01-36). [5]AIDS Fonds (grant 5008). [6]NWO Aspasia (grant 015 000 023)

11.00 Einde presentaties MLDS-projecten

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

Voorzitters: K.N. Faber / L. van der Laan

Voordrachten in het Engels,
spreektijd 10 minuten, discussietijd 5 minuten.

11.00 The human small heterodimer partner (SHP) promoter contains independent and unconventional 9-cis retinoic acid- and bile salt-responsive elements (p. 39)
M.O. Hoeke, J. Heegsma, K.N. Faber, Dept. of Gastroenterology and Hepatology, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands.

11.15 ATP8B1 and CDC50A physically interact and co-localize in the canalicular membrane of polarized WIF-B9 cells. (p. 40)
D.E. Folmer, K.S. Ho-Mok, R.P.J. Oude Elferink, C.C. Paulusma, AMC Liver Center, Academic Medical Center, Amsterdam, The Netherlands

11.30 Unconjugated bile salts shuttle through hepatocyte peroxisomes for glycine or taurine conjugation. (p. 41)
K. Rembacz, J. Woudenberg, E. Jonkers, F.A.J. van den Heuvel, T.E. Vrenken, H. Moshage, F. Stellaard, K.N. Faber. Dept of Gastroenterology and Hepatology, University Medical Center Groningen, The Netherlands

11.45 The active metabolite of leflunomide, A77 1726, protects rat hepatocytes against bile acid-induced apoptosis (p. 42)
T.E. Vrenken, M. Buist-Homan, A.J. Kalsbeek, K.N. Faber, H. Moshage. Dept of Gastroenterology and Hepatology, University Medical Center Groningen, The Netherlands

12.00 Einde programma, lunchbuffet.

Nederlandse Vereniging voor Gastrointestinale Chirurgie **Brabantzaal**

12.30 Inschrijving, koffie

Voorzitters: E. van der Harst / R. van Hillegersberg

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

13.00 Diagnostic algorithm for pretreatment staging of patients with oesophageal cancer (p. 43)
M. van Heijl[1], J.M.T. Omloo[1], N.J. Smits[2], S.S.K.S. Phoa[2], J.J.G.H.M. Bergman[3], G.W. Sloof[4], P.M.M. Bossuyt[5], J.J.B. van Lanschot[1,6]. Depts of Surgery[1], Radiology[2], Gastroenterology[3], Nuclear Medicine[4] and Clinical Epidemiology[5], Academic Medical Centre at the University of Amsterdam Presently: Dept of Surgery[6], Erasmus Medical Centre, Rotterdam.

13.10 No additional value of bronchoscopy after EUS in the preoperative assessment of patients with oesophageal cancer at or above the carina (p. 44)
J.M.T. Omloo[1], M. van Heijl[1], J.J.G.H.M. Bergman[2], M.G.J. Koolen[3], M.I. van Berge Henegouwen[1], J.J.B. van Lanschot[1,4]. Depts of Surgery[1], Gastroenterology[2] and Pulmonary Diseases[3], Academic Medical Centre at the University of Amsterdam, Amsterdam and presently: Dept of Surgery[4], Erasmus Medical Centre, Rotterdam, The Netherlands

13.20 Improving staging accuracy in colorectal carcinomas by sentinel node mapping: a comparative study. (p. 45)
E. van der Zaag[1], C.J. Buskens[1], H.M. Peeters[2], B.W. van den Berg[3], W.H. Bouma[1]. Depts of Surgery[1], Pathology[2] and Gastro-enterology[3], Gelre Hospitals, Apeldoorn, The Netherlands

13.30 Are micro-metastases in colon cancer a predictor for the delopment of distant metastases? (p. 46)
E. Hermans, P.M. van Schaik, J.C. van der Linden, M.F. Ernst, K. Bosscha. Dept of Surgery, Jeroen Bosch Hospital, `s-Hertogenbosch, The Netherlands

13.40 Laparoscopic liver resections: initial experience in a University Hospital setting (p. 47)
J.H.M.B. Stoot, R.M. van Dam, M.C.G. van der Poll, S.W.M. Olde Damink, M.H.A. Bemelmans, C.H.C. Dejong. Dept. of Surgery, Academical Hospital Maastricht, Maastricht, The Netherlands

13.50 Management in patients with liver cirrhosis and an umbilical hernia: conservative versus elective surgical treatment (p. 48)
H.A. Marsman, J. Heisterkamp, J.A. Halm, H.W. Tilanus, H.J. Metselaar, G. Kazemier, Dept. of Surgery, Erasmus MC, University Medical Center Rotterdam, The Netherlands

14.00 Reappraisal of diagnostic laparoscopy for periampullary tumours (p. 49)
N.A. van der Gaag[1], M.I. van Berge Henegouwen[1], K. Harmsen[1], O.R.C. Busch[1], T.M. van Gulik[1], D.J. Gouma[1]. Dept of Surgery[1], Academic Medical Center, Amsterdam, The Netherlands

14.10 Predictive indicators of symptomatic and objective outcome after surgical reintervention for failed antireflux surgery; a multivariate analysis (p. 50)
E.J.B. Furnée[1], W.A. Draaisma[1], I.A.M.J. Broeders[1], A.J.P.M. Smout[2], H.G. Gooszen[1]. Depts of Surgery[1] and Gastroenterology[2], University Medical Centre Utrecht, Utrecht, The Netherlands

14.20 Failure of gastric banding: is biliopancreatic diversion with duodenal switch a solution? (p. 51)
F. Polat, R.J. Oostenbroek, W.L.E.M. Hesp. Dept of Surgery, Albert Schweitzer Ziekenhuis, Dordrecht, The Netherlands

14.30 Proximate® Linear Cutter 100 failure: a word of caution (p. 52)
J. Wind, F. Safiruddin, M.I. van Berge Henegouwen, J.F.M. Slors, W.A. Bemelman. Dept of Surgery, Academic Medical Center, Amsterdam, The Netherlands

14.40 Anal fistula plug for closure of difficult perianal fistulas - a prospective study. (p. 53)
P.J. van Koperen[1], A. D'Hoore[2], A.M. Holthuis[2], W.A. Bemelman[1], J.F.M. Slors[1]. Dept of Surgery[1], Academic Medical Center Amsterdam, The Netherlands, Dept of Abdominal Surgery[2], Gasthuisberg, University Clinics Leuven, Belgium

14.50 Long-term health related quality of life in patients treated for their enterocutaneous fistulas (p. 54)
R.G.J. Visschers[1], S.W.M. Olde Damink[1], M. van Bekkum[2], P.B. Soeters[1], W.G. van Gemert[1]. Dept of Surgery[1], University Hospital Maastricht, Faculty of Health, Medicine and Life Sciences[2], Maastricht University, Maastricht, The Netherlands

15.00 Theepauze

Minibattle Ned. Vereniging voor Gastrointestinale Chirurgie **Brabantzaal**

'Endoscopische versus operatieve behandeling van gastroesofageale reflux'

Voorzitters: E.J. Kuipers en W.A. Bemelman

15.30 Reflux behandeling anno 2007, how we do it.
Dr. I.A.M.J. Broeders, chirurg, UMC Utrecht

16.00 Endoscopische therapie is de behandeling voor de toekomst.
N. Bouvy, chirurg, AZM, Maastricht.

16.20 Antireflux chirurgie is de beste enig effectieve therapie
Prof. dr. H.G. Gooszen, chirurg, UMC Utrecht

16.40 Discussie

17.00 Einde programma

Nederlandse Vereniging voor Gastroenterologie **Brabantzaal**

17.00 **Uitreiking AstraZeneca Gastrointestinale Research Award**
door de voorzitter van de jury, prof. dr. J.W.M. Greve,
gevolgd door een erevoordracht

17.15 **Uitreiking van de Dicke medaille aan prof. dr. S.W. Schalm**

17.30 Congresborrel in expositiehal

18.00 Diner in Genderzaal

Symposium Neurogene ziekten — Baroniezaal

Voorzitters: R.J.F. Felt-Bersma / J.W. Straathof

13.00 Het enterisch zenuwstelsel: de software van de darm
P. van den Berghe, Afdeling MDL, KU Leuven

13.30 Achalasie
M. Costantini, University of Padua, Italië

14.00 Chronische Idiopathische Intestinale Pseudo-obstructie
V. Stanghellini, University of Bologna, Italie

14.30 Obstipatie
R.J.F. Felt-Bersma, Afdeling MDL, VUmc, Amsterdam

15.00 Theepauze (expositiehal)

Nederlandse Vereniging voor Gastroenterologie — Baroniezaal

Voorzitters: C.H.C. Dejong / A.A.M. Masclee

15.30 Describing computed tomography findings in severe acute pancreatitis with descriptive terms: an international interobserver agreement study (p. 55)
H.C. van Santvoort[1], T.L. Bollen[2], M.G. Besselink[1], M.A. Boermeester[3], C.H. van Eijck[4], J. Hermans[5], M.S. van Leeuwen[6], J.S. Lameris[7], H.G. Gooszen[1]. Depts of Surgery[1] ,Radiology[6], University Medical Center Utrecht, Dept of Radiology[2], St Antonius Hospital, Nieuwegein, Depts of Surgery[3], Radiology[7], Academic Medical Center, Amsterdam, Dept of Surgery[4] and Radiology[5], Erasmus Medical Centre, Rotterdam, The Netherlands, and the members of the International Reviewer Group

Donderdag 4 oktober 2007

15.40 *Abstract teruggetrokken*
Quality of life one year after a single attack of acute pancreatitis
B.W.M. Spanier[1], M.G.W. Dijkgraaf[2], M.J. Bruno[1]. Depts of Gastroenterology and Hepatology[1], and Clinical Epidemiology and Biostatistics[2], Academic Medical Center, Amsterdam, The Netherlands

15.50 Randomised controlled trials of intravenous antibiotic prophylaxis in severe acute pancreatitis: meta-analysis and relationship between methodological quality and outcome (p. 57)
A.C. de Vries[1], M.G.H. Besselink[2], E. Buskens[3], M. Schipper[4], K.J. van Erpecum[5], H.G. Gooszen[2] for the Dutch Acute Pancreatitis Study Group. Dept of Gastroenterology and Hepatology[1], Erasmus Medical Centre, Rotterdam, Dept of Surgery[2], University Medical Centre Utrecht, Dept of Epidemiology[3], University Medical Centre Groningen, Centre for Biostatistics, Utrecht university and Dept of Gastroenterology[5], University Medical Centre Utrecht, The Netherlands

16.00 Impact of small bowel capsule endoscopy on patient management:
a 1-year follow-up study (p. 58)
A.P.J. de Graaf, R.K. Weersma, W.J. Thijs, A.J. Limburg, J.J. Koornstra. Dept of Gastro-enterology and Hepatology, University Medical Center Groningen, The Netherlands

16.10 Efficacy of fecal therapy for recurrent Clostridium difficile associated diarrhea (p. 59)
J.J. Keller, M. Nieuwdorp, H. van Heukelem, C. Visser, E.J Kuijper, P. Speelman en J.F.W.M. Bartelsman, Depts of Gastroenterology, Medicine and Microbiology, AMC Amsterdam. Department of Microbiology, LUMC Leiden, Dept of Gastroenterology, Slotervaart Hospital Amsterdam, The Netherlands

16.20 Effect of droplet size of a fat emulsion delivered in the small intestine on satiety and food intake in healthy volunteers (p. 60)
P.W.J. Maljaars[1], R.J.P. van der Wal[2], E.A. Haddeman[3], H.P.F. Peters[3], C. Beindorff [3], A.A.M. Masclee[1]. Division of Gastroenterology-Hepatology[1], Dept of Internal Medicine, University Hospital Maastricht, Dept of Gastroenterology-Hepatology[2], Leiden University Medical Centre, Leiden, Unilever Food and Health Research Institute[3], Vlaardingen, The Netherlands

16.30 Enteral administration of isotopically labeled alanyl-[2-15N]glutamine results in a higher enrichment of [15N]citrulline and [15N]arginine compared to the parenteral route, despite equal arginine release from the kidney (p. 61)
G.C. Ligthart-Melis[1], M.C.G. van de Poll[2], P.G. Boelens[1], M.P. van den Tol1[1], L. Cynober[3], N.E.P. Deutz[2], C.H.C. Dejong[2], P.A.M. van Leeuwen[1]. Dept of Surgery[1], VU University Medical Centre, Amsterdam, Dept of Surgery[2], University Hospital Maastricht, Maastricht, The Netherlands and Dept of Clinical Biochemistry[3], Université Paris Descartes, Paris, France*

16.40 The Citrulline Generation Test (CGT): a new enterocyte function test (p.62)
J.H.C. Peters[1], N.J. Wierdsma[2], T. Teerlink[3], P.A.M. van Leeuwen[4], C.J.J. Mulder[1], A.A. van Bodegraven[1]. Depts of Gastroenterology[1], Small Bowel Diseases Unit, Nutrition and Dietetics[2], Clinical Chemistry[3] and Metabolic Laboratory and Experimental Surgery[4], VU University Medical Center, Amsterdam, The Netherlands

16.50 Mid-upper arm circumference, weight and height in Dutch children (p. 63)
J.J.Schweizer[1], W.J. Gerver[2]. Dept of Paediatrics[1], Leiden University Medical Center, Leiden and Dept of Paediatrics, Free University Medical Center, Amsterdam, Dept of Paediatrics[2], University Hospital Maastricht, The Netherlands

17.00 Einde programma in deze zaal

Voor het plenaire programma kunt u zich begeven naar de Brabantzaal
17.00 uur: uitreiking AstraZeneca Gastrointestinale Research Award
17.15 uur: uitreiking Dicke medaille aan prof. dr. S.W. Schalm

Donderdag 4 oktober 2007

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

Voorzitter: H. Moshage / J.P.H. Drenth

Voordrachten in het Engels,
spreektijd 10 minuten, discussietijd 5 minuten.

13.00 Intravenous immunoglobulins reduce allogeneic T-cell activation after liver transplantation by modulating the interaction between Dendritic Cells and Natural Killer Cells (p. 64)
T. Tha-In[1], H.J. Metselaar[1], H.W. Tilanus[2], Z.M.A. Groothuismink[1], P.M. van Hagen[3], E.J. Kuipers[1], R.A. de Man[1], J. Kwekkeboom[1]. Depts of Gastroenterology and Hepatology[1], Surgery[2] and Internal Medicine[3], Erasmus MC – University Medical Center, Rotterdam, The Netherlands

13.15 Glutathione, but not catalase is important in protection of Hepatic Stellate Cells against oxidative stress (p. 65)
S. Dunning, R.A. Hannivoort, L. Conde de la Rosa, M. Buist-Homan, K.N. Faber, H. Moshage. Dept of Gastroenterology and Hepatology, University Medical Center Groningen, The Netherlands

13.30 Hepatic glucose-6-phosphate metabolism is perturbed in LXRalpha-null mice* (p. 66)
M.H. Oosterveer[1], T.H. van Dijk[1], A. Grefhorst[1], V.W. Bloks[1], R. Havinga[1], F. Kuipers[1], D-J. Reijngoud[1]. Center for Liver, Digestive and Metabolic Diseases[1], Laboratory of Pediatrics, University Medical Center Groningen, The Netherlands

13.45 The Adrenoleukodystrophy Protein (ALDP) and the 70-kDa Peroxisomal Membrane Protein (PMP70) are differentially associated with lipid microdomains (p. 67)
J. Woudenberg, A. Pellicoro, K.P. Rembacz, F.A.J. van den Heuvel, M. Hoekstra, A.J. Moshage, K.N. Faber. Dept of Gastroenterology and Hepatology, University Medical Center Groningen, The Netherlands

14.00 **Algemene ledenvergadering**
Nederlandse Vereniging voor Hepatologie

14.30 Theepauze

Symposium Inherited Liver Diseases — Parkzaal

Voorzitter: J.P.H. Drenth

15.00 Opening of the symposium
J.P.H. Drenth, Nijmegen, The Netherlands

15.02 Did the Dutch contribute to the elucidation of genetic liver disorders?
R.J. Oude Elferink, Amsterdam, The Netherlands

15.30 Genetic disorders in iron metabolism
A. Pietrangelo, Modena, Italy

16.00 Genetic predisposition to gall stone disease
F. Lammert, Bonn, Germany

16.30 Genetic Correlates in hepatitis C
M. Thursz, London, UK

17.00 End of session

Voor het plenaire programma kunt u zich begeven naar de Brabantzaal
17.00 uur: uitreiking AstraZeneca Gastrointestinale Research Award
17.15 uur: uitreiking Dicke medaille aan prof. dr. S.W. Schalm

Donderdag 4 oktober 2007

President Select (plenair) **Brabantzaal**

Voorzitter: J.B.M.J. Jansen

20.00 The arteriovenous fistula: a feasible alternative to deliver home parenteral nutrition (p. 68)
M.W. Versleijen[1], M. Kock[1], L.G. van Rossum[1], M.C. Willems[2], G.J. Wanten[1]. Depts of Gastroenterology and Hepatology[1] and Vascular Surgery[2], Radboud University Medical Centre, Nijmegen, The Netherlands

20.15 Results of the first screening program for colorectal cancer in The Netherlands (p. 69)
A.F. van Rijn[1], L.G. van Rossum[2], P. Fockens[1], R.J. Laheij[2], E. Dekker[1], J.B. Jansen[2], [1]Dept of Gastroenterology, Academic Medical Centre, Amsterdam, [2]Dept of Gastroenterology, Radboud University Nijmegen Medical Center, Nijmegen, Netherlands

20.30 CEA in activated macrophages: a new prognostic or diagnostic factor for early detection of local recurrence of colorectal neoplasms? (p. 70)
D. Japink[1], M. Nap[2], M.P.G. Leers[3], M.N. Sosef[1]. Depts of Surgery[1], Clinical Pathology[2] and Clinical Chemistry[3], Atrium Medical Center Heerlen, The Netherlands

20.45 Tolerance to gliadin peptides can be restored by enteral administration of lactococcus Lactis bio-engineered to deliver the immunodominant antigen to sensitized NOD AB^0 DQ8 transgenic mice (p. 71)
I.L. Huibregtse[1], E.V. Marietta[2], S. Rashtak[2], F. Koning[3], P. Rottiers[4], C. David[2], S.J.H. van Deventer[1], J.A. Murray[5]. CEMM[1], Academic Medical Center, Amsterdam, The Netherlands, Dept of Immunology[2], Mayo Clinic, Rochester MN, USA, Dept of Hematoimmunology[3], University Medical Center Leiden, The Netherlands, Dept of Molecular Biomedical Research[4], VIB, Ghent, Belgium and Dept of Gastroenterology and Hepatology[5], Mayo Clinic, Rochester MN, USA

21.00 **Nycomed-lecture** - "How to keep up with science as an endoscopist",
Gary W. Falk, MD, MS, Professor of Medicine, Cleveland Clinic Lerner College of Medicine, Director, Center for Swallowing and Esophageal Disorders Department of Gastroenterology & Hepatology, Cleveland Clinic Foundation

21.30 **Ledenvergadering Nederlandse Vereniging voor Gastroenterologie**

Casuïstiek **Brabantzaal**

Voorzitter: W. Hameeteman

08.30 Casuïstische patiëntenbespreking

Sectie Gastrointestinale Endoscopie **Brabantzaal**

Voorzitter: W. Hameeteman

09.00 Narrow-band imaging (NBI), indigo carmine chromoscopy (ICC) and acetic acid chromoendoscopy (AAC) have little clinical relevance in Barrett's imaging: a study comparing the evaluation of 4 different enhancement techniques by expert and non-expert endoscopists (p. 72)
W. Curvers[1], L. Baak[2], R. Kissliech[3], A. van Oijen[4], T. Rabinstein[5], K. Ragunat[6], J.F. Rey[7], P. Scholten[8], U. Seitz[9], P. Fockens[1], J. Bergman[1]. Dept. of Gastroenterology and Hepatology[1], Academic Medical Center, Amsterdam, Dept. of Gastroenterology and Hepatology[2], OLVG, Amsterdam, The Netherlands, Medical Clinic[3], Johannes Gutenberg University, Mainz, Germany, Dept of Gastroenterology and Hepatology, Medical Center Alkmaar[4], The Netherlands, Dept. of Internal Medicine II[5], HSK, Wiesbaden, Germany, Wolfson Digestive Disease Centre[6], Queens Medial Center, Nottingham, Great Britain, Dept. of Gastroenterology and Hepatology[7], Institute Arnault Tzanck, St Laurent duVar, France, Dept. of Gastroenterology and Hepatology, St Lucas Andreas Hospital[8], Amsterdam, The Netherlands, Dept. of Interdisciplinary Endoscopy[9], University Medical Center Hamburg-Eppendorf, Hamburg, Germany.

09.10 Novel combined modality therapy for Barrett's esophagus containing early neoplasia: endoscopic resection followed by circumferential and focal radiofrequency ablation (p. 73)
R.E. Pouw[1], J.J. Gondrie[1], C.M. Sondermeijer[1], W.D. Rosmolen[1], F.P. Peters[1], W.L. Curvers[1], F.J. ten Kate[2], K.K. Krishnadath[1], P. Fockens[1], J.J. Bergman[1]. Depts of Gastroenterology and Hepatology[1] and Pathology[2], Academic Medical Center, Amsterdam, The Netherlands

Vrijdag 5 oktober 2007

09.20 Implementation of EUS-FNA for lung cancer staging (p. 74)
J.T. Annema[1], M.E. Smits[2], B.G. Taal[2], S. Burgers[3], R. Bohoslavsky[1], H. van Tinteren[4], K.F. Rabe[1], Depts of Lung Diseases, LUMC, Leiden[1] and Gastroenterology[2], Lung Diseases[3] and Statistics[4], Antoni van Leeuwenhoek Ziekenhuis, Amsterdam, The Netherlands

09.30 Role of high resolution endoscopy, narrow-band imaging and autofluorescence imaging for the classification of polyps in patients with hyperplastic polyposis (p. 75)
K.S. Boparai, F.J.C. van den Broek, P. Fockens, E. Dekker. Dept of Gastroenterology and Hepatology, Academic Medical Centre, University of Amsterdam, The Netherlands

09.40 Interobserver variability and accuracy of colonic pit patterns by narrow band imaging and color by autofluorescence imaging (p. 76)
F.J.C. van den Broek, W.L. Curvers, J.C. Hardwick, J.B. Reitsma, J.J.G.H.M. Bergman, P. Fockens, E. Dekker. Dept of Gastroenterology and Hepatology, Academic Medical Center Amsterdam, The Netherlands

09.50 Validation of the new Olympus virtual reality colonoscopy simulator (p. 77)
A.D. Koch[1], J. Haringsma[1], E.J. Schoon[2], R.A. de Man[1], E.J. Kuipers[1]. Dept of Gastro-enterology[1], Erasmus Medical Centre[1], Rotterdam, Dept. of Internal Medicine[2], Catharina Hospital, Eindhoven, The Netherlands

10.00 Einde sessie vrije voordrachten

Symposium Hepatitis B en C / richtlijn **Brabantzaal**

Voorzitters: H.L.A. Janssen, H.R. Reesink en R. Adang

10.00 Richtlijnen HBV therapie:
Dr. K.J. van Erpecum, Universitair Medisch Centrum Utrecht

10.35 Nieuwe therapeutische ontwikkelingen HBV
Drs. E.H.C.J. Buster, Erasmus Universiteit Rotterdam

11.00 Richtlijnen HCV therapie
Dr. H.W. Reesink, Academisch Medisch Centrum, Amsterdam

11.35 Nieuwe therapeutische ontwikkelingen HCV
Prof. dr .J.P.H. Drenth, Universitair Medisch Centrum St. Radboud, Nijmegen

12.00 Einde symposium

Symposium Maagcarcinoom **Baroniezaal**

Voorzitters: A. Cats en P.D. Siersema

08.30 Familiair maagcarcinoom
Drs. I. Kluijt, klinisch genetica,
Polikliniek Familiaire Tumoren, AVL

08.45 Genetische veranderingen bij maagcarcinoom
Dr. N.C.T. van Grieken, patholoog,
Afdeling pathologie, VUmc

09.00 Detectie, surveillance en therapie van premaligne afwijkingen
Prof. dr. E.J. Kuipers, MDL-arts,
Afdeling Maag-, Darm- en Leverziekten, EMC

09.15 Stadiering
Dr. F. Vleggaar, MDL-arts,
Afdeling Maag-, Darm- en Leverziekten, UMCU

09.30 Peri-operatieve behandeling van maagcarcinoom
Dr. A. Cats, MDL-arts,
Afdeling Maag-, Darm- en Leverziekten, AVL-NKI

09.50 Panel discussie

10.00 Einde symposium, koffiepauze

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

10.30 An increase in the number of risk-alleles is associated with an increased risk for Crohn's disease and a more severe disease course (p. 78)
R.K. Weersma[1], P.C. Stokkers[2], A.A. van Bodegraven[3], R.A. van Hogezand[4], H.W. Verspaget[4], D.J. de Jong[5], C.J. van der Woude[6], B. Oldenburg[7], R.K. Linskens[8], G. van der Steege[9], D.W. Hommes[4], J.B. Crusius[10], C. Wijmenga[9], I.M. Nolte[1], G. Dijkstra[1]. Dept of Gastroenterology[1], University Medical Center Groningen, Dept of Gastroenterology[2], Academic Medical Center, Amsterdam, Dept of Gastroenterology[3], VU Medical Center, Amsterdam, Dept of Gastroenterology[4], University Medical Center Leiden, Dept of Gastroenterology[5], UMCN, Dept of Gastroenterology[6], Erasmus MC, Rotterdam, Dept of Gastroenterology[7], University Medical Center Utrecht, Dept of Gastroenterology[8], St Anna Ziekenhuis, Geldrop, Depts of Genetics[9] and,Epidemiology[10], University Medical Center Groningen and Dept of Immunogenetics[11], VU Medical Center, Amsterdam, The Netherlands

10.40 Gender-related differences in disease perception in inflammatory bowel disease patients (p. 79)
Z. Zelinkova[1], J. Baars[1], T. Markus[2], E.J. Kuipers[1], C.J. van der Woude[1]. Dept of Gastro-enterology and Hepatology[1], Erasmus Medical Center, Rotterdam, Dutch patients' association of Crohn's disease and Ulcerative Colitis[2] (CCUVN), Breukelen, The Netherlands

10.50 Considerable gastric cancer risk during first year after diagnosis of gastric MALT lymphoma (p. 80)
L.G. Capelle[1], A.C. de Vries[1], M.K. Casparie[2], G.A. Meijer[3], E.J. Kuipers[1]. Dept of Gastroenterology and Hepatology[1], Erasmus University Medical Center, Rotterdam, PALGA (Pathologisch-Anatomisch Landelijk Geautomatiseerd Archief), the nationwide network and registry of histo- and cytopathology[2], and Dept of Pathology[3], Free University Medical Center, Amsterdam, The Netherlands

11.00 The yield of endoscopic surveillance with random biopsy sampling in patients with intestinal metaplasia and dysplasia of the gastric mucosa. (p. 81)
A.C. de Vries[1], J. Haringsma[1], R.A. de Vries[2], F. ter Borg[3], H. van Dekken[4], E.J. Kuipers[1]. Depts of Gastroenterology and Hepatology[1], and Pathology[4], Erasmus MC University Medical Center, Rotterdam, Dept of Gastroenterology and Hepatology[2], Rijnstate Hospital, Arnhem,Dept of Gastroenterology and Hepatology[3], Deventer Hospital, The Netherlands

11.10 The placement of nasoduodenal feeding tubes by nurses with the assistance of an electromagnetic system (CORTRAK™) (p. 82)
A. Duflou, B.W.M. Spanier, M.A.P.M. van den Bergh, P. Fockens, E.M.H. Mathus-Vliegen. Dept of Gastroenterology and Hepatology, Academic Medical Center, Amsterdam, The Netherlands

11.20 Day-to-day variation in acid reflux patterns in patients with non-erosive reflux disease and erosive reflux disease: clinically relevant or trivial? (p. 83)
P.J.F. de Jonge[1], D.J. Bac[2], I. Leeuwenburgh[3], R.J.Th. Ouwendijk[2], M. van Leerdam[1], E.J. Kuipers[1], P.D. Siersema[1]. Dept of Gastroenterology and Hepatology[1], Erasmus MC- University Medical Center Rotterdam, Dept of Internal Medicine[2], Ikazia Hospital Rotterdam and Dept of Internal Medicine[3], St Franciscus Gasthuis Rotterdam, The Netherlands

11.30 Effective removal of oncogenetic alterations after radiofrequency energy ablation of barrett's esophagus containing high-grade dysplasia (p. 84)
J.J. Gondrie[1], A.R. Rygiel[1], R.E. Pouw[1], C.M. Sondermeijer[1], P. Fockens[1], F.J. ten Kate[2], K.K. Krishnadath[1], J.J. Bergman[1]. Depts of Gastroenterology[1] and Pathology[2], Academic Medical Centre, Amsterdam

11.40 Can the presence of intestinal metaplasia and dysplasia in columnar-lined esophagus be predicted? - A multivariable analysis (p. 85)
M. Kerkhof[1], E.W Steyerberg[2], J.G Kusters[1], E.J Kuipers[1], P.D Siersema[1]. Depts of Gastroenterology and Hepatology[1], and Public Health[2], Erasmus MC - University Medical Center Rotterdam, The Netherlands

11.50 Esophageal capsule endoscopy in patients with gastro-esophageal reflux disease and Barrett's esophagus: improvement of diagnostic accuracy (p. 86)

P.J.F. de Jonge[1], B.C. van Eijck[1], H. Geldof[2], F.C. Bekkering[2], E.J. Kuipers[1], P.D. Siersema[1]. Dept of Gastroenterology and Hepatology[1], Erasmus MC - University Medical Center Rotterdam and Dept of Gastroenterology and Hepatology[2], IJsselland Hospital, Capelle aan den IJssel, The Netherlands

12.00 Einde programma, lunchbuffet in expositiehal.

Nederlandse Vereniging voor Hepatologie (klinisch) Parkzaal

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

08.30 Paroxysmal Nocturnal Hemoglobinuria in Budd-Chiari Syndrome – Results of the EN-Vie Study (p. 87)

J. Hoekstra[1], S. Darwish Murad[1], A. Plessier[2], M. Hernández-Guerra[3], D.C. Valla[2], J.C. Garcia-Pagan[3], E. Elias[4], M. Primignani[5], F.W. Leebeek[6], H.L.A. Janssen[1], For the EN-Vie Study Group. Depts of Gastroenterology and Hepatology[1], Hematology[6], Erasmus MC, University Medical Center, Rotterdam, The Netherlands, Dept of Hepatology[2], Hôpital Beaujon, Clichy, France, Liver Unit[3], Hospital Clinic, Barcelona, Spain, Liver Unit[4], Queen Elizabeth University Hospital, Birmingham, UK and Dept of Hepatogastroenterology[5], IRCSS Ospedale Maggiore di Milano, Milan, Italy

08.40 Clinically significant infections in adult cadaveric and living donor liver transplant recipients (p. 88 + 89)

M.A.J. van den Broek[1], F.H. Saner[2], S.W.M. Olde Damink[1], P.M. Rath[3], A. Paul[2], S. Nadalin[2], C.E. Broelsch[2], M. Malagò[2,4]. Dept of Surgery[1], University hospital Maastricht, Maastricht, The Netherlands, Dept of General, Visceral and Transplantation Surgery[2] and Institute of Medical Microbiology[3], University hospital Essen, Germany, Dept of Surgery[4], University College London, London, United Kingdom.

08.50 No beneficial effects of probiotics in primary sclerosing cholangitis (PSC): a randomized placebo-controlled cross-over study (p. 90)
F.P. Vleggaar[1], J.F. Monkelbaan[1], K.J. van Erpecum[1]. Dept of Gastroenterology[1], University Medical Centre, Utrecht, The Netherlands

09.00 Psychiatric side-effects and the fluctuations in related amino acids in the treatment of chronic hepatitis C infection (p. 91)
G. Bezemer[1], A.R. van Gool[2], J.M. Vrolijk[1], D. Fekkes[3], B.E. Hansen[1], S.W. Schalm[1], H.L.A. Jansen[1], R.J. de Knegt[1]. Depts of Gastroenterology and Hepatology[1], Psychiatry[2] and Neuroscience[3], Erasmus MC - University Medical Center, Rotterdam, The Netherlands

09.10 Development of a flexible accurate limited sampling model for monitoring tacrolimus after orthotopic liver transplantation: towards C4-monitoring (p. 92)
P. Langers[1], S.C.L.M. Cremers[2], R.R. Press[3], J. den Hartigh[3], A. Baranski[4], D.W. Hommes[1], B. van Hoek[1]. Depts of Gastroenterology and Hepatology[1], Clinical Pharmacy and Toxicology[3], and Surgery[4], Leiden University Medical Center, Leiden, The Netherlands, Dept of Medicine[2], Columbia University, New York, NY, USA

09.20 FibroScan superior to APRI in detecting significant liver fibrosis in chronic hepatitis B and C patients (p. 93)
J.F. Bergmann, C. Verveer, B.E. Hansen, H.L.A. Janssen, R.J. de Knegt, Dept of Gastentero-logyand Hepatology, Erasmus MC, University Medical Center Rotterdam, The Netherlands

09.30 Dilated portal tract veins are associated with a lower incidence of ischemic type biliary lesions after liver transplantation (p. 94)
W.R.R. Farid[1], A. Demirkiran[1], J. de Jonge[1], P. Zondervan[2], H.J. Metselaar[3], H.W. Tilanus[1], R. de Bruin[1], G. Kazemier[1]. Depts of Surgery[1], Pathology[2], and Gastroenterology and Hepatology[3], Erasmus MC University Medical Center Rotterdam, The Netherlands

09.40 TIPS for treatment of ascites: PTFE-covered stents superior to bare stents (p. 95)
J.J. Kuiper[1], H.R. van Buuren[1], P.M.T. Pattynama[2], R.A. de Man[1]. Depts of Gastroenterology and Hepatology[1], and Radiology[2], Erasmus MC, University Medical Center Rotterdam, The Netherlands

Vrijdag 5 oktober 2007

09.50 Predicting sustained HBeAg loss after treatment with peginterferon alpha-2b: development and validation of a practical model (p. 96)
E.H.C.J. Buster[1], B.E. Hansen[1,2], S. Zeuzem[3], S.W. Schalm[1], E.W. Steyerberg[4], H.L.A. Janssen[1]. Depts of Gastroenterology and Hepatology[1], Epidemiology and Biostatistics[2], and Public Health[4], Erasmus MC University Medical Center Rotterdam, The Netherlands, Medizinische Klinik I[3], Klinikum der Johann Wolfgang Goethe-Universität, Frankfurt am Main, Germany

Sectie Experimentele Gastroenterologie — Parkzaal

Voorzitters: R.C. van Tol en A. te Velde

10.30 Omeprazole treatment in rats leads to bacterial overgrowth in the proximal digestive tract and altered bile acid metabolism with increased amounts of conjugated deoxycholic acid (p. 97)
R.R. Sital[1], I.A. Boere[2], L.H. van Damme[3], F.W.M. de Rooij[4], J.L.D. Wattimena[4], R.W.F. de Bruin[2], A.H.M. van Vliet[1], H.Ph. Endtz[3], E.J. Kuipers[1], J.G. Kusters[1], P.D. Siersema[1]. Depts of Gastroenterology and Hepatology[1], Surgery[2], Medical Microbiology[3], and Internal Medicine[4], Erasmus MC - University Medical Center Rotterdam, The Netherlands

10.40 Dextran sodium sulfate-accelerated tumorigenesis in a novel conditional Apc mutant mouse model of colorectal cancer (p. 98)
P.J. Koelink[1], H.W. Verspaget[1], C. Breukel[2], C. Bosch[2], R. Fodde[3], R. Smits[3], E.C. Robanus Maandag[2]. Depts of Gastroenterology and Hepatology[1], Human Genetics[2], Leiden University Medical Center, Leiden and Dept of Experimental Pathology[3], Josephine Nefkens Institute, Erasmus University Medical Center, Rotterdam, The Netherlands

10.50 Colorectal neoplasia after liver transplantation is associated with higher proliferative activity, lower apoptosis and increased β-catenin expression compared with controls (p. 99)
M. Blom, W. Boersma-van Ek, G. Dijkstra, R.C. Verdonk, S. de Jong, J.H. Kleibeuker, E.B. Haagsma, J.J. Koornstra. Dept of Gastroenterology and Hepatology, University Medical Center Groningen, The Netherlands

11.00 MRP1 differentially modulates T lymphocyte and intestinal epithelial cell apoptosis (p. 100)

A. van Steenpaal[1], G. Dijkstra[1], H.H.J. Geuken[1], L.I.H. Bok[1], H. Moshage[1], M. Peppelenbosch[2], K.N. Faber[1]. Depts of Gastroenterology and Hepatology[1], and Cell biology[2], University Medical Center Groningen, University of Groningen, The Netherlands

11.10 High fat nutrition; a physiologic way to attenuate inflammation (p. 101)

T. Lubbers[1], J. De Haan[1], M. Hadfoune[1], M.D. Luyer[1], C.H. Dejong[2], W.A. Buurman[1], J.W. Greve[2]. Dept of General surgery[1], University of Maastricht and Dept of General surgery[2], University hospital Maastricht, The Netherlands

11.20 High expression of p53 and Kl67 and aneuploidy predict neoplastic progression in Barrett Esophagus (p.102)

M. Sikkema[1], M. Kerkhof[1], J.G. Kusters[1], P.M.H. van Strien[1], E.W. Steyerberg[2], H. van Dekken[3], E.J. Kuipers[1], P.D. Siersema[1]. Depts of Gastroenterology and Hepatology[1], Public Health[2] and Pathology[3], Erasmus MC – University Medical Center, Rotterdam, The Netherlands

11.30 Essential fatty acid deficiency in mice impairs intestinal function as reflected by fat malabsorption and reduced lactose digestion* (p. 103)

S. Lukovac, E.L. Los, F. Stellaard, E.H.H.M. Rings, H.J. Verkade. Groningen University Institute for Drug Exploration (GUIDE), Center for Liver, Digestive and Metabolic Diseases, Pediatric Gastroenterology, University Medical Center Groningen, University of Groningen, The Netherlands

11.40 Molecular mechanisms of microvillous inclusion disease* (p. 104)

M.R. Golachowska[1], J.F. Baller[2], R. Prekeris[3], D. Hoekstra[1], E.H. Rings[2], S.C.D. van IJzendoorn[1]. Depts of Cell Biology[1], section Membrane Cell Biology, Pediatrics[2], University Medical Center Groningen, The Netherlands and Dept of Cellular and Developmental Biology[3], School of Medicine, University of Colorado Health Sciences Centre, Denver, USA

Vrijdag 5 oktober 2007

11.50 Depletion of the colonic stem cell compartment upon conditional activation of the Hedgehog pathway (p. 105)
W.A. van Dop[1], A. Uhmann[2], M. Wijgerde[3], G.J. Offerhaus[4], G.E. Boeckxstaens[5], M.A. van den Bergh Weerman[6], D.W. Hommes[7], J.C. Hardwick[7], H. Hahn[2], G.R. van den Brink[1,7]. Center for Experimental Molecular Medicine[1], Dept. of Gastroenterology & Hepatology[5], Dept. of Pathology[6], Academic Medical Centre, Amsterdam, Dept of Reproduction and Development[3], Erasmus University Medical Centre, Rotterdam, Dept. of Pathology[4], University Medical Centre Utrecht, Dept. of Gastroenterology & Hepatology, University Medical Centre Leiden[7], The Netherlands, Institute of Human Genetics[2], Georg August University of Göttingen, Germany

12.00 Einde programma

Nederlandse Vereniging voor Gastroenterologie **Brabantzaal**

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

13.30 Early presence of intestinal tissue damage in multiple trauma patients (p. 106)
J.J. de Haan[1], J.P.M. Derikx[1], B. Relja[2], T. Lubbers[1], M.D. Luyer[1], W.A. Buurman[1], J.W. Greve[1], I. Marzi[2]. Dept of General Surgery[1], Maastricht University, Academic Hospital Maastricht, The Netherlands and Dept of Trauma Surgery[2], University Hospital, Johann Wolfgang Goethe University, Frankfurt am Main, Germany

13.40 Performance characteristics of faecal occult blood tests: which test to use for colorectal cancer screening (p. 107)
F.A. Oort[1], J.S. Terhaar sive Droste[1], M.E. Craanen[1], R.W.M. van der Hulst[2], H.A. van Heukelem[3], R.J.L.F. Loffeld[4], I.C.E. Wesdorp[5], R.L.J. van Wanrooy[1], L. de Baay[1], E.M. Mutsaers[1], S. van der Reijt[1], C.J.J. Mulder[1], Dept. of Gastroenterology and Hepatology[1], VU University Medical Centre, Amsterdam, Dept. of Gastroenterology and Hepatology[2], Kennemer Gasthuis, Haarlem, Dept. of Gastroenterology and Hepatology[3], Slotervaart Hospital, Amsterdam, Dept. of Internal Medicine[4], Zaans Medical Centre, Zaandam, Dept. of Gastroenterology and Hepatology[5], St. Lucas Andreas Hospital, Amsterdam, The Netherlands

13.50 Primary colonoscopy screening for colorectal cancer in a workplace-based community: first results of participation and acceptance (p.108)
C. Khalid-de Bakker, D. Jonkers, W. Hameeteman, A. Masclee, R. Stockbrügger. Dept of Gastroenterology, University Hospital Maastricht, The Netherlands

14.00 Risk stratification among individuals attending population-based sigmoidoscopy screening (p. 109)
L. Hol, M.E. van Leerdam, M. van Ballegooijen, E.J. Kuipers. Depts of Gastroenterology and Hepatology, and Public Health, Erasmus MC, University Medical Center, Rotterdam, The Netherlands

14.10 First Report: Triage for colorectal cancer with CT colonography with limited bowel preparation in a FOBT positive screening population (p. 110)
M.H. Liedenbaum[1], A.F. van Rijn[2], A. de Vries[1], P. Fockens[2], E. Dekker[2], J. Stoker[1], [1]Department of Radiology, Academic Medical Centre, Amsterdam, [2]Department of Gastroenterology, Academic Medical Centre, Amsterdam, The Netherlands

14.20 How safe are Dutch guidelines for endoscopic follow-up of colonic adenomas? (p. 111)
B.K. Deressa, B.E. Schenk, J. Vecht. Dept of Gastroenterology, Isala Klinieken Zwolle, The Netherlands

14.30 Autofluorescence endoscopy improves the detection of colorectal adenomas in subjects with hereditary non polyposis colorectal cancer or familial colorectal cancer; a back-to-back colonoscopy study (p. 112)
D. Ramsoekh[1], J. Haringsma[1], J.W. Poley[1], H. van Dekken[2], E.W. Steyerberg[3], M.E. van Leerdam[1], E.J. Kuipers[1] Depts of Gastroenterology and Hepatology[1], Pathology[2], Public Health[3], Erasmus MC University Medical Center, Rotterdam, the Netherlands

14.40 Proton pump inhibitors and the risk of colorectal cancer (p. 113)
E.M. van Soest[1,2], L.G.M. Van Rossum[4], J.D. Dieleman[2], M.G.H. van Oijen[2,4], P.D. Siersema[1], M.J.C.M. Sturkenboom[2,3], E.J. Kuipers[1]. Depts of Gastroenterology and Hepatology[1], Medical Informatics[2], Epidemiology and Biostatistics[3], Erasmus University Medical Center, Rotterdam and Dept of Gastroenterology and Hepatology[4], Radboud University Nijmegen Medical Center, The Netherlands

14.50 Efficacy of colonoscopy, sigmoidoscopy and barium enema in reducing the incidence of CRC (p. 114)
S.A. Mulder[1], E. van Soest[2], J. Dieleman[2], M.E. van Leerdam[3], L.G. van Rossum[4], R.J.Th. Ouwendijk[1], E.J. Kuipers[3]. Dept of Gastroenterology[1], Ikazia Hospital Rotterdam, Medical Informatics[2], Dept of Gastroenterology and Hepatology[3], Erasmus University Medical Center, Rotterdam and Dept of Gastroenterology and Hepatology[4], Radboud University Nijmegen Medical Center, Nijmegen, The Netherlands

15.00 Association between JC virus and the development of colorectal neoplasia after liver transplantation (p. 115). *M. Blom[1], M. Selgrad[2], S. de Jong[1], L. Fini[2], G. Dijkstra[1], R.C. Verdonk[1], S. Williams[2], R. Meyer[2], A. Goel[2], J.H. Kleibeuker[1], E.B. Haagsma[1], L. Ricciardiello[2], C.R. Boland[2], J.J. Koornstra[1]. Dept of Gastroenterology and Hepatology[1], University Medical Center Groningen, The Netherlands and Dept of Gastroenterology[2], Baylor University Medical Center, Dallas, TX, USA*

15.10 Sequential versus combination chemotherapy with capecitabine, irinotecan, and oxaliplatin in advanced colorectal cancer (ACC).
A Dutch Colorectal Cancer Group (DCCG) phase III study (p. 116)
A. Cats[1], M. Koopman[2], J. Douma[3], J. Wals[4], A.H. Honkoop[5], F.L.G. Erdkamp[6], R.S. de Jong[7], C.J. Rodenburg[8], L. Mol[2], N.F. Antonini[1], C.J.A. Punt[2]. Dept. of stomach-intestine-liver[1], Netherlands Cancer Institute, Amsterdam, Dept. of Internal Medicine[2], Radboud University Medical Centre, Nijmegen, Dept. of Internal Medicine[3], Rijnstate Hospital, Arnhem, Dept. of Internal Medicine[4], Atrium Medical Centre, Heerlen, Dept. of Internal Medicin[5]e, Isala Hospital, Zwolle, Dept. of Internal Medicine[6], Maasland Hospital, Sittard, Dept. of Internal Medicine[7], Martini Hospital, Groningen, Dept. of Internal Medicine[8], Meander Hospital, Amersfoort, The Netherlands

15.20 Einde programma, theepauze in expositiehal.

Consensus / Richtlijn CBO Perioperatieve Voeding *(NESPEN en NVGIC)* **Baroniezaal**

Voorzitters: P. Go en C.H.C. Dejong

13.30 Implementation of Guidelines – Opportunities and Threats
Mevr. dr. T. van der Weijden,
Afdeling Huisartsgeneeskunde, Universiteit Maastricht

13.55 The Guideline – Forcipal Delivery or Vacuum Extraction?
Mevr. drs . E.B. Haverkort,
Afdeling Diëtetiek, Academisch Medisch Centrum

14.15 Changing Perioperative Practice in the Netherlands: the CBO Breakthrough Project Periop 1&2
Mevr. J. Maessen,
Afdeling Chirurgie, Academisch Ziekenhuis Maastricht

14.35 Changing Perioperative Practice: the Arctic Circle Upper GI Experience
Dr. K. Lassen,
Dept of Gastrointestinal Surgery, University Hospital of Tromso, Norway

15.00 Einde programma, theepauze (expositiehal)

Tytgat lecture **Parkzaal**

Voorzitter: P.L.M. Jansen.

13.30 Vascular liver diseases
Professor Dominique-Charles Valla, Service d'Hépatologie
Pôle des Maladies de l'Appareil Digestif, Hôpital Beaujon, Clichy, France

International Teaching Session **Parkzaal**

Voorzitters: G. Bouma en G. Dijkstra

14.00 The role of PPARs as fatty acid sensors controlling metabolism and inflammation
Dr. S. Kersten, Ph.D., Voeding, Metabolism and Genomics group, Division of Human Nutrition Wageningen University

14.30 PPAR agonists in gastroenterology and hepatology".
Dr. Pierre Desreumaux, Clinique des Maladies de l'Appareil Digestif et de la Nutrition, Hopital Swynghedauw, Lille Cedex, France.

15.00 Einde programma, theepauze (expositiehal)

Vrijdag 5 oktober 2007

Sectie Endoscopie Verpleegkundigen en Assistenten **Diezezaal**

10.00 – 10.30 uur	Ontvangst met koffie
10.30 – 11.30 uur	Sessie over de verpleegkundig endoscopist Met de volgende sprekers: *Dr. J.J. Koornstra,MDL-arts, UMC Groningen* *Mevr. M. van de Kerkhof, verpleegkundige, VieCuri Venlo* *Prof. dr. P.D. Siersema, MDL-arts, UMC Utrecht*
11.30 – 11.40 uur	Forumdiscussie met deze drie sprekers
11.45 – 12.30 uur	Ledenvergadering
12.30 – 13.45 uur	Lunchbuffet in Kempenhal
13.45 – 14.15 uur	Clostridium en M.R.S.A., *De heer H. Immink, desinfectie expert Nijmegen*
14.15 – 14.45 uur	Kwaliteitsmeting biopsietangen, *Mevr. C. de Jong, verpleegkundige, LUMC Leiden*
14.45 – 15.00 uur	Bekkenbodemproblematiek, *Mevr. dr. S. Veltkamp, chirurg, Ziekenhuis Amstelland. Amstelveen*
	Einde programma

Vereniging voor Maag Darm Lever Verpleegkundigen **Auditorium**

09.30 - 09.45 uur	Ontvangst met koffie en thee
09.45 - 10.00 uur	Welkomstwoord *W. Goverde, voorzitter VMDLV*
10.00 - 10.20 uur	Ischemie poli *Dr. J.J. Kolkman, MDL-arts, MST Enschede*
10.20 -10.40 uur	Ischemie poli *Mw. A. Goossens, verpleegkundige, Ischemie poli MST Enschede*
10.40 - 11.10 uur	Preventie van infecties o.a. clostridium *Mw. M. Vrijaldenhoven, AMD, UMC St. Radboud Nijmegen*
11.10 –11.30 uur	Clostridium bestrijding met faecesdonatie *Prof. dr. J.F.W.M. Bartelsman, MDL-arts, AMC Amsterdam*
11.30 - 12.00 uur	Ondervoeding en risico op refeeding in het ziekenhuis *Mevr. J. van de Broek, diëtiste, UMC St. Radboud Nijmegen*
12.00 - 13.30 uur	Lunch
13.30 - 14.00 uur	Acute pancreatitis, Landelijke studie *Drs. M.G.H. Besselink, UMC Utrecht*
14.00 - 14.30 uur	Nieuwe medicatie en toediening bij IBD *Dr. D.J. de Jong, MDL-arts, UMC St. Radboud Nijmegen*
14.30 - 14.50 uur	IBD nurse practioners *Mw. J. Gaarenstroom, Nurse Practioner, UMC Utrecht*
14.50 -15.00 uur	Afsluiting *Dhr. W. Goverde*
15.00 - 16.00 uur	Borrelen en netwerken

Does ursodeoxycholic acid protects against apoptotic liver injury?

T.E. Vrenken, L. Conde de la Rosa, M.H. Schoemaker, M. Buist-Homan, H. Moshage. Dept of Gastroenterology and Hepatology, University Medical Center Groningen, Groningen, The Netherlands
(MLDS-project MWO 02-1)

Background: Patients with chronic liver diseases like primary biliary cirrhosis, benefit from treatment with the bile acid ursodeoxycholic acid (UDCA). In addition, *in vitro* studies have shown that the taurine-conjugate of UDCA, tauroursodeoxycholic acid (TUDCA), protects against bile acid –induced apoptosis of hepatocytes. The protective effect of TUDCA in other models of liver cell death has not been investigated yet. Therefore, the AIM of the present investigation was to elucidate the mechanism of the protective effect of TUDCA and to investigate whether TUDCA protects against other inducers of hepatocyte death. Materials and Methods: *in vitro* studies were performed using primary cultured rat hepatocytes or the human hepatoma cell line HepG2.ntcp. After attachment, hepatocytes were exposed to death-inducing stimuli: the superoxide anion donor menadione as a representative reactive oxygen species (ROS), the hydrophobic bile acid glycochenodeoxycholic acid (GCDCA), an agonistic antibody against Fas (αFas) and the cytokine tumor necrosis factorα (TNFα) + Actinomycin-D (ActD) as a model for acute liver failure. Necrotic cell death was determined by Sytox green staining and apoptotic cell death by acridine orange staining, caspase-3 activity assay and caspase-3,6,8,9 processing. The MAP kinases JNK, ERK and p38 and the PI-3-kinase/Akt pathway were inhibited using specific inhibitors. Results: TUDCA inhibited GCDCA-induced apoptosis, even when added 2 hrs after GCDCA. The protective effect was dependent on intact ERK and PI-3-kinase signaling, but not related to NF-kB-activation or ROS-scavenging by TUDCA. Furthermore, GCDCA-induced apoptosis was dependent on JNK-activity. TUDCA did not protect against superoxide anion-induced cell death or TNF/ActD-induced cell death.
Conclusion: TUDCA protects against bile acid induced liver cell toxicity, but not against other inducers of apoptotic cell death. Therefore, our results suggest that TUDCA is protective in liver diseases associated with elevated bile acid levels, such as chronic cholestatic liver diseases, but not in cytokine/imm une-mediated liver diseases, like acute liver failure. The protective effect of TUDCA is dependent on intact ERK and PI-3-kinase signaling.

Investigation of the applicability of antimicrobial peptides against *Helicobacter pylori*

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(MLDS-project WS 01-42)

Symptomatic *Helicobacter pylori* infections demand triple therapy to eradicate the bacterium. Antimicrobial peptides provide a rapid expanding source of new bactericidal agents that are indispensable for filling-in the gap in potent therapeutics inflicted by increased resistance of bacteria to conventional antibiotics. Antimicrobial peptides generally have a net positive charge and an amphipatic character, endowing interaction with the membrane of the micro-organism. The membrane is destabilized and essential molecules can leak out. The unique conditions of the niche of *H. pylori* as present in the stomach, e.g., low pH, proteolytic activity, and a mucous environment, hamper the bactericidal activity of defence systems. The purpose of this study was to investigate whether antimicrobial peptides are efficacious *in vitro* against *H. pylori*, considering its niche. *H. pylori* was screened against previously developed synthetic antimicrobial peptides, that effectively kill a large series of bacterial pathogens, including antibiotic-resistant variants using a sensidisk-assay and a modification of the 'MIC method for cationic antimicrobial peptides' according to Hancock. One particular compound, the human cathelicidin peptide LL-37, emerged as potential candidate. Further study on LL-37 revealed the following: The all-D isomer possessed a higher bactericidal activity indicating proteolytic cleavage of LL-37 by *H. pylori*. Sub-lethal doses of LL-37 increased the sensitivity toward the antibiotic amoxicillin in a clinical amoxicillin-resistant strain of *H. pylori.* A second generation of LL-37 variants were designed that were smaller and less sensitive to pepsin digestion. The fragment of LL-37 corresponding to the amino acids 13-31 appeared the smallest optimal anti-helicobacter peptide. Sublethal dosis of this peptide reduced the killing concentration of amoxicillin by a factor four. Conclusively, variants of the human cathelicidin peptide are membrane active antimicrobial peptides that shows potential activity against *H. Pylori*.

Role of L-SIGN in pathogenesis, antigen presentation and cellular interactions

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Maag Lever Darm Stichting[4] (grant WS 01-36), AIDS Fonds[5] (grant 5008), NWO[6] Aspasia *(grant 015 000 023)*

The C-type lectin L-SIGN is expressed on liver sinusoidal endothelial cells (LSEC) in the liver. These LSECs, with antigen presentation and tolerisation functions, form a fenestrated endothelium lining the sinusoid. The L-SIGN homologue DC-SIGN, expressed on dendritic cells (DCs), was identified as a receptor for HIV-1 envelope glycoprotein gp120. By now a plethora of pathogen and cellular ligands for DC-SIGN have been described. In this project the function of L-SIGN was investigated, describing its carbohydrate binding characteristics, pathogen and cellular ligands.
The interaction of both L-SIGN and DC-SIGN with hepatitis C envelope proteins was investigated using HCV virus like particles (VLPs) composed of the highly glycosylated envelope proteins E1 and E2. We demonstrate that both DC-SIGN and L-SIGN specifically bind to HCV VLPs. Our data further demonstrate that DC-SIGN is the main receptor on DCs to capture and internalize HCV. Strikingly, in contrast to other ligands, HCV is not targeted to lysosomal compartments but is retained in early endosomes. Consequently, HCV circumvents rapid lysosomal degradation, which may be vital to its dissemination. In addition, *in situ* binding studies to liver tissue revealed HCV binding to the L-SIGN-expressing LSECs but not to its main target the hepatocyte. These data suggest that HCV employs DC-SIGN and L-SIGN for viral dissemination. However, using a combination of HCV VLPs with anti-HCV antibodies, combined to immune complexes, we demonstrate that both L-SIGN and DC-SIGN are able to present HCV-IC derived antigens to $CD4^+$ T cells. Therefore L-SIGN could have a dual function in HCV infections by mediating both viral dissemination and antigen presentation.
Besides pathogen derived ligands, L-SIGN also interacts with self ligands. We demonstrated that L-SIGN is able to interact with colon carcinoma cell-derived antigens, neutrophils and monocytes. In the case of neutrophils, L-SIGN is able to mediate tethering and rolling of neutrophils over an L-SIGN-positive cell layer under shear stress mimicking the blood flow in the sinus. This indicates a role for L-SIGN in the targeting of these cells to the liver sinusoid.
Altogether our data demonstrate a role for L-SIGN in homeostasis by interacting with neutrophils and monocytes, and a role in pathogenesis by interaction with and internalization of HCV.

The human small heterodimer partner (SHP) promoter contains independent and unconventional 9-cis retinoic acid- and bile salt-responsive elements

M.O. Hoeke, J. Heegsma, K.N. Faber, Dept of Gastroenterology and Hepatology, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands

The small heterodimer partner (SHP) is an important regulator of bile salt homeostasis. It represses key genes in liver and intestine involved in bile salt homeostasis. SHP itself is positively regulated by the Farnesoid X Receptor (FXR). FXR functions as a heterodimer with the Retinoid X Receptor α (RXRα). FXR is activated by the bile salt cheno-deoxycholic acid (CDCA) and RXRα by the vitamin A derivative 9-cis retinoic acid (9cRA). Previously, a FXR-responsive element (FXRE) was identified at position -291/-279 in the hSHP promoter (Goodwin et al., 2000). Recently, we found that 9cRA differentially affects CDCA-induced FXR target gene expression. 9cRA simultaneously stimulates and fully represses CDCA-induced expression of SHP and the bile salt export pump (BSEP), respectively. In vitro binding studies revealed that 9cRA inhibits binding of FXR/RXRα to the FXRE. Here, we studied the molecular mechanism of the co-stimulatory effect of CDCA and 9cRA on SHP expression in a human intestinal cell line.DLD-1 (human colon carcinoma) cells were transiently transfected with hFXR- and hRXRα-expression plasmids and cultured with/without CDCA and/or 9cRA. Deletion mutants of a 579bp hSHP promoter element in a luciferase reporter plasmid were generated to determine the location of CDCA and/or 9cRA responsive elements. Transcription of hSHP was quantified by Q-PCR and the promoter activity of hSHP was determined by luciferase reporter assays.CDCA and 9cRA induce transcription of SHP in DLD-1 cells 39- and 12-fold, respectively. Maximal SHP expression (98-fold) was observed when DLD-1 cells are co-exposed to both ligands. Similar regulation was observed for the -569/+10 hSHP promoter element. SHP promoter fragments that were 5' truncated up to position -122 still showed CDCA-induced luciferase expression. This DNA fragment does not contain a sequence similar to the previously identified FXREs. 9cRA dependent activation was lost when truncating the hSHP promoter to -278. Induction of transcription by CDCA and 9cRA were dependent of FXR and RXRThe hSHP promoter contains a novel bile salt-responsive element, which is different from the previously suggested FXRE at position -291/-279. A separate RXRα/9cRA-response element is present at position -303/-279. Independent regulation of hSHP by bile salts and 9cRA may be important to maintain adequate levels of bile salt synthesis and transport during cholestatic conditions that are associated with reduced vitamin A levels.

ATP8B1 and CDC50A physically interact and co-localize in the canalicular membrane of polarized WIF-B9 cells.

D.E. Folmer, K.S. Ho-Mok, R.P.J. Oude Elferink, C.C. Paulusma. AMC Liver Center, Academic Medical Center, Amsterdam, The Netherlands

Mutations in *ATP8B1* cause progressive familial intrahepatic cholestasis type 1, benign recurrent intrahepatic cholestasis type 1, and are associated with intrahepatic cholestasis of pregnancy. ATP8B1 is a type 4 P-type ATPase involved in phosphatidylserine translocation, and has an important role in maintaining the resistance of the hepatocyte canalicular membrane to hydrophobic bile salts.
We have recently shown in non-polarized cells that ATP8B1 requires an accessory protein, termed CDC50, for endoplasmic reticulum exit and phosphatidylserine translocase activity at the plasma membrane. The aim of this study was to determine whether an ATP8B1-CDC50 interaction is important in the liver.
Using real-time PCR, we examined the relative expression levels of *CDC50* mRNA in liver and WIF-B9 cells, a hepatocyte model cell line that forms large apical vacuoles that are equivalent to the bile canalicular lumen. Stable WIF-B9 cell lines co-expressing green fluorescent protein-tagged ATP8B1 (ATP8B1-GFP) and HA-tagged CDC50 (HA-CDC50) were generated by lentiviral transduction. In these cells, we studied the localization of the proteins using confocal laser scanning microscopy. Physical interaction of ATP8B1-CDC50 was studied by co-immunoprecipitation using anti-HA and anti-CDC50A antibody.
Real-time PCR revealed that both mouse liver and WIF-B9 cells preferentially express *CDC50A* mRNA, whereas *CDC50B* mRNA is hardly detectable. In polarized WIF-B9 cells, ATP8B1-GFP and HA-CDC50A co-localized in the canalicular membrane and in subapical vesicles. We also observed some co-localization of ATP8B1-GFP and HA-CDC50A in the basolateral membrane of WIF-B9 cells. In addition, ATP8B1-GFP co-precipitated with both HA-CDC50A and endogenous CDC50A.
In conclusion, we demonstrate that ATP8B1-GFP and HA-CDC50A are binding partners in WIF-B9 cells. Our data suggest that CDC50A is the potential accessory protein for ATP8B1 in the hepatocyte, and an important determinant for ATP8B1-mediated activity. Hence, mutations in the *CDC50A* gene potentially play a role in cholestatic syndromes associated with ATP8B1 deficiency.

Unconjugated bile salts shuttle through hepatocyte peroxisomes for glycine or taurine conjugation

K. Rembacz, J. Woudenberg, E. Jonkers, F.A.J. van den Heuvel, T.E. Vrenken, H. Moshage, F. Stellaard, K.N. Faber. Dept of Gastroenterology and Hepatology, University Medical Center Groningen, The Netherlands

Bile salts are synthesized in the liver and are required for efficient dietary fat digestion. Efficient function and enterohepatic cycling of bile salts require that they are conjugated to taurine or glycine. We showed that the enzyme responsible for bile salt conjugation, bile acid-CoA:amino acid N-acyltransferase, resides in hepatocyte peroxisomes (Pellicoro et al., Hepatology 2007). This implies the presence of yet unknown bile salt transporters in the peroxisomal membrane. In this study we use deuterium-labeled cholic acid (D4-CA) to study trans- and intra-cellular bile salt transport in cultured rat hepatocytes.

Primary rat hepatocytes were cultured on collagen-coated plates in William's medium E (WME). Twenty four (24) hours after plating, the cells were exposed to different concentrations D4-CA (here presented for 100 μM). In time, media and cell samples were collected and the levels of D4-CA, D4-tauro-CA (D4-TCA) and D4-glyco-CA (D4-GCA) were quantified by liquid chromatography-tandem mass spectrometry (LC/MS/MS). Rat hepatocytes were exposed for 30 min to D4-CA and analyzed by digitonin assays to establish the subcellular location of D4-CA, D4-TCA and D4-GCA. Release of marker proteins (GAPDH for cytosol; catalase for peroxisomes) was determined by Western blotting.

Within 24 hours, cultured rat hepatocytes efficiently converted D4-CA (input 100 uM) to D4-TCA (± 23 uM) and D4-GCA (± 68 uM) in the medium. The high level of D4-GCA was due to the presence of glycine in WME. D4-TCA and D4-GCA were already detectable in hepatocytes after 5 minutes of exposure to D4-CA. Maximal intracellular accumulation of D4-TCA (± 220 uM) and D4-GCA (± 380 uM) was observed 3 hours after addition of D4-CA to the medium. Treatment of D4-CA-exposed hepatocytes with 30 ug/ml digitonin led to the complete release of GAPDH and D4-CA from hepatocytes, indicating a cytosolic location of D4-CA. Significant amounts of D4-TCA were retained in the cell fraction after treatment with 30 or 150 ug/ml digitonin, showing a similar extraction profile as the peroxisomal marker catalase.

We established an in vitro assay to study the dynamics of bile salt conjugation and intra- and trans-cellular transport in cultured rat hepatocytes. Significant amounts of de novo conjugated bile salts accumulate in an intracellular compartment with biochemical characteristics of peroxisomes. This is the first evidence that unconjugated bile salts shuttle through intracellular organelles for conjugation.

The active metabolite of leflunomide, A77 1726, protects rat hepatocytes against bile acid-induced apoptosis

T.E. Vrenken, M. Buist-Homan, A.J. Kalsbeek, K.N. Faber, H. Moshage. Dept of Gastro-enterology and Hepatology, University Medical Center Groningen, The Netherlands

Background Leflunomide is an immunosuppressive and anti-inflammatory drug belonging to the DMARD (disease-modifying antirheumatic drug) class of drugs. Leflunomide is converted to its active metabolite teriflunomide (A77 1726). It has been postulated that the anti-inflammatory and immunosuppressive effects of leflunomide on inflammatory and immune cells are due to inhibitory effects on signal transduction pathways, in particular the JNK and the NF-κB pathway. These signaling pathways are critically involved in the regulation of apoptosis in hepatocytes.
Aim Does teriflunomide (A77 1726) protects hepatocytes against apoptosis induced by different stimuli?
Methods Primary rat hepatocytes were exposed to glycochenodeoxycholic acid (GCDCA, 50 μM, 4 hrs), to TNFα (20 ng/ml) in combination with actinomycin D (200 ng/ml, TNF/ActD) for 16 hrs, or to a cytokine mixture (CM, 16 hrs) consisting of mTNFα, hIL-1β, rIFNγ and LPS, or to the superoxide anion donor menadione (50 μM, 12 hrs). A77 1726 (1-50 μM) was added prior to the apoptotic stimuli. LY294002 (50 μM) was used to block the PI3-kinase/Akt signaling pathway. ERK, JNK and p38 MAP kinases were inhibited using 10 μM U0126, 5 μM SP600125 or 10 μM SB203580, respectively. The mRNA-level of the NF-κB-regulated gene iNOS was measured by qPCR. Caspase-3-like activity was measured with a fluorometric assay, and necrosis was monitored using Sytox Green.
Results A77 1726 dose-dependently reduces GCDCA-induced caspase-3 activity, but has no effect on TNF/ActD- or menadione-induced apoptosis. A77 1726 was still protective when added up to 2 hrs after GCDCA. Furthermore, A77 1726 does not induce necrosis in GCDCA-treated cells. Both U0126 and SB203580 partially reduce the protective effect of A77 1726, whereas the other inhibitors had no effect. CM-induced iNOS mRNA levels were not affected by A77 1726. A77 1726 did not induce caspase-3 activity in TNF-treated hepatocytes.
Conclusion A77 1726, the active metabolite of leflunomide, is protective against bile acid induced apoptosis, but not against cytokine or oxidative stress induced apoptosis. ERK and p38, the anti-apoptotic MAP-kinase family members, play a major role in the protection of A77 1726. Furthermore, A77 1726 does not inhibit cytokine-induced NF-κB activation, and does not sensitize hepatocytes to TNF-induced apoptosis. Thus, leflunomide could be used as treatment in chronic liver diseases accompanied by elevated bile acid levels and inflammation.

Diagnostic algorithm for pretreatment staging of patients with oesophageal cancer

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Introduction: Guidelines for diagnosis and treatment of oesophageal cancer recommend a set of investigations for the standard preoperative work-up: computed tomography of chest and abdomen (CT), endoscopic ultrasonography (EUS) and external ultrasonography of the neck (US). Yet there is no recommended order for these investigations.
Methods: To construct an algorithm, the three recommended staging modalities (CT/EUS/US) were examined based on data collected in a series of consecutive patients. The six possible algorithms that can be constructed were evaluated in terms of: efficiency, accuracy and burden. Efficiency was assessed by comparing the algorithms on the minimal number of investigations needed to detect all patients with incurable disease due to distant metastases or local irresectability. Accuracy of the various algorithms was assessed by comparing the total number of false-positives. Test burden was evaluated using results from a previous study (modified Likert scale).
Results: Between October 2002 and December 2005, 315 patients with oesophageal cancer were evaluated. Incurable disease due to distant metastases or local irresectability was observed in 73 patients. Calculating efficiency, the minimal number of investigations needed to detect these incurable patients were: US-CT-EUS 151, US-EUS-CT 138, CT-US-EUS 135, CT-EUS-US 118, EUS-US-CT 115, EUS-CT-US 111. Without using an algorithm, a total of 219 investigations would be needed. Evaluating accuracy of the various algorithms, numbers of false-positive test results were: US-CT-EUS 10, US-EUS-CT 9, EUS-US-CT 7, CT-US-EUS 7, EUS-CT-US 6, CT-EUS-US 5. Performing all three investigations in every patient results in a total of 17 false-positive test results. Mean burden scores for every algorithm to detect all patients with incurable disease were: US-CT-EUS 8.8, US-EUS-CT 8.8, EUS-US-CT 7.9, EUS-CT-US 7.6, CT-US-EUS 7.0, CT-EUS-US 6.3. The total burden score for a patient undergoing all three tests is 13.5.
Conclusion: The algorithm CT-EUS-US proved to be most accurate and induced the least burden. Although ranking only third best in efficiency, results differed only marginally from the two algorithms which ranked best in efficiency. Introduction will probably require some logistic adjustments. However, decreasing the number of unnecessary investigations by using this algorithm in pretreatment staging of patients with oesophageal cancer would improve the diagnostic process considerably.

No additional value of bronchoscopy after EUS in the preoperative assessment of patients with oesophageal cancer at or above the carina

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Introduction: Oesophageal cancer is an aggressive disease with a strong tendency to infiltrate into surrounding structures. Especially tumours at or above the carina are associated with early invasion of the tracheobronchial tree, precluding radical surgical resection. Endoscopic ultrasonography (EUS) is considered the most accurate diagnostic modality to determine the T-stage of the tumour. In the preoperative work-up for patients with tumours at or above the carina, it is recommended to perform a bronchoscopy (with biopsy on indication) to exclude airway invasion. Aim of the present study is to determine the additional value of bronchoscopy (with biopsy on indication) for detecting invasion of the tracheobronchial tree after having performed EUS in the preoperative assessment of patients with oesophageal cancer at or above the carina. Methods: Between January 2003 and December 2006, 45 patients were analysed in our department for histologically proven oesophageal cancer at or above the carina. All patients underwent both EUS and bronchoscopy (with biopsy on indication) in the preoperative assessment of local resectability. Results: After extensive diagnostic work-up 19 of 45 patients (42%) were eligible for potentially curative oesophagectomy. Distant metastases were found in 13 of 26 patients (50%) not suitable for curative surgery. In the 13 other patients (50%) local irresectability (T-stage 4) due to invasion of vital structures was described on EUS: invasion of the aorta in three patients, invasion of the lung in eight patients; in two patients invasion of the tracheobronchial tree was described, which was confirmed by bronchoscopy with positive biopsy results. Therefore, no additional value of bronchoscopy after EUS was seen in this cohort of patients.
Conclusion: For patients with newly diagnosed oesophageal tumours at or above the carina, no additional value of bronchoscopy (with biopsy on indication) to exclude invasion of the tracheobronchial tree is seen after performing EUS in a specialised centre. Even though based on small numbers, we conclude that bronchoscopy is not indicated if no invasion of the airways is identified on EUS.

Improving staging accuracy in colorectal carcinomas by sentinel node mapping: a comparative study

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In patients with colorectal carcinoma the prognosis is highly dependent on lymph node stage. However, 25-30% of patients with Dukes B (N0) carcinoma develop local recurrences or distant metastases within 5 years. This suggests that current staging techniques are insufficient. The aim of this study was to analyse whether sentinel node (SN) mapping improves staging in these patients. Patent blue (1-2cc) was injected intratumorally in 54 patients with colonic carcinoma and 22 patients with rectal carcinoma direct after colonic resection or total mesorectal excision (TME). Patients with T4 tumours were excluded. Patients with rectal carcinoma received pre-operative short course radiotherapy. Neo-adjuvant chemotherapy was not administered. All lymph nodes were examined by conventional haematoxylin and eosin stained sections. If the sentinel node was negative for metastasis, additional sections were immunostained with antibodies against cytokeratines (Cam5.2 and CK20) and polyglycopeptides (BerEp4) for the detection of micrometastatic disease.A SN was identified in 65 of 76 patients (85%). It accurately predicted nodal status in 62 patients with three false negative SNs (sensitivity 95%). In eight of the 22 lymf node positive patients, the sentinel node was the only positive node. Of the 43 lymph node negative (N0) patients, eight were upstaged by immunohistochemistry (19%). The detection of micrometastatic disease in N0 patients was related to depth of tumour invasion ($p<0.05$). There was a significant difference in SN identification in patients who underwent colonic resection compared to TME. Ten out of the 11 unsuccessful SN procedures were found in the TME group. False negative sentinel nodes were more frequently found in patients who received pre-operative radiotherapy ($p=0.02$).
Conclusion: Sentinel node mapping can accurately predict nodal status in patients with colonic carcinomas. Additional immunohistochemical analysis upstages almost 20% of N0 patients, which might identify a patientgroup that may benefit from adjuvant therapy. However, sentinel node mapping is less reliable in patients with rectal carcinomas who underwent TME with pre-operative short course radiotherapy.

Are micro-metastases in colon cancer a predictor for the delopment of distant metastases?

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Colon cancer is the second most commonly diagnosed malignancy in the Netherlands. One of the most important predictors for survival in patients with colon cancer is the lymph node status. In most countries, patients with curatively resected colon cancer without nodal tumor involvement do not receive adjuvant therapy (chemotherapy) because there is still no evidence that this is beneficial.However, more than 30% of these patients will develop loco-regional recurrence or distant metastases. A possible reason could be that more than 70% of the positive lymph nodes are < 2 mm or less and that they are likely to be missed during conventional gross pathological examination of the specimens.The purpose of this study was to evaluate if patients with micro-metastases are at higher risk for developping distant metastases.In the period January 2000 to January 2002, 137 patients underwent curative surgery for colon cancer. If the patients had a Dukes B colon carcinoma additional staining and sectioning on the lymph nodes were performed retrospectively. Lymph nodes were examined using 4 multilevel sections at 250-µm intervals and stained with Pan-Cytokeratine (LU-5).There were 61 patients with a Dukes B colon carcinoma.The mean age was 76 years(43-89), ratio man:women 33:28 with a median follow-up of 47 months(1-89 months).Thirteen patients developped metastases in time and 48 patients did not develop metastases. The mean number of lymph nodes was 7 (1-12). After additional staining and sectioning in 4 of the 13 (31%) and 7 of the 48 (15%) patients micro-metastases were detected.
Conclusion: Patients with micro-metastases develop significant more distant metastases in time. Further studies are needed to investigate whether these patients benefit from adjuvant therapy.

Laparoscopic liver resections: initial experience in a University Hospital setting

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Laparoscopic liver resections are gaining popularity world wide, but experience in the Netherlands is still limited. This study was conducted to assess the feasibility and safety of laparoscopic liver surgery in our unit. All patients treated with laparoscopic liver resections in the years 2003 to 2007 were included in this retrospective study using a prospectively collected database. This group was matched with a group of patients undergoing the same type of liver resection as an open procedure. Pre-operative diagnosis included benign and malignant liver lesions. Pre-operative assessment consisted of pre-operative multi-disciplinary consent and tumour limited to the left lateral liver segments requiring anatomical resection of segment II and III. In the laparoscopic approach group, liver transection was performed with harmonic scalpel, portal pedicles and hepatic veins were stapled. Primary outcomes were complications. Secondary outcomes were conversion, blood loss, length of operation, and length of stay. Data were analysed according to the intention to treat principle.The laparoscopic approach for left lateral resection (bisegmentectomy 2 and 3) was performed in eight patients (group I, one male, seven female) with a median age of 52 [range 34-82] years. In the open group, eight of 34 patients were matched for the same type of resection (group II, five male, three female, median age 63.5 [range 32-77] years). There were two minor complications in the laparoscopic group compared with two moderate complication in the open group. In the laparoscopic group there were 2 conversions (25%) due to tumour size and close relation with the liver vein. The median blood loss was 100cc [range 50-750] in the laparoscopic group versus 550cc [range 250-750] in the open group. The median operation time in group I was 119 [range 106-261] minutes compared to 176 [range 97-229] minutes in group II. The median length of stay was 7 [range 5-10] days in group I versus 6 [4-10] days in group II. There were no deaths. In the laparoscopic group there were 6 benign lesions and 3 malignant tumours (median tumour size 3.6 [range 1-10.5] cm). In the open group there was one benign lesion and 8 malignant tumours (median tumour size 2.5 [range 1.3-10] cm).Left lateral resection of liver tumours is feasible and safe using laparoscopic approach. It may be appropriate to consider this as the standard approach in young females with benign liver tumours in the not too distant future.

Management in patients with liver cirrhosis and an umbilical hernia: conservative versus elective surgical treatment

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Patients with liver cirrhosis and ascites are at high risk of developing an umbilical hernia. The expectance that surgical management in these patients is associated with high morbidity and mortality often leads to avoidance of operative treatment. However, conservative management may ultimately lead to serious complications as well. The objective of this study was to compare the outcome in our series of operative versus conservative treatment of these patients. In the period from 1990 to 2004, 34 patients with an umbilical hernia combined with liver cirrhosis (based on clinical, biochemical or histological findings) and ascites (diagnosed with either ultrasound or computed tomography) were identified from our hospital database. 21 patients underwent surgical treatment in the elective setting and 13 patients were initially treated conservatively. Model of End Stage Liver Disease (MELD) scores and mean age were not significantly different between the two groups. Elective hernia repair was successful in 16 out of 21 patients (76%). Complications occurred in 3 of these 21 patients (14%), consisting of wound related problems (infection, necrosis and haematoma) and a hernia recurrence in 4 out 17 (24%). Success rate of the initial conservative management was only 23%; hospital admittance due to incarcerations occurred in 10 of 13 patients (77%) of which six patients required hernia repair in an emergency setting. Two patients of the initially conservative managed group died due to complications of the umbilical hernia. One patient died after admittance for a spontaneous rupture and evisceration through the eroded skin of an umbilical hernia. Emergency surgery was complicated by bacterial peritonitis, further decompensation of liver failure and ultimately development of multiple organ failure. The second patient died on the 8th day after liver transplantation due to an incarceration followed by intestinal necrosis and sepsis. The complication rates between conservative management and elective surgical management (77% and 14% respect-tively) were significantly different, P=0.0002.
Conclusion: Conservative management of umbilical hernias in patients with liver cirrhosis and ascites leads to a high rate of incarcerations with subsequent hernia repair in an emergency setting whereas elective repair can be performed with less morbidity and is therefore advocated.

Reappraisal of diagnostic laparoscopy for periampullary tumours

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A significant number of patients, scheduled for explorative laparotomy (EL) for a suspected periampullary malignancy, undergo a palliative bypass procedure due to distant metastases (liver, peritoneal) and/or locoregional ingrowth. Controversy still exits on the additional value of a diagnostic laparoscopy (DL) as an upstaging modality to preclude a noncurative EL. Routine DL was eliminated in 1998 from the diagnostic protocol in our institution since a prospective study revealed a yield of only 13% for distant metastases. Objective: To evaluate the rationale of a strategy without routine use of DL, for patients undergoing an EL for a suspected periampullary malignancy, in terms of resection vs. bypass ratio and to analyze the indications for performing a bypass procedure. Methods: Between 1993-2006 987 patients underwent an EL for the suspicion of periampullary malignancy, potentially resectable on radiological imaging. Between 1993-1998 (period I) 288 patients had a DL performed as a routine diagnostic procedure, whereas between 1999-2006 (period II) 583 patients had no routine DL performed. Patient characteristics and pathological findings in each period were analyzed, as well as rates of resection and bypass procedures and the indications to perform a bypass. Results: Patient characteristics did not significantly differ between periods. Pathological findings after resection were (period I/II): solid neoplasm 89%/78%, cystic neoplasm 1%/11%, benign 10%/11%. Resection rate was 67% (n=193/288) in period I and 66% (n=383/583) in period II, whereas the bypass rate was 33% (95/288) in period I and 34% (200/583) in period II. Locoregional ingrowth as indication for a bypass decreased from 76% (n= 72/95) in period I to 53% (n= 105/200) in period II. Distant metastases as indication for a bypass increased from 24% (n= 23/95) in period I to 48% (n=95/200) in period II ($p<0.05$).
Conclusion: The overall resectability rate for periampullary malignancies has remained unchanged. Irresectability due to locoregional ingrowth declined during the study period, probably as a result of the introduction of advanced radiological techniques and the application of well-defined criteria for resection. However, a proportional increase in distant metastasis was found, which might have been due to the implementation of a diagnostic protocol without routine use of DL. Further studies might identify a subgroup of patients in which a DL can prevent an unnecessary exploration.

Predictive indicators of symptomatic and objective outcome after surgical reintervention for failed antireflux surgery; a multivariate analysis

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Recurrent gastro-esophageal reflux disease (GERD) and troublesome dysphagia after primary antireflux surgery is successfully treated by reoperation in 70% of patients. The reasons for failure after re-intervention, however, remain unclear. Therefore, if risk factors predicting outcome of reoperation could be identified, reoperation could be confined to a selected population to obtain optimal results in this notoriously difficult population. The purpose of the present study was to identify pre- and intra-operative factors predicting outcome in patients re-operated for recurrent GERD or troublesome dysphagia after primary antireflux surgery.Between 1994 and 2005, surgical re-intervention was performed in 83 patients (47 males, mean age 47.2 ± 14.4 years) for recurrent GERD and in 47 (18 males, mean age 50.7 ± 13.4 years) for troublesome dysphagia after primary antireflux surgery. For both groups of patients, the predictive value of different objective variables, anatomical abnormalities found during re-intervention and outcome parameters of preoperative esophageal manometry and 24-hr pH monitoring, was analysed for symptomatic as well as for objective outcome of surgical re-intervention, using logistic regression analysis.Preoperative symptoms improved or were resolved in 66.7% of patients re-operated for troublesome dysphagia and in 73.3% of patients re-operated for recurrent GERD. In the latter group, pathological reflux was absent at follow-up in 66.7% of patients. In the multivariate analysis, none of the variables were of predictive value for both symptomatic and objective outcome in patients re-operated for recurrent GERD. In patients re-operated for troublesome dysphagia, however, independent predictors of the effect of reoperation were the amplitude of the distal esophageal contractions (odds ratio (OR) 1.613, 95% confidence interval (CI) 1.087 – 2.393, p = .017), intrathoracic wrap migration (OR 0.077; 95% CI 0.003 – 1.755; p = .108) and the fact that an abdominal approach was chosen (OR 0.012; 95% CI 0.001 – 0.337; p = .009).
Conclusions: No predictors could be detected for symptomatic and objective outcome in patients re-operated for recurrent GERD. In patients re-operated for troublesome dysphagia, however, a low amplitude of the distal esophagus significantly predicted persisting of dysphagia and herniation of the wrap as well as the abdominal approach were negative predictors of symptomatic outcome.

Failure of gastric banding: is biliopancreatic diversion with duodenal switch a solution?

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Obesity is the most frequent form of malnutrition in the developed world and is increasing. Morbid obesity defined as a body mass index (BMI) of ≥40 kg/m^2 is a disease which can lead to morbidity like hypertension, diabetes, arthritis, obesity-hypoventilation syndrome, infertility and psychosocial problems.
Conservative treatment attempts at sustained weight loss in this population are almost always unsuccessful.
Surgery of the morbid obesity is the only effective treatment at the short and long term. Bariatric surgery can divided in two types. The first one is the restrictive procedures like the laparoscopic adjustable silicone gastric banding (LASGB) and the second one the malabsorptive procedures like biliopancreatic diversion with duodenal switch (BPD-DS).
LASGB is the most frequent performed technique in Holland and in Europe as a treatment of morbid obesity. Scopinaro introduced in 1980 biliopancreatic diversion which was modified in 1990 by Marceau to BPD-DS. This is a technique which that it was possible to decrease nutrient absorption by shortening the functional intestinal length and decrease fat absorption further by diverting biliopancreatic juices. The major advantage of this bariatric procedure is the preservation of normal eating behaviour. A major disadvantage is malabsorption of the fat-soluble vitamins, calcium and iron.
Despite the frequency and experience with LASGB it has a failure rate of 25%. This group of patient are advised a malabsorptive procedure. In our hospital we advise these patients BPD-DS.
We present hereby or results of the BPD-DS after unsuccessful LASGB.
Between august 2004 and January 2007 we performed BPD-DS as a treatment of an unsuccessful weight loss after LASGB in 20 patients. Follow-up was performed by the surgeon with our specialized obesity nurses.
The mean BMI preoperative was 45,5 kg/m^2 (30,8-57,3). After a mean follow-up of 20 months the mean BMI was decreased to 36,4 kg/m^2 (25,1-47,6). Absolute weight loss was 25,5kg (13,2-53,2).
There was no mortality in our group. 11 patients had complications. There were 9 minor (1x ileus, 2x wound infection, 4x pneumonia and 2x infection of the urinary tract) and 6 major (1x abdominal abscess, 2x spleen injury, 1x pylorusstenosis and 2x serious low levels of potassium).
BPD-DS is an effective technique as a treatment of morbid obesity after an unsuccessful LASGB.

Proximate® Linear Cutter 100 failure: a word of caution

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Background: Although staplers and cutters are widely used and generally effective, any mechanical device possesses the potential to malfunction. A linear staple line failure discovered during stapling of an ileal pouch alerted us to investigate linear cutter malfunctioning. The problem causing the observed staple line failure might be situated near the proximal end of the 100 mm Proximate® linear cutter (Ethicon) where the tissue lock is not completely secure to prevent cutting without stapling. Following this incident, we investigated whether suboptimal function of linear cutters occurred during cross stapling of a pig's large bowel. Methods:To investigate whether insufficiency of the proximal staple line would occur if cross stapling of the bowel was performed according to the user manual three different lengths of linear cutters (Proximate® 55 mm-TLC55, 75 mm-TLC75 and 100 mm-TLC10, Ethicon) were used to cross staple the large bowel of a pig. Representatives of the involved company were present during the experiment. Results: Cross stapling of the pig's large bowel demonstrated that even if the tissue was not advanced further than the marks on the stapling device, insufficiency of the proximal stapling line occurred. This accounted particularly for the 100 mm stapler, where the staples overlap was the least. Inspection of the three sizes of linear staplers tested demonstrated that particularly the 100 mm stapler had an insufficient staple overlap of the tissue lock.
Conclusion: Both the case report and the animal model demonstrated that the 100 mm Proximate® linear cutter (TLC 100) is not completely safe due to insufficient overlap of the staples at the proximal end of the linear staple line.

Anal fistula plug for closure of difficult perianal fistulas -a prospective study-

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Submucosal, intersphincteric, and low transsphincteric fistulas, in the lower one-third of the external sphincter complex are easy to treat by simple fistulotomy, with a favorable success rate and relatively little impact on fecal continence. Complex high and recurrent fistulas remain a surgical challenge. Simple division i.e. fistulotomy will likely result in fecal incontinence. Various surgical treatment options for these fistulas have shown disappointing results. Recently a biologic anal fistula plug was developed to treat these high transsphincteric fistulas. To assess the results of the anal fistula plug in patients with complex high perianal fistulas a prospective two-center clinical study was undertaken. Between April 2006 and October 2006 a consecutive series of patients with difficult therapy-resistant high fistulas were enrolled. During surgery the internal fistula tract opening was identified. A conical shaped collagen plug was pulled through the fistula tract. Any remaining portion of the plug that was not implanted in the tract was removed. The plug was fixed at the internal opening with a deep 3/0 polydioxanone suture.Seventeen patients with a median age of 45 years (range 27-75) were included. Of these patients 71 percent (12 out of 17) were male. Twelve patients had a history of perianal fistula surgery. The remaining patients had, among other things, anal stenosis, anal fibrosis, and problems with hemorrhoidal tissue. At a median length of follow-up of 7 months (range 3-9), seven of the 17 fistulas had healed (41 percent). In ten patients the fistula recurred.
Conclusions: In these small series of 17 patients with difficult high perianal fistulas a success rate of 41 percent is noted. Larger series preferably in trial setting, must be done to establish the efficacy of the anal fistula plug in perianal fistula.

Long-term health related quality of life in patients treated for their enterocutaneous fistulas

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Objective: The treatment of patients with enterocutaneous fistulas (ECF) is complex and often associated with intensive care and re-operations. There are no data available about the health related quality of life (HRQL) after treatment of patients with ECF. Therefore, in the present study we wanted to assess the long term effects on HRQL in patients who were treated for their ECF. Methods: Patients were eligible for this study at least two years after treatment. Between 1990 and 2005, 135 patients with ECF were treated according to a standardised protocol. Informed consent was obtained by telephone. HRQL was assessed by the Karnofsky Scale (KS), the short form 36 (SF36) and the inflammatory bowel disease questionnaire (IBDQ). These questionnaires are assessed with a scale ranging from 0 to 100, which represents the maximal HRQL. Additionally, patients were asked to report about perceived health before and during treatment and in their present situation, on a five-point scale, in which five is the highest score. Finally, patients were asked to furnish information regarding co-morbidity. The Mann-Whitney U test and the Friedman test were used to assess the significance of the results. Post-test analysis was done with the Wilcoxon Signed Ranks Test using the Bonferroni correction. Results: Forty-four patients died, twelve declined participation and fourteen could not be retrieved. Sixty-five patients gave their consent, of whom sixty-two returned all questionnaires (95%). Perceived health of these patients differed significantly between the three time-points ($P<0.001$). In post-test analysis patients judged their present perceived health significantly lower when compared with the pre-treatment period ($P=0.024$), independent of the aetiology of the ECF. However, the present perceived health was significantly higher than during the treatment period ($P<0.001$). The current median KS was 80, the median total SF36 score was 57 and the median total IBDQ score was 80. In a univariate analysis, lower total SF36 score was significantly associated with the presence of malignancy (61.1 vs. 38.3, $P=0.040$), neurological disorder (61.1 vs. 35.6, $P=0.007$) and depression (62.4 vs. 37.4, $P=0.002$).
Conclusion: The intensive treatment of patients with ECF results in a good long-term HRQL. Differences in long-term HRQL are independent from the aetiology of ECF but related to current co-morbidity.

Describing computed tomography findings in severe acute pancreatitis with descriptive terms: an international interobserver agreement study

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Introduction: Severe acute pancreatitis (AP) is associated with pancreatic necrosis and a wide variety of intra-abdominal collections. Computed tomography (CT) is used most commonly to differentiate between these complications. The current definitions (e.g. pseudocyst, pancreatic abscess) are based on the 1992 Atlanta Symposium. Recently, an interobserver study on the Atlanta definitions for describing CT findings showed very poor interobserver agreement (Besselink Pancreas 2006). This can potentially lead to miscommunication and patient mismanagement. The use of objective, strict descriptive terminology might be a valuable alternative but has unknown interobserver agreement. Aims & Methods: The aim of this international study was to determine the interobserver agreement for descriptive terms for CT findings in AP. 17 reviewers (8 radiologists and 9 clinicians) considered experts on AP participated in the following centers:Netherlands: 1) University Medical Center, Utrecht (2) Academical Medical Center, Amsterdam, and 3) Erasmus University Medical Center, Rotterdam; Germany: 4) University of Heidelberg; UK: 5) Royal Liverpool University Hospital; USA: 6) University of Washington Medical Centre, Seattle, 7) Brigham and Women's Hospital, Harvard Medical School, Boston and 8) Mayo Clinic, Rochester. The reviewers scored 9 descriptive items on 55 CT scans of patients with severe AP. Percentage agreement (PA) was calculated. RESULTS: Overall agreement was good to very good for the terms presence of a collection (PA= 100%; interquartile range [IQR], 68-100%), relation with pancreas (PA= 100%; IQR, 68%-100%), content (PA= 88%; IQR, 87%-100%) shape (PA= 100%; IQR, 78%-100%), mass effect (PA= 78%; IQR, 62%-100%) loculated gas bubbles (PA= 100%; IQR, 100-100%) and air fluid level (PA= 100%; IQR, 100-100%). Overall agreement was moderate for extent of pancreatic nonenhancement (PA= 60% IQR, 46%-88%) and encapsulation (PA= 56%; IQR, 48%-69%). PA was significantly greater among radiologist than clinicians for the terms extent of pancreatic nonenhancement (PA= 75% vs 57%, P= 0.008), encapsulation (PA= 67%; vs 46%, P= 0.001) and content of collection (PA= 100% vs 78%, P= 0.008).
Conclusion: Interobserver agreement for descriptive terms for CT findings in AP is good. Therefore, it is recommended to no longer use subjective definitions to describe CT findings in AP, such as pseudocyst, pancreatic abscess etc.

Quality of life one year after a single attack of acute pancreatitis

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Abstract teruggetrokken

Randomised controlled trials of intravenous antibiotic prophylaxis in severe acute pancreatitis: meta-analysis and relationship between methodological quality and outcome

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Background: Meta-analyses on the use of intravenous antibiotic prophylaxis in severe acute pancreatitis have shown conflicting results. The outcome of the second placebo-controlled randomised controlled trial (RCT) on this topic has not been included in any of the previous meta-analyses. The methodological quality of the various RCTs has frequently been criticized but was never formally assessed. Aim: To perform a meta-analysis of RCTs of antibiotic prophylaxis in severe acute pancreatitis and evaluate the methodological quality in relation to outcome. Methods: The MEDLINE, EMBASE and Cochrane databases were searched for RCTs that studied the effectiveness of intravenous antibiotic prophylaxis in severe acute pancreatitis. Meta-analysis was performed with a random effects model. Methodological quality was quantified by a previously published scoring system (range 0-17 points). Results: Six studies, with a total of 397 participants, obtained a methodological score of at least 5 points and were included. Systemic antibiotic prophylaxis had no significant effect on infection of pancreatic necrosis (absolute risk reduction (ARR) 0.055; 95% CI 0.084 to 0.194) and mortality (ARR 0.058, 95% CI -0.017 to 0.134). Linear regression analysis showed an inverse association between methodological quality and ARR for mortality (regression coefficient -0.871, p = 0.02).
Conclusions: At present, adequate evidence for the routine use of antibiotic prophylaxis in severe acute pancreatitis is lacking. The inverse relationship between methodological quality and impact of antibiotic prophylaxis on mortality emphasizes the importance of high-quality RCTs.

Impact of small bowel capsule endoscopy on patient management: a 1-year follow-up study

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Capsule endoscopy (CE) is a relatively new diagnostic modality in the evaluation of patients with suspected small bowel pathology. While many studies are available on the diagnostic yield of CE, less is known about the impact of CE on patient management. It is also unclear to what extent referring physicians are able to predict the clinical consequences of CE. We therefore analysed data from consecutive CE studies performed between September 2003 and December 2005 in our institution. Prior to CE, referring physicians were asked to estimate the consequences of CE according to potential different CE outcomes. The influence of CE on patient management was retrospectively investigated with at least one year follow-up. The actual consequences of CE were compared with the physicians' predicted consequences of CE. Management consequences were defined as major if they consisted of surgical intervention, endo-scopic intervention or medical therapy based on positive findings at CE. Consequences were considered as minor when no specific therapy was started (e.g. iron therapy) or when no further diagnostic tests had been performed.180 CE studies were reviewed in 179 patients (mean age 55 years, range 16-90, 42 % male). The indication for CE was occult or overt gastrointestinal bleeding in 72 % of cases. The overall diagnostic yield of CE was 42.2 %. CE led to major management consequences in 32 % of cases. These consisted of surgery (4 %), endoscopic interventions (19 %) and medical therapy (9 %). Patients, in whom CE initiated minor management changes, consisting of iron supplementation therapy in most cases, experienced no further bleeding during follow-up. In 78 % of cases, the actual consequences of CE matched the predicted consequences.
In conclusion, CE had a major impact on patient management in about one third of investigations. In the majority of cases, physicians adequately predicted the clinical consequences of CE.

Efficacy of fecal therapy for recurrent Clostridium difficile associated diarrhea

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Aim: Recurrent Clostridium difficile associated diarrhea (CDAD) is an increasing problem partly due to the highly virulent ribotype 027 toxinotype III strain. Antibiotic therapy for a first recurrence of CDAD fails in approximately 50 % of cases and treatment of a subsequent recurrence even less successful illustrating an urgent need for more powerful treatment strategies. We describe our results with the injection of donor stool (fecal therapy) in patients with multiple relapses of CDAD. Methods: Patients with a proven relapse of CDAD (diarrhea and positive ELISA for C. difficile toxin) after at least 2 courses of antibiotic treatment were included. Patients were pre-treated with vancomycin 500 mg qid during 4-7 days followed by bowel lavage with polyethyleenglycol and infusion of donor feces in the coecum or jejunem. Fresh donorfeces were donated by healthy relatives of the patients that were screened for infectious agents (fecal bacterial pathogens and parasites, HIV, and hepatitis viruses). Donorfeces (150-200 mg) were dissolved in 0.9% saline resulting in a solution of ~ 400 cc. After infusion of donor feces, resolution of diarrhea and clearance of fecal C. difficile toxin was assessed. Results: Seven patients (aged 48-82 years, 4 males and 3 females) were treated with fecal therapy. Two patients were infected with the ribotype 027 strain. Patients were treated with antibiotics for CDAD during a median time of 70 (range 55-139) days prior to fecal therapy, and isolation precautions were required during a median duration of 80 (range 72-151) days for hospitalised patients (n=5). In 5 of 7 patients, diarrhea resolved within 4 days after donor feces infusion. In 2 patients, CDAD recurred but was successfully treated with subsequent courses of fecal therapy using another stool donor. Clostridium difficile toxin test and culture was repeatedly negative after resolution of diarrhea in 6 of 7 patients. In one patient, toxin test and culture remained positive and he was considered an asymptomatic carrier after successful treatment with fecal therapy. One patient died 4 weeks after fecal therapy due to respiratory insufficiency unrelated to donor stool infusion.
Conclusion: Fecal therapy seems a promising treatment strategy for recurrent CDAD, also in patients with the antibiotic resistant and hypervirulent ribotype 027 strain. A randomised trial to compare the efficacy of fecal therapy with conventional antibiotics for recurrent CDAD will be initiated.

Effect of droplet size of a fat emulsion delivered in the small intestine on satiety and food intake in healthy volunteers

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We have shown that ileal as compared to oral delivery of small amounts of fats decreases hunger and food intake through activation of the ileal brake. However, a direct comparison between duodenal (D) and ileal (I) fat infusion on hunger has never been made. Furthermore, reducing the droplet size of fat particles has been shown to increase rate of fat digestion and that might affect hunger. Therefore we compared the effect of small amounts of lipid emulsions differing in droplet size (fine=F vs coarse=C emulsion) and in site of delivery (D vs I) on postprandial hunger, meal intake, gastric emptying half time (GE T1/2) and small bowel transit time (SBTT), using a single-blind crossover design. Fifteen healthy normal-weight volunteers (3 male, mean age 23yrs, mean BMI 21.6kg/m2) were intubated with a naso-ileal tube. Each subject received all 4 treatments on 4 consecutive days in a randomized order. After consumption of a fat-free drink (145 kcal) at t=0 min, 6 g of F or C emulsion was infused into D from t=30-90 min or into I from t=105-165 min. Surface-weighted mean diameter was 0.65 and 5.40 micron for F and C, implying a 8 times larger droplet surface for F. Hunger parameters (VAS) were assessed for the subsequent 240 min, when food intake was assessed in an ad libitum meal. SBTT was assessed by lactulose H2 breath test, gastric emptying by 13C breath test. All parameters were analyzed using ANOVA with subjects as blocks and location (D, I) and size (F, C) as factors, and (where appropriate) baseline values as covariates.Food intake was lower in I (169 g) than D (192g; $P<0.001$), while reduction in F (174 g) vs C (187 g) approached significance ($P=0.06$). Consistent with these results, hunger scores were also affected by both location (only for t=120-240 min: D vs I 60.0 vs 53.6 mm/min, $P<0.05$), and droplet size (only for t=0-120 min: F vs C 36.7 vs 41.9 mm/min, $P<0.05$). Other satiety parameters (e.g. fullness) showed similar results. When infused in the duodenum, the smaller droplets delayed GE T1/2 compared to C (D-F vs D-C: 148 vs 129 min, $p<0.05$). Droplet size had no effect on SBTT, but I significantly delayed SBTT compared to D (I vs D: 129 vs 85 min, $p<0.05$).
Conclusions: A smaller fat droplet size enhanced the ability of a given amount of fat to reduce food intake and hunger and to delay gastric emptying. Compared to duodenal infusion, ileal fat infusion significantly reduced food intake and hunger and significantly inhibited SBTT.

Enteral administration of isotopically labeled alanyl-[2-15N]glutamine results in a higher enrichment of [15N]citrulline and [15N]arginine compared to the parenteral route, despite equal arginine release from the kidney

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We previously established the existence of a pathway from glutamine into citrulline and arginine in humans. The aim of present study was to establish the hydrolysis of the dipeptide alanyl-glutamine (Ala-Gln) with enteral (EN) or intravenous (IV) administration. In addition we studied whether Ala-Gln derived citrulline (Cit) contributes to arginine (Arg) synthesis in humans.
16 patients undergoing upper gastrointestinal surgery received an IV or EN administration of Ala-[^{15}N]Gln (10±0.5 mmol/kg/hr). Blood was sampled from an artery (A), portal vein (PV) and the right renal vein (RV). Plasma concentrations of Ala-Gln, amino acids and enrichments (TTR%) of [^{15}N] labeled substrates were measured. Net balances of Ala-Gln across the portally drained viscera (PDV) and [^{15}N]arginine across the kidneys were calculated: ([A]–[V])*plasma flow. Results are expressed in means ± SEM. T-tests were applied ($p<0.05$ was considered significant).
Arterial plasma levels of the dipeptide were 1.0±0.6 and 0.1±0.0 mM in the IV and EN group respectively. EN administered Ala-[^{15}N]Gln was almost completely taken up by the PDV, in contrast with IV administration (IV:0.04±0.07 vs. EN:9.7±0.5 mmol/kg/hr). EN administration resulted in a higher TTR% of [^{15}N]Cit IV:4.9±0.4 vs. EN:8.4±0.7) and [^{15}N]Arg (IV:1.0±0.1 vs. EN:1.5±0.1) when compared to the IV route. More [^{15}N]Cit was delivered to the kidneys with EN administration (IV:0.26±0.04 vs. EN:0.55±0.08 mmol/kg/hr). In contrast, this did not result in a higher release of [^{15}N]Arg by the kidneys (IV:0.13±0.13 vs. EN:0.10±0.10 mmol/kg/hr).
In conclusion: The dipeptide is avidly hydrolysed with both routes of administration. EN administered Ala-[^{15}N]Gln is almost completely taken up by the PDV. The higher [^{15}N] citrulline and arginine enrichments observed with EN administration, were not accompanied by a higher renal release of [^{15}N]arginine, suggesting the existence of another site for arginine synthesis.

The Citrulline Generation Test (CGT): a new enterocyte function test

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The amino acid citrulline is mainly produced by enterocytes from conversion of glutamine. Fasting plasma citrulline concentration has been suggested to be a biomarker of intestinal failure. However, test characteristics proved to be disappointing in clinical setting. We propose a Citrulline Generation Test (CGT) to assess enterocyte function, in which oral glutamine is used to induce production of citrulline by the enterocyte. The aim of the study was to assess the feasibility of a CGT in healthy subjects and patients with decreased enterocyte mass. Twenty healthy subjects (HS), 8 patients with coeliac disease (CD), 6 patients with refractory coeliac disease (RCD) and 8 patients with short bowel syndrome (SBS) were given an oral bolus of 20 grams of the dipeptide alanine-glutamine. Subsequent changes in plasma citrulline and other amino acids concentrations were determined for 3 hours by venous blood sampling. Baseline and peak concentrations of citrulline, time to peak, the area under the citrulline curve and changes in plasma glutamine, alanine and arginine were determined using reverse-phase high-performance liquid chromatography (HPLC). Following the oral bolus of alanine-glutamine, plasma citrulline concentrations showed a time dependent rise in HS of 44 ± 13% (38 to 54 µmol/L, $p < 0.0001$) with peak concentrations at 77 ± 16 minutes. The slope from baseline plasma citrulline to peak concentrations was 0.22, 0.13 and 0.09 µmol/L.min-1 in HS, CD and RCD, respectively (HS vs. CD $p < 0.05$, HS vs. RCD $p < 0.001$). In contrast, using fasting plasma citrulline concentrations, a statistically significant difference was detected between HS and RCD only ($p < 0.01$). In patients with SBS, the CGT was able to distinguish between non-adapted and adapted SBS (i.e. < or > then 24 months following final digestive circuit modification, respectively) by means of the incremental area under the CGT curve till 90 minutes (iAUC T90). The iAUC T90 was 469 and 1187 µmol/L.min in non-adapted and adapted SBS, respectively ($p = 0.04$). Again, fasting citrulline concentrations could not differentiate between these groups ($p = 0.07$).
In conclusion, an oral bolus of alanine-glutamine induces a time-dependent rise in plasma citrulline concentration to an extent dependent on the existence of villous atrophy or enterocyte hyperplasia in coeliac disease, and adapted short bowel syndrome, respectively.

Mid-upper arm circumference, weight and height in Dutch children

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In developing countries mid-upper arm circumference (MUAC) is used to screen groups of children for malnutrition. In developed countries MUAC has been shown to correlate with body composition and BMI. However, in practice MUAC test performance for nutritional status expressed as weight/height or BMI has low specificity.
Because 22% of paediatric patients in the Netherlands is malnourished we decided to investigate the uselfulness of MUAC to estimate weight and height in healthy dutch children.
Participants were healthy Dutch children who were studied previously for anthropometric purposes. Gender, age, height (cm), weight (kg) and MUAC (cm) were available. The cohort was randomly divided in 2 groups. In group 1 the correlation between MUAC-weight and MUAC-height were calculated with correlations and regression analysis. In group 2 the models calculated in group 1 were used to calculate predicted weight and a predicted height based on MUAC. Subsequently correlations between weight-predicted weight and height-predicte height were calculated
There were 2101 participants (54% boys, median age 11.9 years, 2.0-17.9). In group 1 were 1082 participants, in group 2, 1019. There were no significant differences between the groups regarding gender, age, height, weight and MUAC.
Group 1: The correlation between MUAC and weight was 0.94 ($p<0.0001$) for boys and 0.93 ($p<0.0001$) for girls.
The following models were made.

- Boys: weight (kg) = - 60.4 + 4.7*MUAC (cm) ($p<0.0001$)
- Boys: height (cm) = -184.8 + 24.5*MUAC (cm) + -0.4*MUAC (cm)^2 ($p<0.0001$)
- Girls: weight (kg) = - 53.3 + 4.2*MUAC (cm) ($p<0.0001$)
- Girls: height (cm) = -246.6 + 30.4*MUAC (cm) + -0.6*MUAC (cm)^2 ($p<0.0001$)

Group 2: The correlation between weight and predicted weight was 0.94 ($p<0.0001$) for boys and 0.93 ($p<0.0001$) for girls. The correlation between height and predicted height was 0.84 ($p<0.0001$) for boys and 0.89 ($p<0.0001$) for girls.
Conclusions: Weight can be accurately predicted from MUAC in healthy Dutch children. This method is suitable to establish weight in children that are difficult to weigh (traction, casts, intensive care) but also to screen groups of children. Height can be reasonably accurately predicted from MUAC. Further research is needed to establish the accuracy of this method in patient groups with altered body composition (muscular dystrophy, encephalopathy).

Intravenous immunoglobulins reduce allogeneic T-cell activation after liver transplantation by modulating the interaction between Dendritic Cells and Natural Killer Cells

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We have shown that intravenous immunoglobulins (IVIg) reduce the incidence of acute rejection after liver transplantation from 31% to 13% and suppress the allogeneic T-cell priming by dendritic cells (DC). Here, we investigated the mechanism by which IVIg prevent immune activation after liver transplantation.
Human DC, NK-cells and T-cells were isolated from blood of healthy individuals. DC were stimulated with TNFα/IL1β in absence or presence of IVIg. IVIg were then removed and allogeneic NK-cells were added. NK-cell phenotype and apoptosis of DC were determined by flowcytometry. T-cell priming capacity of DC was assessed by culturing DC with allogeneic T-cells with or without NK-cells using ^{3}H-thymidine incorporation and CFSE-dilution techniques. *Ex vivo* changes in peripheral blood leukocyte populations were monitored in patients treated with IVIg (N=11).
DC matured in presence of IVIg (IVIg-DC) activated allogeneic NK-cells and increased their interferon-γ production, compared to control-DC. Subsequently, the activated NK-cells induced apoptosis of IVIg-DC, as shown by increased Caspase-3 expression and increased 7-AAD staining (IVIg-DC: 33±9% 7-AAD positive, control-DC: 17±8%, $p<0.01$). In presence of NK-cells, IVIg-DC were impaired in their allogeneic T-cell priming capacity by 81%±15 ($p<0.05$) compared to control-DC. This was due to NK-cell mediated Antibody Dependent Cytotoxicity (ADCC) to IVIg-DC, which can be abrogated by blockade of FcγRIII on NK-cells. This effect of IVIg could be mimicked by aggregates of a humanized monoclonal antibody, indicating that ADCC of DC is restricted to multimers in IVIg preparations. Furthermore, IVIg-DC promoted *in vitro* expansion of $CD56^{bright}CD16^{-}CCR7^{+}$ lymph node type NK-cells, which correlated with a decrease in the numbers of circulating NK-cell after IVIg- treatment.
In conclusion, IVIg reduce the incidence of acute rejection after liver transplantation by promoting NK-cell mediated ADCC of DC, which subsequently reduces the allogeneic T-cell priming. By modulating the early control switch of antigen-presentation, IVIg can prevent T-cell activation, and may therefore be a promising candidate for future non toxic immunosuppressive regimen after liver transplantation.

Glutathione, but not catalase is important in protection of Hepatic Stellate Cells against oxidative stress

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Background: We have previously shown that activated HSCs are sensitive to both superoxide anion and hydrogen peroxide induced cell death. HSC have different mechanism to detoxify oxidative stress such as peroxisomal catalase, superoxide dismutases and anti-oxidants like glutathione. Aim: 1) to evaluate the importance of catalase and glutathione in the protection against oxidative stress-induced cell death. 2) to evaluate the effect of oxidative stress on mRNA levels of antioxidant enzymes and activation markers of HSCs. Methods: Primary rat hepatocytes and serum-starved culture-activated rat HSCs were exposed to menadione (5-50μM; superoxide anion donor) or hydrogen peroxide (0.2-5mM). Apoptosis and necrosis were determined by Acridine Orange and Sytox Green nuclear staining, respectively. mRNA expression of genes was determined by quantitative RT-PCR. Catalase was inhibited using 3-aminotriazole (20mM). Glutathione levels were depleted by treatment with buthionine sulfoximine (BSO) at 200μM. Results: Menadione dose-dependently induced apoptotis, not necrosis. Glutathione depletion did not modulate menadione-induced cell death. Hydrogen peroxide only induced necrosis at concentrations of 5 mM. However, glutathione depletion dramatically increased the sensitivity of HSCs to hydrogen peroxide, resulting in >80% necrosis at 1 mM hydrogen peroxide. Blocking catalase did not sensitize HSCs but sensitized hepatocytes to hydrogen peroxide induced necrosis. In accordance, the relative expression of catalase mRNA was 13-fold higher in hepatocytes compared to HSCs. Menadione and hydrogen peroxide both induced the oxidative stress responsive gene HO-1 and this induction was further increased by GSH-depletion. The mRNA levels of the anti-oxidant enzymes catalase, Mn-SOD, Cu/Zn SOD and the activation markers TGF-, α-SMA and collagen type 1 mRNA expression were not substantially altered by oxidative stress.
Conclusion: In contrast to hepatocytes, catalase is not important in the protection of activated HSCs against hydrogen peroxide toxicity. Depletion of glutathione increases oxidative stress in activated HSCs, shown by further induction of HO-1 and increased sensitivity of HSC to hydrogen peroxide induced necrosis. Our results indicate that other hydrogen peroxide detoxifying enzymes, e.g. GSH-peroxidase, are important in activated HSCs. Targeting these enzymes may be a strategy to deplete activated HSCs as anti-fibrotic therapy, without affecting hepatocytes.

Hepatic glucose-6-phosphate metabolism is perturbed in LXRalpha-null mice

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LXR is a nuclear hormone receptor that coordinates lipid and cholesterol metabolism upon activation by oxysterols.Recently, it was proposed that LXR acts as a glucose sensor in the liver and that glucose and its metabolite glucose-6-phosphate are able to activate LXR in vitro at physiological concentrations.The aim of this study was to assess the functional relevance of the major hepatic LXR isoform in the control of hepatic and peripheral glucose metabolism in mice. Glucose metabolism was studied in fasted male LXR-alpha knockout (KO) mice and their wildtype (WT) littermates by infusing [U-13C]glucose, [2-13C]glycerol, [1-2H]galactose and paracetamol for 6 hours, followed by mass isotopomer distribution analysis.Although 9-hour fasting blood glucose levels were similar in LXRalpha null mice compared to wildtype littermates, they were reduced during steady state infusion in LXRalpha KO mice (KO 7.3±0.5 WT 8.7±1.9 mmol/l, $p<0.05$).Hepatic glycogen content was significantly higher in fasted LXRalpha KO mice (KO 306±120 WT 138±53 umol/g, $p<0.05$).Whole body glucose turnover was significantly lower in (KO 129.6±12.8 WT 159.1±26.2 µmol/kg/min, $p<0.05$).LXRalpha deficiency did not affect gluconeogenic flux (KO 97.9±9.5 WT 109.4±17.1 µmol/kg/min, NS).However, all fluxes affecting the glucose-6-phosphate pool, i.e. through glycogen synthase (Gs), glycogen phosphorylase (Gp), glucose-6-phosphatase (G6pase) and glucokinase (Gk) were significantly lower in LXRalpha null mice compared to wildtype littermates.Expression levels of genes encoding Pyruvate Kinase (Pk), Gk and Gp were significantly reduced by LXRalpha deficiency.Glucose balance, i.e., the difference between G6pase and Gk fluxes was lower in LXRalpha null mice (KO 119.5±11.9 WT 142.8±27.1 µmol/kg/min, $p<0.05$).Glycogen balance, i.e., the difference between Gs and Gp fluxes was not altered in LXRalpha null mice (KO -14.4±8.1 WT -20.6±18.5 µmol/kg/min, NS).Metabolic clearance of glucose was not affected by LXRalpha deficiency (KO 18.2±2.7 WT 16.9±1.8 µmol/kg/min, NS).In summary, LXRalpha deficiency does not affect hepatic gluconeogenesis in mice.However, hepatic glucose-6-phosphate metabolism is disturbed. As a result, hepatic glucose output is impaired, leading to decreased blood glucose levels.

The Adrenoleukodystrophy Protein (ALDP) and the 70-kDa Peroxisomal Membrane Protein (PMP70) are differentially associated with lipid microdomains

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Peroxisomes are multifunctional organelles that are especially enriched in the liver. Hepatocyte peroxisomes are the sole site of bile acid conjugation to glycine or taurine and of β-oxidation of (very) long chain fatty acids (VLCFAs). The Adrenoleukodystrophy protein (ALDP/ABCD1) and the 70-kDa peroxisomal membrane protein (PMP70/ABCD3) are highly homologous ATP-binding cassette (ABC-) transporters that transport (V)LCFAs across the peroxisomal membrane. Several (hepatic) ABC-transporters have been shown to be associated with detergent-resistent lipid microdomains (DRMs). Surprisingly little is known about the membrane embedding of PMPs. Moreover, peroxisomal DRMs have not been described to date. Here, we studied the putative association of PMPs to DRMs.

Cells from the hepatoma cell line HepG2 were lysed in the presence of 1% Triton X-100 (v/v) or 1% Lubrol WX (w/v). DRMs were isolated by flotation gradient centrifugation. Gradient fractions were analyzed by Western blotting using antibodies against ALDP, PMP70 and marker proteins for DRMs (c-Src), cytosol (GAPDH) and cytoskeleton (actin). Co-immuneprecipitation experiments were performed using anti-PMP70 anti-bodies. HepG2 cells were cultured in the presence of 10 μM lovastatin (Lov) and 2 mM methyl-β-cyclodextrin (CD) for *in vivo* disruption of DRMs. mRNA and protein expression were analyzed by Q-PCR and Westernblotting, respectively. Subcellular location of ALDP and PMP70 was determined by immunofluorescence microscopy.
Significant amounts of PMP70 were detected in the TX-100-resistant DRM fraction showing a similar gradient distribution as c-Src, while ALDP was completely extracted. In contrast, ALDP was detected in Lubrol WX resistant DRMs together with PMP70 and c-Src. Anti-PMP70 co-precipitated PMP70 with another peroxisomal membrane protein (Pex14p) from DRMs without precipitating c-Src. Lov/CD-treatment of HepG2 cells led to the dissociation of ALDP and PMP70 from Lubrol WX-DRMs, inefficient sorting of ALDP as well as peroxisomal biogenesis abnormalities.
This is the first demonstration of DRMs in the human peroxisomal membrane that exist *in vivo* independently from plasmamembrane DRMs. Remarkably, ALDP and PMP70 showed differential association with peroxisomal DRMs eventhough they are highly homologous. Cellular depletion of cholesterol leads to the dissociation of ALDP and PMP70 from DRMs and affects peroxisomal protein sorting.

The arteriovenous fistula: a feasible alternative to deliver home parenteral nutrition

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The success of a home parenteral nutrition (HPN) program is mainly determined by the occurrence of vascular access-related complications. With central venous catheters (CVC) these problems are frequent and mainly comprise occlusions and catheter-related infections which can be life-threatening. Our centre has an ongoing experience with HPN for 37-years and has remained unique in the world by using arteriovenous fistulae (AVF) for venous access in HPN. In the present investigation we evaluated complications related to AVF in comparison with CVC's. The medical records of all our current HPN-patients were reviewed by two independent reviewers. Comparison of complications during CVC or AVF use was performed by regression analysis. In 68 patients (24 male, mean age 51 yrs), who had been on HPN for 6.5 yrs (range 3.5 mnths-30.2 yrs), 484 routes for venous access (range 1-24/patient) had been created comprising 393 CVC's, mainly Hickman (211) and Porth a Cath's (119), and 91 AVF. Sixty fistulae (66%) became functional; the creation of 6 failed due to immediate occlusion or the absence of appropriate blood vessels and 25 occluded during maturation. Complications during CVC placement consisted of rebleeding, hemato- and/or pneumothorax (9%). Immediate rebleeding was observed in 9 fistulae (10%). The infection incidence rate (number/-access yr) was significantly lower in the AVF (0.02) when compared to PAC (0.72), Hickman (1.56) or untunnelled catheters (2.76). The occlusion rate was not significantly different between the untunnelled catheters (0.53), PAC (0.35) and AVF (0.52) but was lower for Hickman catheters (0.18).
Conclusions: AVF have a higher rate of initial failure but once functional, the blood stream infection rate is much lower than during CVC use whereas the occlusion rate is not increased. Considering the very low rate of infections, which clinically are the most serious venous access-related complications, we conclude that AVF are a valuable alternative for CVC's in the administration of HPN.

Results of the first screening program for colorectal cancer in The Netherlands

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Colorectal cancer (CRC) is the second cause of cancer death in the Western World. The fecal occult blood test (FOBT) is the only screening technique with proven mortality reduction. In many countries a form of screening for CRC is advised. The number of countries implementing screening programs for CRC has increased over the last two decades. We report the results of the first population-based program for CRC in The Netherlands. Between May 2006 and January 2007, people aged 50 to 75 years who lived in the Amsterdam or Nijmegen in The Netherlands were recruited for our study. A total of 20,000 individuals were randomly selected to receive either a guaiac based FOBT (Hemoccult) or an immunochemical based FOBT (OC-sensor). Both groups were sent a package containing either the Hemoccult or the OC-sensor accompanied by a letter and an extensive information leaflet on CRC and screening. After two weeks a reminder was sent. The primary outcome parameter was participation to the screening program by performing the FOBT. In case of a positive test participants were invited to two academic hospitals and were offered a colonoscopy. Of the 20.623 individuals invited for this study the overall response was 53.2% (n=10,972) 46.7% for Hemoccult and 59.7% for OC-sensor (p<0,001). This response was higher for the Nijmegen area than for the Amsterdam area (56.6% vs 49.6%; p<0,001), higher in women than in men (56.9% vs 49.2%, p<0,001), and highest in the 60-69 age group (57.3%). The overall positive rate was 5,8% (2.4% Hemoccult, 8.5% OC-sensor; p<0,001 RR 3.7 (95%-CI; 3.1-4.6)). The uptake of colonoscopy among participants with a positive test result was 79.3%. The positive predictive value for CRC was 5.1%. Adenomas were diagnosed in 64.6% of all performed colonoscopies, of which 61.6% were advanced adenoma. Conclusion: This is the first of FOBT screening for CRC in The Netherlands. The study population was chosen because of being representive for the entire Dutch population. Thus, implementation of a nation wide screening program seems feasible and should lead to mortality reduction in The Netherlands.

CEA in activated macrophages: a new prognostic or diagnostic factor for early detection of local recurrence of colorectal neoplasms?

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The Carcinoembryonic Antigen (CEA) is a protein that can be found in increased concentration in the blood of patients with colorectal cancer. It is used during follow-up for the detection of local tumor recurrence or metastases. 45 to 60 percent of these patients show neither an elevated CEA at the time of primary diagnosis, or during follow-up. Tumors demonstrate a continuous imbalance of cell proliferation and cell death,after which parts of these cells enter the circulation. This principle should make it possible to find free tumorparticles containing CEA, in the circulation. As macrophages phagocytize these tumor fragments, an analysis of CEA in activated macrophages could be a more sensitive parameter than CEA in serum. Detection of CEA in activated macrophages could be of value for the detection of local recurrence or metastases as well as the determination of prognoses. The goal of this prospective study is to determine if CEA in activated macrophages can be measured reliably; to ascertain to what extent this can be seen as an oncologic prognostic factor, and if CEA in activated macrophages has a clear advantage over the standard CEA-measurement in serum during the follow-up of colorectal cancer. Blood samples were taken pre-and postoperatively from patients (n=41) with colorectal pathology. The intracellular CEA in activated macrophages (CD14+/CD16+) was measured in EDTA-blood. Cell membranelabeling (CD14-APC,CD16-FITC), followed by a fix-and-perm intracellular CEA-coloringstep (CEA-rPE). The labeled cells were subsequently analyzed using flowcytometry,and separated by computer on coloringbasis. A standard CEA-test was also performed in serum. The first results showed that CEA in macrophages was detectable in patients with colorectal pathology. The serum-CEA-negative patients (ref:0-5,0)(n=11,range<1,0–4,7;mean CEA 2,1) with colorectal cancer showed a percentage of CEA-containing macrophages that was elevated (range4,3%-31,4%;mean16,0%). In this group of patients it was shown that the percentage of activated macrophages is higher in patients with metastases than in patients with local colorectal cancer with and without positive lymph nodes. The fraction of CEA-containing macrophages in metastasized patients is higher (n=3,range16,4%-79,6%; mean:42,3%) than in patients without proven metastases (n=9;range7,5%-31,4%;mean:17,1%). The measurement of CEA-containing macrophages could be a promising diagnostic and/or prognostic factor for the use in patients with colorectal cancer.

Tolerance to gliadin peptides can be restored by enteral administration of lactococcus Lactis bio-engineered to deliver the immunodominant antigen to sensitized NOD AB0 DQ8 transgenic mice.

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Introduction: Antigen-specific immune suppression is an attractive therapeutic goal for the treatment of several gastro-intestinal diseases especially celiac disease. Active delivery of recombinant autoantigens or allergens at the intestinal mucosa by genetically modified *Lactococcus lactis* (LL) provides a novel therapeutic approach for the induction of tolerance. For this purpose we genetically engineered deamidated DQ8 epitope secreting LL (LL-eDQ8d) and evaluated local and systemic immune responses in gluten-sensitized NOD AB^{o} DQ8 class II transgenic mice after oral supplementation.
Methods: Mice were sensitized with 10 µg deamidated DQ8 epitopes and fed for 10 days with BM9 (negative control), LL-pT1NX (empty vector) or LL-eDQ8d (1x10^{9} CFU/day). Tolerance induction was assessed by DTH responses, ex vivo proliferation assays, cytokine measurements and FACS analysis on regulatory T cell markers.
Results: Daily intragastric administration of LL-eDQ8d in sensitized transgenic mice led to a significant suppression of the delayed-type hypersensitivity (DTH) response compared to the sensitized control mice. These data were accompanied by a decreased proliferative capacity of the splenocytes and inguinal lymph node cells, which was critically dependent on the combination of IL-10 and TGF-β. Moreover the LL-eDQ8d treatment induced a significant Foxp3 upregulation in the splenic and GALT CD4+CD25- T-cell population as well as in the splenic CD4+CD25+ population compared to the immunized BM9 and LL-pT1NX treated group.
Conclusion: Mucosal delivery of immunodominant gliadin epitopes by genetically modified LL induces suppression of local and systemic T cell responses in peptide sensitized mice NOD AB^{o} DQ8 transgenic mice, by the induction of Foxp3^{+} regulatory T cells. Our data provide promise for the development of effective therapeutics for treatment of several common autoimmune, inflammatory and/or allergic diseases by autoantigen- and/or allergen-secreting L.lactis. Finally, we believe that these results can be rapidly translated into a therapy for an important and frequently occurring ailment, celiac disease.

Narrow-band imaging (NBI), indigo carmine chromoscopy (ICC) and acetic acid chromoendoscopy (AAC) have little clinical relevance in Barrett's imaging: a study comparing the evaluation of 4 different enhancement techniques by expert and non-expert endoscopist.

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Introduction: ICC, AAC and NBI combined with magnification endoscopy have been reported to recognize typical arrangements of mucosal and or vascular patterns in Barrett's esophagus (BE) that may correlate with histology. The aim of this study was to compare images obtained with magnifying high-resolution white light endoscopy (WL), NBI, ICC and AAC in order to determine the best technique for use in BE. Methods In 14 BE patients upper endoscopy was performed by one endoscopist (JB). Areas selected by the discretion of the endoscopist were first imaged with WL followed by NBI, ICC and ACC (after gently washing off the indigo carmine). From 22 areas (8 areas with high-grade dysplasia (HGD) or early cancer (EC)) good quality images with all 4 techniques were obtained. These images were evaluated by 7 endoscopists with no specific expertise in BE or advanced imaging techniques and by 5 international experts in this field. Endoscopists scored the images for the following items: overall image quality, mucosal image quality, vascular image quality. In addition, they evaluated the mucosal and vascular patterns (regular vs. irregular) and the presence of abnormal blood vessels. The WL images of all 22 areas were first evaluated separately. Subsequently, NBI, ICC and AAC images, each with the corresponding WL image, were evaluated in a random order. Finally, all 4 techniques were evaluated together. Results: In overall, all enhance-ment techniques were better appreciated than WL. NBI was best appreciated for overall and vascular imaging quality and AAC was best appreciated for mucosal imaging quality. Expert endoscopists had a more explicit appreciation of the enhancement techniques compared to WL than non-expert endoscopists. The inter-observer agreement for mucosal and vascular patterns and the presence of abnormal blood vessels as well as the sensitivity for detecting HGD/EC did not improve by adding NBI, ICC or AAC. This applied for non-expert endoscopists as well as expert endoscopists. Conclusion: Although the imaging qualities of NBI, ICC and AAC are in general better appreciated than WL, the addition of these enhancement techniques, in the setting of this study, did not lead to an improvement of inter-observer agreement or sensitivity. The enthusiasm regarding the diagnostic potential of additional enhancement techniques may be biased by the subjective improvement of imaging quality which may have little clinical relevance.

Novel combined modality therapy for Barrett's esophagus containing early neoplasia: endoscopic resection followed by circumferential and focal radio-frequency ablation.

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Endoscopic resection (ER) allows for removal of high-grade dysplasia (HGD) and early cancer (EC) in Barrett's esophagus (BE) with histological verification of resection margins. Focal ER, however, is associated with recurrent lesions in non-resected areas, while radical ER is associated with a significant stricture rate. Ablation with PDT or APC may allow for treatment of remaining BE after ER, but is associated with residual BE, dysplasia, buried Barrett's, and stenosis. A newer ablative therapy, radiofrequency ablation (RFA), may be successful in eliminating residual intestinal metaplasia (IM) and dysplasia after focal ER. Aim of this study was to assess safety and efficacy of focal ER followed by RFA of residual BE, in BE pts with HGD/EC. Eligible pts had BE <10cm, visible lesions with HGD/EC, and no signs of submucosal infiltration/lympnode metastases on endoscopy or EUS. ER was performed with the cap-technique or multi-band ligation (MBL) device. Circumferential ablation (CA) was performed with the balloon-based HALO360 System (BÂRRX Medical, Sunnyvale, CA, USA) and focal ablation (FA) with the HALO90 System. 6wks after ER, CA was performed, followed every 2mos by CA or FA until BE eradication. 2 mos after the last ablation, EGD with Lugol's staining and large cup biopsy (4Q/1cm) was performed. Histology was reviewed by 1 expert pathologist.19 pts (14 M, 58 (53-72)yrs, BE length 7 (5-9)cm) had ER (n=8 cap, n=11 MBL; n=8 en-bloc, n=11 piecemeal (median 2 (2-3) res/pt)). 3 pts had acute bleeding after ER, treated with hemoclips. ER-specimens: EC (n=8), HGD (n=8), LGD (n=3); all clear vertical margins. Remaining BE after ER: HGD (n=13), LGD (n=6). Median was FU 17 (11-23) mos. Complete histological and endoscopic eradication of dysplasia and IM was achieved in all pts after 1.4 (SD 0.50) CA and 1.7 (SD 0.81) FA sessions. 1 pt had persisting HGD after 2 CA and 3 FA, resected with MBL as escape treatment. 2 pts developed stenosis at the ER site after CA (no. resections 2 and 3), which resolved after dilatations. 0/533 biopsies obtained from neosquamous mucosa during FU contained subsquamous IM.
Conclusion: BE pts with HGD/EC can be effectively and safely treated with a combined modality therapy of focal ER followed by RFA of residual BE. A complete response rate for IM and dysplasia of 95% was achieved, with escape ER resulting in an overall success rate of 100%. These results compare favorably to other regimens, such as radical ER, PDT, or APC.

Implementation of EUS-FNA for lung cancer staging

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Objective: To test an implementation strategy of EUS-FNA for the staging of lung cancer.Background: Transesophageal ultrasound- guided fine needle aspiration (EUS-FNA) can prevent up to 70% of scheduled surgical staging procedures in patients with non-small cell lung cancer (1). Whether these results - obtained by experts - are reproducible in community hospital settings is as yet unknown. Methods: Chest physicians and gastroenterologists participated in a dedicated EUS training for lung cancer staging consisting of a hands-on training which involved the investigation of approximately 45 patients. Subsequently, trainees performed EUS-FNA in consecutive patients with (suspected) lung cancer that were candidates for surgical staging. In case EUS-FNA did not assess N2/N3 disease, surgical staging or thoracotomy with mediastinal dissection occurred. Results of the five test centers were compared with that of the expert center.Primary outcome: Assessment of mediastinal (N2/N3) metastases or tumor invasion (T4). Results: 321 patients were included, 196 (62%) in the five test centers combined and 125 (38%) in the expert center. N2/N3 metastases or tumor invasion were assessed in 43,9 % of patients in the test centers compared to 42,3 % in the expert center [p=0.88]. The negative predictive value of EUS-FNA regarding mediastinal staging was equal in both groups (7.8% vs 10.7%) [p=0.96] as was the prevalence of mediastinal metastases (49% vs51%) [p=0.96].
Conclusion: Chest physicians or gastroenterologists without prior EUS experience can obtain results comparable with that of experts following adequate training.Implication: the current strategy could be used to facilitate large scale implementation of EUS-FNA for lung cancer staging

Role of high resolution endoscopy, narrow-band imaging and autofluorescence imaging for the classification of polyps in patients with hyperplastic polyposis

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Hyperplastic polyposis syndrome (HPS) is a condition in which multiple hyperplastic polyps (HPs) are spread throughout the colon. Patients with HPS are at increased risk of developing colorectal cancer (CRC) through a HP-serrated adenoma (SA)-CRC pathway. In the general population SAs are rare, but may have a premalignant potential as well. However the distinctive endoscopic appearance of SAs has never been described. Novel endoscopic techniques, like narrow-band imaging (NBI) and autofluorescence imaging (AFI), may improve the endoscopic diagnosis of SAs. The aims of this study were to assess the use of high resolution endoscopy (HRE), NBI and AFI for the classification of HPs, SAs and adenomas in patients with HPS. Seven patients with HPS were evaluated by colonoscopy using endoscopic trimodality imaging (ETMI), which incorporates HRE, NBI and AFI in one system. All detected polyps were analysed with NBI for Kudo pit pattern (I-V) and with AFI for polyp colour (green, ambiguous or purple). The accuracy of NBI and AFI in differentiating the detected polyps was determined by using histology as a gold standard. At colonoscopy, 21 HPs, 31 SAs and 14 adenomas were detected. The median size of HPs, SAs and adenomas was 2mm (interquartile range 1-3mm), 3mm (1-8mm) and 2mm (1-3mm) respectively ($p=0.001$ for SAs). Macroscopically 6 HPs (32%), 5 SAs (17%) and 1 adenoma (7%) were classified as sessile. Flat appearance was found in 13 HPs (68%), 25 SAs (83%) and 8 adenomas (93%). On NBI, 18 (95%) HPs showed Kudo pit pattern type I-II versus 21 (70%) of SAs (n.s.). Of all adenomas, only 2 (14%) had Kudo type I-II ($p<0.001$). On AFI, all 21 (100%) HPs were green/ambiguous in colour versus 28 (90%) SAs (n.s.). Only 2 (14%) adenomas were green/ambiguous ($p<0.001$). The accuracy of NBI in discriminating SAs from HPs was 55% and for AFI this was 45%. The accuracy of NBI and AFI in discriminating adenomas from HPs or SAs was 81% and 92% respectively.

Conclusion: In patients with HPS, serrated adenomas tend to be larger and flat in appearance compared to HPs, which are more often sessile. Endoscopic discrimination between HPs and SAs using HRE, NBI and AFI proved to be unsatisfactory. However, discrimination of HPs/SAs from adenomas was very well possible with NBI and AFI. To prevent potential progression of SAs to CRC, we suggest regular surveillance and removal of all polyps, irrespective of endoscopic appearance, in patients with HPS.

Interobserver variability and accuracy of colonic pit patterns by narrow band imaging and color by autofluorescence imaging

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Pit patterns of colonic polyps can be used for the prediction of histology. Narrow band imaging (NBI) is a novel endoscopic technique which enhances mucosal pit patterns by applying special filters to the endoscopic light. Autofluorescence imaging (AFI) is another technology which utilizes endogenous tissue fluorophores for color reproduction. During AFI, neoplasia appears purple while non-neoplastic lesions appear green. We evaluated the interobserver variability and accuracy of the Kudo pit pattern by NBI and of polyp color by AFI.
We randomly selected images of 50 polyps from our database. From each polyp an AFI image and NBI image were available. After a short systematic training session in pit pattern analysis (NBI) and color assessment (AFI), 3 expert and 4 non-expert endoscopists assessed all NBI and AFI images, and finally the combined NBI-AFI images. Images were displayed in a random order and assessors were blinded for histology.
The NBI images were judged on quality for pit pattern recognition and then scored for Kudo pit pattern (I-V). The AFI images were judged on quality for color assessment and scored as green, ambiguous or purple. For analysis, Kudo type I-II and green color were considered non-neoplastic. During the assessment of combined NBI-AFI images, green lesions as well as ambiguous colored lesions with Kudo I-II were considered non-neoplastic.
Pit patterns could not or poorly be classified in 6% of NBI images and the color of polyps could not or poorly be determined in 3.2% of AFI images. Overall interobserver agreements for Kudo classification and polyp color were moderate (kappa 0.52 and 0.47, respectively). The overall interobserver agreement for the combined use of NBI-AFI was substantial (κ 0.65). Experts had the highest interobserver agreement for NBI (κ 0.77) and non-experts for combined NBI-AFI (κ 0.72).
The overall sensitivities of NBI, AFI and combined NBI-AFI were 78%, 83% and 71% respectively; corresponding specificities were 51%, 66% and 90%. There were no differences in accuracy between experts and non-experts.
Conclusion: The overall interobserver agreement in endoscopic diagnosis increases when using NBI-AFI together. The highest sensitivity for a correct endoscopic diagnosis is obtained by AFI; the highest specificity by the combined use of NBI-AFI. The most remarkable result was that overall accuracy was highest by combining NBI-AFI for both expert and non-expert endoscopists.

Validation of the new Olympus virtual reality colonoscopy simulator

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Introduction: Simulators are increasingly used in training physicians in diverse medical fields. Data on systematic evaluation of the performance of endoscopy simulator devices are scarce compared to their use in general practice. The Olympus virtual reality simulator is a newly developed simulator for colonoscopy. The objectives of this study were to determine expert validity, construct validity, and the didactic value of the simulator as judged by experts. Aims & Methods: Participants were allocated to one of two groups depending on the endoscopic experience. Novices were defined as participants without any flexible endoscopy experience, experts had all performed more than 1000 colonoscopies.All participants were asked to fill out a questionnaire on demographics, endoscopic experience, and their appreciation of the haptic and visual realism of the colonoscopy exercises performed. Appreciation was expressed on a visual analogue scale (VAS) varying from very unrealistic (0) to very realistic (10). Experts were asked to evaluate the Olympus simulator for use as a teaching device for novices. Exercises included one eye-hand coordination game and a virtual colonoscopy.Test-parameters used were points acquired in the game, time to reach the cecum, maximum insertion force and patient pain. Data were analysed using a 2-tailed Mann-Whitney U Exact test. Results: Novices (N=23) scored a mean of 774 points (range 1511), experts (N=23) scored 1009 points (range 1286). This difference did not reach significance (P=0,058)Experts performed virtual colonoscopy significantly faster than novices (877 vs 273 sec, P<0.001) but used more insertion force (14.2 vs 12.8N, P=0.022). Average maximum pain score was higher in the expert group: 86% vs 68%. (P=0.008). Appreciation of the realism of the colonoscopy performed was graded 5.7 (range 7.2) on a 10-point scale. Experts considered the Olympus simulator beneficial for the training of novice endoscopists with a mean grade of 7.4 on a 10-point scale.
Conclusion: The novel Olympus VR simulator discriminates excellently between the measured levels of expertise (construct validity). The prototype offers a marginal realistic representation of colonoscopy according to experts (expert validity). Although software development is ongoing, the device may already be implemented in the training program of novice endoscopists.

An increase in the number of risk-alleles is associated with an increased risk for Crohn's disease and a more severe disease course

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Background and aims: Inflammatory bowel diseases –consisting of Crohn's disease (CD) and ulcerative colitis (UC)- have a complex genetic background. The IBD5 locus, DLG5 and CARD15 were already confirmed to be associated with CD in the Dutch population. More recently ATG16L1 was also found to be associated with CD in the Dutch population (OR=1.19; CI: 1.07–1.32; p=0.0005), specifically with ileal localization and stricturing behavior. The aim of this study was to assess the risk for both CD development and CD progression by combining information from the four genes listed above. Methods: 2937 patients with IBD (1696 CD, 1099 UC and 142 Indeterminate Colitis) and 1484 controls from 7 University Medical Centres in the Netherlands were included. Phenotypic details were available for 2091 patients (1316 CD and 775 UC). The most informative SNPs for ATG16L1 (rs2241880), the IBD5 locus (rs2522027) and DLG5 (rs2289310) together with the three known risk associated polymorphisms for CARD15 were used to determine interaction between the genes. Odds ratios (ORs) were calculated in a binary logistic regression analysis with the number of risk alleles as an independent variable, and compared to controls with zero or one risk allele. Ordinal regression analysis was performed to test whether a more complex course of CD was associated with an increased number of risk alleles. Results: Individuals carrying an increasing number of risk alleles are at an increased risk for CD. The progressive increase in ORs is consistent with an independent effects multiplicative model. CD patients carry more risk alleles compared to controls ($p=9.44e^{-11}$). CD patients with a more severe disease course or operations had significantly more risk alleles compared to non-stricturing, non-penetrating behavior (p=0.0005) or patients without operations (p=0.0067).
Conclusion: We showed that CD is a multigenic disorder and that an increasing number of risk alleles is associated with an increased risk for CD and with a more severe disease course. Combining information from the known common risk polymorphisms may enable clinicians to predict the disease course of inflammatory bowel disease patients in the future.

Gender-related differences in disease perception in inflammatory bowel disease patients

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Background: Clinical practice shows that gender-related issues in inflammatory bowel disease (IBD) are of great importance. However, there are no data available concerning differences in quality of life between female and male patients. Aim: To assess gender-related differences in quality of life perception in IBD patients. Methods: Between December 2006 and January 2007, a patient empowerment study has been performed as a patients-initiated study in cooperation with Dutch Patients' Crohn`s and Colitis association (CCUVN). All patients willing to participate completed the online questionnaire on the CCUVN website consisting of multiple-choice questions. A chi-square test was used for statistical analysis of the gender-related differences. Results: In total 1067 (Crohn`s disease/ulcerative colitis, 617/450) patients, mainly females (703 females/364 males, 66%/34%) replied.Significantly more females (F) than males (M) found that the disease limited them in everyday activities (53% F vs. 45% M, p=0.014). Only 9% of participating female patients vs. 19% of males almost never experienced disease-related limitations. Significantly more females compared to males encountered serious limitations in professional life such as work (42% F vs. 33% M, p=0.015) and study (36% F vs. 19% M, p<0.001). Furthermore, the disease was limiting more females than man in family life (31% F vs. 21% M, p=0.002), social life (35% F vs. 23% M, p<0.001) and sport (44% F vs. 34% M, p=0.004). No differences in the impact of disease on these activities were observed with regards to the type of the disease.In addition, as a result of the disease, significantly less female then male patients (44% and 55%, respectively; p=0.002) found that they were able to meet their daily expectations with regard to work or study, household, family and social activities.
Conclusion: The negative impact of inflammatory bowel disease on the quality of life is more frequently present in female than in male patients.

Considerable gastric cancer risk during first year after diagnosis of gastric MALT lymphoma

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Gastric mucosa associated lymphoid tissue (MALT) lymphomas and gastric adenocarcinomas are both consequences of chronic H. pylori infection. In addition, increased progression of pre-malignant gastric lesions in patients with gastric MALT lymphoma has been reported. However, the gastric cancer risk in patients with MALT lymphoma is unknown. The aim of this study was to evaluate the risk of gastric cancer in patients with gastric MALT lymphoma in the Netherlands. Patients with a first diagnosis of MALT lymphoma between 1991 and 2006 were identified in the Dutch nationwide histopathology registry (PALGA). Within this cohort, the number of gastric cancer diagnoses during follow-up was evaluated. In total, 1297 patients (672 males; 625 females) (median age 67.0 years) were newly diagnosed with MALT lymphoma during the investigated period. The cohort consisted of 1072 (82.6%) patients with low-grade MALT lymphoma, 113 (8.7%) with high-grade MALT lymphoma and 112 (8.6%) with intermediate or undefined MALT lymphoma. The incidence of MALT lymphoma increased from 1991 (37 patients) to 1997 (152 patients). After this period, the number of diagnoses of MALT lymphoma declined to 64 patients in 2006. Overall, 31 (2.4%) patients (14 males; 17 females) (median age 72.0 years) were diagnosed with gastric cancer, 15 (1.2%) patients with low-grade MALT, 4 (0.3%) with high-grade MALT lymphoma and 12 (0.9%) with intermediate or undefined MALT lymphoma. Of the 31 patients with MALT lymphoma and gastric cancer, 11 (35.5%) were simultaneously diagnosed with both disorders, 8 (25.8 %) patients developed gastric cancer within 1 year, and 12 (38.7%) patients within 1 to11 years. Gastric cancer risk within 5 years after a diagnosis of MALT lymphoma did not change over time during the observation period ($p=0.38$ for comparison of lymphomas diagnosed before and after 1997).
Conclusions: Patients with MALT lymphoma are at substantial risk of gastric cancer. Most cancer are diagnosed simultaneously with or within one year after diagnosis of a MALT lymphoma. These findings emphasize the need of accurate endoscopic and histological re-evaluation of the gastric mucosa in particular within the first year after diagnosis of a gastric MALT lymphoma.

The yield of endoscopic surveillance with random biopsy sampling in patients with intestinal metaplasia and dysplasia of the gastric mucosa

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Endoscopic surveillance with random biopsy sampling in patients with pre-malignant gastric lesions, i.e. atrophic gastritis (AG), intestinal metaplasia (IM) and dysplasia (DYS), could identify patients at risk for gastric cancer. However, the yield of this strategy is unclear.To evaluate the yield of endoscopic surveillance with random biopsy sampling, a gastroscopy was performed in patients with a previous diagnosis of IM or DYS of the gastric mucosa. During gastroscopy targeted biopsies were taken from all macroscopically visible gastric lesions. In addition, random biopsies were obtained from standardized sites: 4 from the antrum, 4 from the corpus, 2 from the angulus and 2 from the cardia. Furthermore, H. pylori was cultured from corpus and antrum biopsies. An expert pathologist, blinded for endoscopic findings, assessed all biopsy specimens according to the updated Sydney System and revised Vienna classification.Sixty-one patients with IM (median age 61.0 yrs) and 10 patients with DYS (59.0 yrs) were included in this study. Targeted biopsies were obtained in 11 patients with IM and 3 patients with DYS; these biopsies showed low grade DYS in respectively 2 and 1 patients, and high grade DYS in respectively none and 1 patient. Random biopsy sampling showed no pre-malignant lesion in respectively 23 (38%) and 2 (20%) patients with an initial diagnosis of IM and DYS. However, random biopsy sampling was crucial for detection of DYS in 3 (5%) patients with an initial diagnosis of IM, including 1 patient with high grade DYS, and in 1 (10%) patient with an initial diagnosis of DYS. With regard to intragastric distribution of lesions, IM was detected in the antrum in 41% of cases, in 34% at the angulus, in 25% at the lesser curvature of corpus, in 20% at the greater curvature of the corpus and in 21% at the cardia. DYS was detected in the antrum in 5 (7%) patients and at the lesser curvature of the corpus in 3 (4%) patients. H. pylori culture was positive in only 5 (6%) patients.
Conclusions: Presence of pre-malignant gastric lesions is often not confirmed during surveillance gastroscopy. Random biopsy sampling during endoscopic surveillance seems important for an adequate diagnosis of both severity and intragastric extent of pre-malignant gastric lesions. Biopsies of the lesser curvature of the corpus are essential in this evaluation.

The placement of nasoduodenal feeding tubes by nurses with the assistance of an electromagnetic system (CORTRAK™)

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Background: The endoscopic placement of nasoduodenal feeding tubes is a time-consuming procedure for the endoscopist. New technologies such as an electromagnetic guided system (Cortrak™) that visualises the path of the feeding tube in the patient, may facilitate the placement of feeding tubes by nurses. Aim: To evaluate the feasibility of placement of nasoduodenal feeding tubes by nurses at the patient's bedside without the help of endoscopy and without the need of fluoroscopy. Methods: Patients without aberrant anatomy were eligible. Feeding tubes were positioned at the bedside of the patient. The aim was to reach at least the duodenojejunal flexure. The success rate, procedure time, location of the feeding tube and the confirmation of its site by fluoroscopy and the discomfort for the patient were recorded. Tubes were followed in time with respect to clogging, dislocation, and the possibility of repositioning in case of dislocation. Results: Fifty patients (24 at the ward, 21 at the intensive care (IC), 5 at the out-patient clinic) were included. Patients required a feeding tube for malnutrition (23), gastric paresis (13), pancreatitis (6), artificial ventilation (4), dysphagia and aspiration pneumonia (4). In 36 (72%) patients the procedure was successful, in 20 of the 24 ward patients, in 13 of the 21 IC patients, and in 3 of the 5 outpatients. Thirty-two of the feeding tubes were positioned in the horizontal part of the duodenum in front of (24), at (5) or past (3) the duodenojenunal ligament. Unsuccessful positioning was mainly related to gastric paresis and being on the ventilator. Apparently, there was a learning curve as 21 of the last 25 feeding tubes were positioned successfully in contrast to 15 of the first 25 feeding tubes. The mean procedure time of successfully positioned tubes was 12.4 minutes.Sixteen tubes were removed intentionally, 16 became dislocated and 4 were repositioned with the electromagnetic system, 2 tubes clogged and 2 are still in situ. Nineteen patients had a functioning tube for more than 7 days. Patients scored favourably as to pain and discomfort.
Conclusion: The positioning of nasoduodenal feeding tubes by nurses without the assistance of endoscopy or fluoroscopy is feasible and associated with a high success rate. The path finding system enables a safe, accurate and deep intraduodenal positioning of the feeding tube at the patient's bedside with minimal discomfort for the patient.

Day-to-day variation in acid reflux patterns in patients with non-erosive reflux disease and erosive reflux disease: clinically relevant or trivial?

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An important limitation of 24-hr pH monitoring is the risk of false-negative results due to day-to-day variability in gastro-esophageal reflux patterns. Wireless 48-hr pH recording (BRAVO; Medtronic, MN) may improve the detection of gastro-esophageal reflux disease (GERD). We investigated day-to-day variability in acid reflux patterns using the BRAVO pH system. Symptomatic GERD patients underwent upper endoscopy and subsequent placement of a BRAVO pH capsule at a distance of 6 cm proximal to the squamo-columnar junction. Patients were classified into non-erosive reflux disease (NERD) or erosive reflux disease (ERD). All antisecretory medications were stopped at least 7 days prior to placement. During monitoring, patients were encouraged to resume their daily routine of meals and activity. Total, supine and upright values of % of time pH<4, number of reflux episodes, number of reflux episodes >5 min., and longest reflux episode were compared between NERD and ERD patients and between day 1 and 2 of recording within these groups. In addition, differences in pathologic reflux (total % of time pH<4 (threshold: >5.3%)) between day 1 and 2 were studied.A total of 50 patients underwent pH monitoring (46% male, mean age ± SD: 45±13 yr). Successful 48-hr pH monitoring was performed in 44 (88%) patients, whereas early capsule dislodgement occurred in 6 (12%). Overall, reflux parameters were similar between NERD and ERD patients on day 1 and day 2. For example, the total number of reflux episodes on day 1 was only slightly higher in ERD patients as compared to NERD patients (51±31 vs. 46±30, p=0.63). In addition, no significant differences were found for reflux parameters between day 1 and day 2 within these groups. However, 2/17 (12%) NERD patients and 8/27 (30%) ERD patients had normal esophageal acid exposure on 1 day and pathologic reflux on the other. In 9/17 (53%) NERD patients, pathologic reflux was detected on both days, 1/17 (6%) was positive on day 1 only, 1/17 (6%) was positive on day 2 only and 6/17 (35%) were negative on both days. Of all ERD patients, 14 (54%) were positive on both days, 3 (14%) was positive on day 1 only, 5 (18%) was positive on day 2 only and 5 (18%) were negative on both days.
Conclusion: Patients with symptomatic GERD share similar patterns of acid reflux and show only minimal day-to-day variation. However, the detection of pathologic reflux can be increased by 6-18% if pH recording is extended to 48 hours in both patient groups.

Effective removal of oncogenetic alterations after radiofrequency energy ablation of barrett's esophagus containing high-grade dysplasia

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Radiofrequency energy Ablation (RFA) is a new ablative modality for treating Barrett's esophagus (BE) with dysplasia. RFA eliminates BE and restores a normal appearing neo-squamous epithelium. The aim of this study was to evaluate whether genetic abnormalities, as found in dysplastic BE, are effectively eradicated by RFA and absent in the neo-squamous epithelium.10 consecutive BE patients with high-grade dysplasia (HGD) underwent circumferential RFA using a balloon-based electrode (HALO360 System, BÂRRX Medical, Sunnyvale, CA, USA), followed by focal RFA using an endoscope-mounted electrode (HALO90 System).At baseline and 2 months after the final ablation, patients underwent EGD with 4Q/1cm large cup biopsies from the BE (pre-RFA) or neosquamous mucosa (post-RFA). Additionally, brush cytology specimens were obtained from the BE (pre-RFA), neosquamous mucosa (post-RFA) and proximal squamous mucosa (pre- and post-RFA) using 5-cm and 1-cm cytology brushes (Wilson-Cook, Limerick, Ireland). Biopsy specimens were investigated by the same expert pathologist for dysplasia and intestinal metaplasia (IM). Proliferative activity (Ki67) and p53 accumulation were evaluated using immunohistochemical (IHC) staining.Multi-color fluorescent in-situ hybridization (FISH) was performed on all brush cytology specimens using DNA probes for the centromeric regions of chromosome 1 and 9, and locus-specific probes for 9p(p16) and 17p(p53). Results were analyzed with manual scoring and an automated fluorescence microscope with Spot counting software (Applied Imaging, Newcastle, UK). Normal proximal squamous epithelium was used as control.All patients had complete endoscopic and histological eradication of all dysplasia and IM. Pre-RFA BE biopsies showed abnormal Ki67 and p53 staining in all patients. All post-RFA biopsies showed normal squamous mucosa with normal Ki67 and p53 staining. No areas of "buried" IM were found in any of the 149 post-RFA neosquamous biopsies. All pre-RFA BE cytology brushes showed FISH abnormalities, either numerical chromosomal changes (60%), loss of p16/p53 (90%) or both (30%). In contrary to these pre-RFA findings, all post-RFA neo-squamous brush cytology specimens showed a normal diploid signal count for all FISH probes.RFA of BE with HGD is effective for removal of dysplasia and intestinal metaplasia. RFA eradicates pre-existing genetic abnormalities and results in restoration of a neosquamous epithelium without these abnormalities.

Can the presence of intestinal metaplasia and dysplasia in columnar-lined esophagus be predicted? - A multivariable analysis

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The histopathological presence of intestinal metaplasia (IM) and the grade of dysplasia in the columnar-lined esophagus (CLE) determine the frequency of endoscopic follow-up, but are both prone to sampling error and interobserver variability. The aim of this study was to evaluate clinical risk factors in patients with presumed Barrett esophagus that could predict the presence of IM and dysplasia in biopsies of CLE regardless the histological results. Second aim was to develop a simple prediction model based on these data. In 908 patients with a CLE of ≥ 2 cm, data on age, gender, reflux symptoms, tobacco and alcohol use, medication use and upper gastrointestinal endoscopy findings were prospectively collected. Multivariable logistic regression analysis was performed, and a model for predicting the histological results was developed with internal validation by bootstrapping. In 127/908 patients, biopsies of CLE did not contain IM (No IM). Of the 781 patients with IM, 663 (85%) patients had no dysplasia (ND), and 118 (15%) low-grade dysplasia (LGD). Most important predictors for the presence of IM were length of CLE, size of hiatal hernia and male gender, while among those with IM age and male gender were most important for the presence of LGD. Multivariable combinations of these predictors yielded reliable models, which were able to discriminate IM well from No IM (area under ROC curve: 0.82), but only reasonably discriminated LGD from ND (area: 0.65).
Conclusions: A simple model based on clinical findings is able to predict the presence of IM in biopsies from CLE. In contrast, predicting the presence of LGD versus ND in IM is more difficult. Predictions from these models may aid in the decision-making on whether surveillance should be performed in a patient with CLE in view of the known sampling error at endoscopy and interobserver variability at histology.

Esophageal capsule endoscopy in patients with gastro-esophageal reflux disease and Barrett's esophagus: improvement of diagnostic accuracy

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PillCam ESO capsule endoscopy (CE) offers a non-invasive approach to visualize the esophagus. However, recent data have shown mixed results in its diagnostic accuracy. We aimed to assess the accuracy and acceptability of CE in evaluating patients with suspected gastro-esophageal reflux disease (GERD), using a new ingestion protocol. As gold standard esophagogastroduodenoscopy (EGD) was performed 1 week prior to CE. The first 28 patients swallowed the capsule following the original ingestion procedure (OIP), in which the patient ingests the capsule in a supine position, followed by gradually raising the body over a period of 6 minutes. The subsequent 30 patients swallowed the capsule following a simplified ingestion procedure (SIP), in which the patient ingests the capsule in a right lateral decubitus position with every 30 seconds taking sips of water. CE videos were reviewed by two independent investigators who were blinded to the EGD findings. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were evaluated. In addition, patient preference, pain, discomfort, and physical symptoms after both procedures were compared using validated questionnaires. Forty-eight consecutive patients underwent both EGD and CE, of whom 24 were diagnosed with reflux esophagitis (67% male, mean age 49.5±13 years), and 24 with Barrett's esophagus (BE) (88%, 55.6±10) by EGD. In addition, both EGD and CE were performed in 10 asymptomatic healthy controls (50%, 45.8±7). The SIP resulted in a faster mean esophageal transit time as compared to the OIP (126±26 vs. 214±33 sec., p=0.04). A complete evaluation of the Z-line was possible in 19/28 (68%) of the OIP as compared to 28/30 (93%) of the SIP (p=0.04). CE accurately assessed the presence of esophagitis in 22 of 24 patients (sensitivity 92%; specificity 88%; PPV 94%; NPV 85%). BE was detected in 23 of 24 patients (sensitivity 96%; specificity 91%; PPV 97%; NPV 88%). EGD and CE were reported to be burdensome by 39 (89%) and 2 (4%) patients, respectively. EGD gave an increase in throat ache (18% vs. 64%) and regurgitation (59% vs. 82%) (all p<0.05). Of the 44 patients evaluated, 41 preferred CE, none preferred EGD and 3 had no preference.
Conclusion: CE is an accurate method and is more comfortable to patients than EGD for detecting GERD-related esophageal findings. The new ingestion protocol improves visualization of the Z-line, which is likely to increase the diagnostic yield of CE.

Paroxysmal Nocturnal Hemoglobinuria in Budd-Chiari Syndrome – Results of the EN-Vie Study

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Approximately 5-10% of cases of Budd-Chiari Syndrome (BCS) is caused by paroxysmal nocturnal hemoglobinuria (PNH). PNH is an acquired disorder of hematopoietic stem cells, characterized by intravascular hemolysis and venous thrombosis. We have studied the relationship between BCS and PNH with respect to clinical characteristics, treatment outcome and prognosis.Data on baseline characteristics, treatment and survival was obtained from the EN-Vie Study, a prospective international multi-center cohort study of 163 patients with BCS. Study guidelines recommended testing for PNH and this was done in 77 patients.From the group of 77 patients tested for PNH, 15 tests were positive (19%). These 15 patients with PNH were compared to the group of BCS-patients without PNH (n=62). Median follow-up for the total tested group was 19 months (range 0-31). Of the patients with BCS and PNH, 10 had already been diagnosed with PNH at an earlier time but only 2 of these patients were on anticoagulant treatment when the diagnosis of BCS was made, both because of previous thrombosis elsewhere. When comparing the PNH-patients to the group of non-PNH-patients, sex ratio, age at diagnosis of BCS, clinical presentation and liver function tests did not differ significantly between the groups. However, BCS-patients with underlying PNH presented with a significantly higher percentage of additional splanchnic vein thrombosis (SVT; i.e. portal, mesenteric or splenic vein thrombosis) (47% vs. 10%, p=0.002) at diagnosis. Despite the higher frequency of SVT in the PNH-group, the number of patients treated with Transjugular Intrahepatic Portosystemic Shunt (TIPS) during follow-up was similar between both groups (6/15 in PNH group vs. 22/62 in non-PNH-group). Of the 15 PNH-patients, 4 successfully underwent bone marrow or stem cell transplantation after the diagnosis of BCS. There was no significant difference in survival between patients with and without PNH.

Conclusions: PNH appears to be a more frequent cause of BCS than previously thought. Despite the high risk of (fatal) thrombosis in PNH, none of the patients known to have PNH before diagnosis of BCS had anticoagulant treatment as primary prophylaxis. Our data show that, despite a higher frequency of additional SVT, short-term prognosis of patients with BCS caused by PNH does not differ from BCS-patients without PNH. Bone marrow/stem cell transplantation and TIPS appear to be safe treatment options for patients with PNH and BCS.

Pulmonary and blood stream infections in adult liver transplant recipients

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Introduction: Infectious complications occur in approximately 50% of cadaveric liver transplant (CLTx) recipients and confer a major risk of mortality after liver transplantation. Theoretically, living donor liver transplant (LDLTx) recipients have lower infection rates as they are better prepared and have shorter ischemic times. We aimed to assess whether the incidence of pulmonary and blood stream infections in LDLTx recipients differed from their CLTx counterparts. Patients and Methods: To detect the expected difference of 50 percent in the incidence of pulmonary and blood stream infections in favour of the LDLTx recipients (i.e. incidence of 25% of pulmonary and blood stream infections in the LDLTx versus 50% in CLTx group), a minimum number of 55 patients had to be included in each arm of this cohort study. Consequently, the clinical course of 55 LDLTx recipients transplanted between December 2002 and December 2006 was analysed. The 173 CLTx recipients who were transplanted in the same period served as a control group. Patients were treated in a single ICU, applying standardized care consisting of triple immunosuppression and antimicrobial prophylaxis. Differences in infectious complications were calculated by means of Fisher´s exact test. Results: Mean MELD-score did not differ between LDLTx and CLTx recipients (14.2 versus 13.3, p=0.4). The overall incidence of pulmonary and blood stream infections for both groups was 8% and 24%, respectively. Pulmonary infections were experienced by 18% of LDLTx versus 5% of CLTx recipients (p=0.005) and blood stream infections occurred in 33% of LDLTx versus 21% of CLTx recipients (p=0.1). One year survival was significantly higher for all recipients who did not experience a pulmonary infection (85% versus 42%, p<0.001).
Conclusion: LDLTx recipients experienced significantly more pulmonary infections when compared with their CLTx counterparts. There was a trend towards a higher incidence of blood stream infections in the LDLTx group. One year survival rate was significantly higher for both groups when no pulmonary infection occurred. The difference in incidence of pulmonary and blood stream infections might be explained by the smaller graft weight versus body weight ratio in the LDLTx recipients. Recently, Schindl et al. found a significant relation between remnant liver volume and infectious complications after liver resection, reflecting the important role of the liver in the innate immune defence.

Infectious complications in living donor liver transplant recipients are a major risk factor of early mortality

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Introduction: Living donor liver transplantation has gained increasing acceptance for patients with end-stage liver disease. Despite advances in graft preservation, operating techniques and post-transplant care, recipient morbidity and mortality remain considerably high. We analyzed the influence of post-transplant clinical significant infectious complications on recipient survival after living donor liver transplantation. Patients and Methods: All adult living donor liver transplant recipients transplanted in our Unit between 2004 and 2007 were studied. Patients were treated in a single ICU, applying standardized care consisting of triple immunosuppression, antimicrobial prophylaxis and selective digestive decontamination. The definition of clinical significant infections was standardized and contained pulmonary, intra-abdominal and blood stream infections proven by culture with accompanying symptoms that reacted to therapy. Data are expressed as mean ± standard deviation or median with range. The influence of infections on recipient survival was analysed using Fisher´s exact test. Significance was defined as $p<0.05$. Results: Sixty patients suffering from end-stage liver disease were transplanted with a living donor liver graft during the study period. The study group comprised 35 male and 25 female recipients with a mean age of 49.3 ± 11.6 years. Mean MELD score was 14 ± 1. Indications for liver transplantation were cirrhosis associated HCCs (18), viral hepatitis (11), cholestatic liver disease (7), alcoholic liver disease (5), autoimmune hepatitis (4), acute liver failure (4) and other factors (11). Clinical significant infectious complications arose in 26 (43%) recipients, consisting of 8 pulmonary, 14 peri-hepatic or intra-abdominal and 14 blood stream infections. Sixteen (27%) recipients died during their hospital stay after a median of 18 (0-69) days. The main cause of recipient death was septic multi-organ failure in 10 (63%). The risk of mortality was 5.7 times increased when a clinical significant infection occurred ($p=0.0008$).
Conclusion: Clinical significant infections in living donor liver transplant recipients confer a major risk of early post-transplant mortality. Prevention of such infections is crucial to achieve higher post-transplant survival rates. Therefore, active identification of graft and recipient related risk factors is of key importance to improve living donor liver transplantation outcomes.

No beneficial effects of probiotics in primary sclerosing cholangitis (PSC): a randomized placebo-controlled cross-over study

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Primary sclerosing cholangitis (PSC) often runs an unfavourable course, and no effective therapy is available. Probiotics exert beneficial effects in non-alcoholic fatty liver disease and may improve liver function in cirrhosis, supposedly by decreasing intestinal endogenous bacteria, improving intestinal barrier function and increasing anti-inflammatory cytokines (Hepatology 2004;39:1441-49). We therefore explored potential beneficial effects of probiotics on serum liver tests, pruritus and fatigue in PSC. Fourteen patients with definite PSC based on cholangiography and liver biopsy were included (13 male / 1 female: mean age 45 (range 28-70) years: all concurrent IBD: no biochemical remission on UDCA: mean baseline bili 17 (range 7-58) uM: Alk Phosph 311 (126-621) U/L: GGT 260 (45-581) U/L: AST 101 (33-423) U/L: ALT 119 (35-580) U/L: serum bile salts 79 (13-303) uM: normal PT and Alb). They were randomized in a double-blind fashion to treatment with probiotics or placebo during 3 months. After a 1-month washout period, a cross-over to the other treatment modality was performed, again for three months. Patients were evaluated every month during the study period (serum parameters and visual analog scale for pruritus or fatigue). UDCA was continued in the same dosage during the study. The probiotic mixture was composed of Lactobacillus casei, L. salivarius, Bifidobacterium bifidum, B. infantis and B. lactis (Ecologic 641®: Winclove Bioindustries, Amsterdam). Two patients dropped out within 2 weeks (too demanding protocol resp. submandibular streptococcus abcess). No changes in pruritus and fatigue occurred in the remaining 12 patients. There were no significant changes in liver biochemistry or bile salts at various time points. Mean decreases in serum bilirubin of 13% (SD 34%) and 15% (SD 43%) were found in verum and placebo groups (p=0.89) after 3 months. No significant differences were observed between the treatment with probiotics and placebo after 3 months in alkaline phosphatase (probiotics vs placebo after 3 months -9% vs -9% change from basline; p=0.99), gammaGT (-11% vs -5%; p=0.60), AST (-16% vs -15%; p=0.99), ALT (-27% vs -26%; p=0.97), prothrombin time (0% vs 2%; p=0.37), albumin (0% vs -1%; p=0.87) and serum bile salts (-71% vs -10%; p=0.18).
In conclusion, our data do not support beneficial effects of probiotics in primary sclerosing cholangitis.

Psychiatric side-effects and the fluctuations in related amino acids in the treatment of chronic hepatitis C infection.

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Background: Standard treatment of chronic hepatitis C infection (HCV) consists of PEG-Interferon (PEG-IFN) and ribavirin (RBV), is hampered by side effects and associated with the development of psychopathology. PEG-IFN might induce psychiatric disturbance by influencing tryptophan (Trp) metabolism (the precursor of serotonin) and/or inducing a shortage of tetrahydrobiopterin (BH4), an important co-factor in the biosynthesis of serotonin. The aim of this study was to assess treatment related fluctuations in serotonergic parameters and their role in the induction of psychiatric symptoms. Methods: 23 HCV-patients were treated with PEG-IFN-α2a 180 mcg QW and RBV 1000-1200mg QD. At day 0, 1, 4, 7 and 8 and at week 2, 3, 4 and 6 plasma samples were obtained to measure Trp, Trp/LNAA ratio (an index for the availability of Trp to the brain), biopterin and neopterin (both metabolites of the precursors of BH4) and 5-hydroxyindoleacetic acid (5-HIAA, the metabolite of serotonin). At the same time points patients completed the Profile of Mood States (POMS) assessing the following (mood) states: depression, aggression, fatigue, tension and vigor. Except for vigor, high scores indicate more complaints. Results: During treatment, neopterin levels were immediately (baseline:30.2 nmol/l, day 1:99.8 nmol/l) and continuously elevated (week 6: 58.1 nmol/l) whereas only minor changes were seen in the other laboratory parameters. Most notably, concentrations of Trp and the Trp/LNAA ratio did not change except for Trp at week 3. Most consistently, POMS-scores on the scales on aggression increased significantly compared to baseline (baseline: 4.8, maximum week 2: 9.2). No consistent correlation was found between the serotonergic parameters and POMS-scores.
Conclusions: The increase in neopterin levels indicates immune activation, but does not translate into a decrease of peripheral Trp levels as mentioned in the literature. Aggression is a profound and early side effect of PEG-IFN treatment.

Development of a flexible accurate limited sampling model for monitoring tacrolimus after orthotopic liver transplantation: towards C4-monitoring

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Recent articles suggested that C0-monitoring is not the optimal way for therapeutic drug monitoring of tacrolimus and that other time points better estimate the systemic exposure of this drug. Aim of theis study was to objectify which single time points or combination of time points show best correlation with the 'gold standard' AUC0-12h and build and validate a flexible, practical and accurate limited sampling model for monitoring tacrolimus. 23 patients were divided into two groups based on (AUC/dose). With multiple regression analysis limited sampling formulas were derived of all 11 patients of group 1. With use of the computer package MWwe calculated, based on data of group 1, 2-compartment population-pharmacokinetic limited sampling models and validated this models on group 2 (12 patients). All formulas and models were based on single- or multiple point monitoring. We compared the correlation of the AUC calculated with both formulas and models with the gold standard AUC0-12h which was calculated using the trapezoidal rule. Both formulas and models showed excellent correlation with AUC0-12h concerning single points C4 and C6 (r^2=0.94-0.90 and 0.97-0.97). Multiple point sampling showed an even better correlation especially when using the models (r^2=>0.94). C0 was a less good and imprecise predictor of AUC0-12h in both formulas and models (r^2's 0.68 and 0.87, MAPE 17% and 14%).
Conclusion: C0-monitoring is not a reliable method in assessing systemic exposure of tacrolimus. Single time points C4 and C6 showed very good correlation with AUC0-12h, for the models even better than for the rigid formulas. Multiple-point sampling showed an even better correlation with AUC0-12h, but this doesn't even out the flexible, practical, cost-effective and easy to apply single point limited sampling model C4. Hence we introduced the LSM4h-model with a new calculated target range (AUC 174-261 h*µg/l) into our clinic.

FibroScan superior to APRI in detecting significant liver fibrosis in chronic hepatitis B and C patients

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Background: Stepwise combination of noninvasive markers can increase diagnostic accuracy of detecting fibrosis and might reduce the need for liver biopsy. Our aim was to assess a model including serum AST to platelets ratio (APRI) and transient elastography (FibroScan), in order to diagnose significant (F≥2) or advanced fibrosis (F≥3) by Metavir classification in both chronic hepatitis B (CHB) and C (CHC) patients.
Methods: We evaluated 175 consecutive patients with CHB (n=93) or CHC (n=82) for APRI and FibroScan at the time of liver biopsy (F0=15, F1=67, F2=50, F3=28, F4=15). The minimal length of each liver biopsy specimen was 25 millimeter. Cut-off values used were 1.5 for APRI (F≥2) and 7.1 kPa (F≥2) or 9.5 kPa (F≥3) for FibroScan, as described in the original reports.
Results: Overall, PPV of significant fibrosis was 79% with APRI and 74% with FibroScan. NPV was highest with FibroScan (76% vs. 51%). In CHB the areas under the receiver operating characteristic curve (AUC) of APRI and Fibroscan were 0.73 and 0.84 for F≥2 and 0.67 and 0.92 for F≥3, respectively. Combination of APRI and FibroScan in these patients improved diagnostic performance when detecting significant fibrosis (F≥2), with AUC of 0.85. In CHC the AUC of APRI and FibroScan were 0.66 and 0.83 for F≥2 and 0.76 and 0.91 for F≥3, respectively. Our algorithm using APRI as screening test followed by FibroScan in order to diagnose F≥2, reduced the need for liver biopsy by 48% in CHB and 38% in CHC. However, over-estimation occurred in approximately 10% of CHB and CHC patients.
Conclusion: In daily practice the value of APRI as noninvasive marker for significant fibrosis is limited, despite previous reports in the literature. Combination of APRI and FibroScan can improve diagnostic accuracy in chronic hepatitis B, but not in chronic hepatitis C. Diagnostic performance of FibroScan is superior to APRI and is most valuable in detecting advanced fibrosis.

Dilated portal tract veins are associated with a lower incidence of ischemic type biliary lesions after liver transplantation

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Ischemic type biliary lesions (ITBL) are a major cause of morbidity and mortality after liver transplantation (Tx). Up to date the exact mechanism is not fully understood and therefore identifying factors involved in the pathogenesis of ITBL is of critical importance. This study describes the histopathological findings in liver biopsies taken during transplantation.Twenty-one liver biopsies from twenty-one grafts taken one hour after reperfusion were blindly evaluated by an experienced liver pathologist. Eleven recipients who underwent re-Tx due to confirmed ITBL were selected and compared to matched recipients who did not develop ITBL. None of the recipients with ITBL had been diagnosed with thrombosis of the hepatic artery. Histopathological evaluation of biopsies after recirculation included edema, infiltration, necrosis, fibrosis, steatosis, vasculitis, thrombosis and arterial or vein dilatation/stenosis.Dilated portal tract veins were significantly more seen in biopsies from recipients who did not develop ITBL (n=10, p=0.024, Fisher's exact T-test). The odds ratio was 0.067 (95% CI 0.006-0.745). No significant differences were seen for edema, necrosis of cholangiocytes, steatosis or vasculitis. Arterial or venous thrombi were not seen.
In conclusion, dilated portal tract veins in recirculation biopsies of liver grafts are associated with a lower incidence of ITBL. Evaluation of portal tract veins and analysis of the portal flow may serve as an important criterion to assess the quality of liver grafts.

TIPS for treatment of ascites: PTFE-covered stents superior to bare stents

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In patients with cirrhosis and ascites, transjugular intrahepatic portosystemic shunt (TIPS) placement is an established treatment modality. Most studies conducted thus far involved bare stents, since polytetrafluoroethylene(ptfe)-covered stents have only been used extensively in the past years. The aim of this study was to compare the course after TIPS implantation in cohorts of patients treated with bare and covered stents. All consecutive patients undergoing TIPS procedures for ascites or hepatic hydrothorax between January 1993 – December 2006 were included and a retrospective chart analysis was carried out. Follow-up was until March 1, 2007. Survival, shunt revision and encephalopathy were analyzed using Kaplan-Meier plots and the logrank test.6 months after stent placement 15/24 patients were evaluable in the bare stent group with 7 (47%) free of ascites. For the ptfe-covered stent group this was 25/39 with 11 patients (44%) free of ascites. 1 year after the procedure 12/24 and 18/39 patients were evaluable in the bare and ptfe-covered stent group, with 50% free of ascites. 2 years after stent placement only 2/10 (20%) evaluable patients were free of ascites in the bare stent group while for the ptfe-covered stent group this was 7/9 (88%) patients (p=0.02). 63 patients underwent a TIPS procedure for hepatic hydrothorax (n=3, 5%) or ascites (n=60, 95%). Bare stents were used in 24/63 (38%) patients. Baseline characteristics (sex, age, MELD, Child Pugh score and etiology of liver disease) in both groups were comparable. There was a significant difference in the cumulative incidence of patients requiring shunt modification. In the bare stent group this was 50%, 65%, and 85%, while for the ptfe-covered stent group this was 35% and 50% at 6 months and both 1- and 2 years. (p=0.018). The cumulative incidence of hepatic encephalopathy at 6 months and both 1- and 2 years in the bare stent group was 20% and 25%. For patients with a ptfe-covered stent this was 32% at 6 months, 1- and 2 years (p=0.39). The overall 1-year survival was 55% for the bare stent group and 60% for the ptfe-covered stent group (p= 0.57); 2-year survival was 50% for both groups.
Conclusions: In patients with refractory ascites there seems no major therapeutic difference between TIPS with implantation of bare stents as compared with ptfe-covered stents. However, implantation of covered stents decreases the necessity of shunt revision, with a comparable risk for encephalopathy.

Predicting sustained HBeAg loss after treatment with peginterferon alpha-2b: development and validation of a practical model

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Treatment with peginterferon alpha-2b (PEG-IFN α-2b) alone or in combination with lamivudine results in HBeAg loss in 36% of chronic hepatitis B virus (HBV) infected patients. We developed and validated a multivariable model based on readily available factors for the prediction of response to PEG-IFN in individual patients. *Methods:* Data of patients randomized to PEG-IFN α-2b 100µg per week alone (n=136) or in combination with lamivudine 100mg per day (n=130) for 52 weeks were analyzed. Univariate logistic regression analysis, followed by backward stepwise selection was used to identify predictors of HBeAg loss at 26 weeks post-treatment among the variables age, sex, HBV genotype (A-D), serum HBV DNA (log_{10} copies/ml), ALT (x ULN), GGT (x ULN), treatment allocation and previous interferon or lamivudine therapy. Interactions between variables and nonlinear relationships were investigated. Discrimination was quantified by the area under the receiver-operating characteristic curve (AUC). Bootstrap sampling was used for internal validation to reduce overfit bias. *Results:* 23 patients were excluded because of missing values or infection with HBV genotype other than A-D, leaving 233 patients for analysis. HBV genotype (genotype A, OR 1.00; genotype B, 0.36 [95% CI] [0.10-1.33]; genotype C, 0.21 [0.08-0.59]; genotype D, 0.52 [0.26-1.01] for ALT fixed at 3xULN), serum HBV DNA ([↑1log]; 0.68 [0.48-0.97]), GGT ([↑1xULN]; 1.46 [1.06-2.02]) and previous IFN therapy (0.45 [0.21-0.94]) were found to be independent predictors of HBeAg loss. Since the influence of ALT was dependent on HBV genotype, an interaction between these variables was included (p=0.03 for the interaction). ALT particularly influenced the likelihood of HBeAg loss in genotype B infected patients. A multivariable model based on the above mentioned variables had adequate discriminative ability (AUC 0.73). After bootstrapping, the discriminative ability of the model was found to be somewhat lower (AUC 0.69). A nomogram was generated from the logistic regression formula (figure). The probability of HBeAg loss is calculated by drawing a vertical line from each of the 4 variable axis (ALT-genotype, HBV DNA, GGT and previous IFN) to the top Points axis. The sum of these 4 points is put on the Total score axis, from which a vertical line is drawn to the Chance of HBeAg loss axis.
Conclusion: A multivariable model based on HBV genotype, serum HBV DNA, ALT, GGT and previous IFN therapy provides an adequate prediction of PEG-IFN induced HBeAg loss and will be a useful tool to guide treatment choice of PEG-IFN vs. nucleos(t)ide analogues in individual HBeAg-positive patients.

Omeprazole treatment in rats leads to bacterial overgrowth in the proximal digestive tract and altered bile acid metabolism with increased amounts of conjugated deoxycholic acid

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Proton pump inhibitors (PPIs) are prescribed for the treatment of acid-related disorders. Although PPIs are known for their safety and efficacy, bacterial overgrowth in the upper gastro-intestinal tract as a consequence of acid suppression can be a drawback. Moreover, some overgrowing bacterial species are capable of metabolizing primary bile acids into secondary bile acids, i.e., deoxycholic acid (DCA), which has been demonstrated to have a tumor promoting capacity.
In this study, we investigated whether administration of PPIs to rats was associated with bacterial overgrowth and whether bile acid composition was changed in PPI-treated rats.
Ten Wistar rats were treated with 400 μmol/kg omeprazole (PPI-treated), daily administered by gavage for a period of 6 weeks. In addition, 10 rats underwent gastrectomy with esophagojejunostomy (GEJ-treated) to mimic total achlorhydria, and 10 served as normal controls (non-treated). After 6 weeks, the jejunum, ileum, and colon of all rats were cultured. Bile was collected by cannulating the common bile duct and the composition was determined by high performance liquid chromatography. The anaerobic bacteria *Clostridium perfringens* and/or *Bacteroides* spp, which are capable of dehydroxylating primary into secondary bile acids, were present in the proximal jejunum of 6/10 PPI-treated, in 10/10 GEJ-treated rats, and in 0/10 of the non-treated rats. Of the primary bile acids, only glycine-conjugated cholic acid (GCA) was higher in PPI-treated and GEJ-treated rats compared to non-treated rats (GCA: 6541 ($p=0.043$), 3203 ($p=0.009$), and 895 μmol/L, respectively). Of the secondary bile acids, both taurine-conjugated DCA (TDCA) and glycine-conjugated DCA (GDCA) were increased in PPI-treated and GEJ-treated rats compared to non-treated rats (TDCA: 5651 ($p=0.006$), 4645 ($p<0.001$), and 468 μmol/L, respectively and GDCA: 1597 ($p=0.028$), 821 ($p=0.002$), and 67 μmol/L, respectively). Finally, the total sum of secondary bile acids was also higher in the PPI-treated and GEJ-treated rats compared to non-treated rats (9017 ($p=0.022$) and 7835 ($p<0.001$) versus 1850 μmol/L, respectively).
Conclusion: Use of PPIs in rats is associated with overgrowth of anaerobic bacteria in the small bowel and increased biliary levels of DCA. This implies that long-term use of high-dose PPIs may have the unwanted side effect of contributing to exposure of the upper gastro-intestinal tract to potentially toxic DCA.

Dextran sodium sulfate-accelerated tumorigenesis in a novel conditional Apc mutant mouse model of colorectal cancer

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Introduction: The use of Adenomatous polyposis coli (Apc) mutant mice to study colorectal tumors is limited. $Apc^{Min/+}$ mice develop multiple intestinal tumors with a prevalence of lesions in the small intestine at a young age. $Apc^{1638N/+}$ mutant mice show a few tumors in the small intestine around one year of age. To generate an Apc mutant mouse model with mainly colorectal tumors at adult stage, we generated a novel conditional Apc mutant mouse model. FabplCre;$Apc^{15lox/+}$ mice, carrying one Apc allele with exon 15 flanked by loxP sites, specifically express Cre recombinase in the distal small intestine and large intestine under the influence of the liver fatty acid-binding protein (Fabpl) promoter. Cre-mediated excision of exon 15 of Apc results in a mutant allele, lacking nearly all functional Apc domains, specifically in these regions of the intestine. Aim: We evaluated intestinal tumorigenesis in these FabplCre;$Apc^{15lox/+}$ mice and determined the effect of dextran sodium sulfate (DSS)-induced colitis. Material&Methods: 2% (w/v) DSS was given in the drinking water for 5 days at 5 weeks of age. Mice were sacrificed at 8 weeks of age and examined for intestinal tumorigenesis. Results: At 8 weeks of age, FabplCre;$Apc^{15lox/+}$ mice developed on average 4.50 ± 5.87 tumors (mean ± SD, n=10) mainly in the distal part of the large intestine (6.7 % of the tumors ≥ 2 mm). DSS-induced clinical signs of colitis were bloody diarrhea and loss of body weight (up to 7.37 ± 12.85 %) at the end of the DSS period. DSS-treated FabplCre;$Apc^{15lox/+}$ mice showed a significant increase of tumors: They developed on average 28.92 ± 5.35 tumors (mean ± SD, n=6, $p<0.001$) also in the large bowel (12.4 % of the tumors ≥ 2 mm).
Conclusion: FabplCre;$Apc^{15lox/+}$ mice developed intestinal tumors at 8 weeks of age, mainly in the distal large bowel. DSS-induced colitis caused accelerated intestinal tumorigenesis, with more and relatively larger tumors, in this mouse model. Thus, the FabplCre;$Apc^{15lox/+}$ mouse represents a novel colorectal tumor mouse model, which is in combination with DSS treatment well suited to study colitis-induced cancer.

Colorectal neoplasia after liver transplantation is associated with higher proliferative activity, lower apoptosis and increased β-catenin expression compared with controls

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Liver transplant (LT) recipients have an increased risk of colorectal neoplasia. We recently found a striking predominance of advanced adenomas detected in asymptomatic liver transplant recipients, suggesting that the adenoma-carcinoma sequence may be accelerated in LT recipients (Gut 2007;56:892-3). To investigate this hypothesis, we compared the degrees of apoptosis and proliferative activity and Wnt activation, assessed by β-catenin expression, in colorectal tissues obtained from LT recipients compared with controls. The degrees of apoptosis (M30 immunoreactivity) and proliferation (Ki-67 immunoreactivity) and β-catenin immunohistochemical expression were determined in normal colonic epithelium (n = 15) and adenomatous polyps (n = 40) from LT recipients who were on average 11 years after OLT. Results were compared with normal epithelium (n = 15) and adenomas (n = 40) from a historic cohort of sporadic adenomas, in which adenomas were matched for size, degree of dysplasia and growth type.In normal colonic epithelium, no differences in proliferative activity or apoptosis were found between LT recipients and controls. In adenomas from LT recipients, proliferative activity (mean ± SEM) was higher compared to sporadic adenomas (60.3 ± 3.2 % vs 42.7 ± 2.8 %, $p < 0.001$), whereas apoptotic indices were lower in LT recipients (0.29 ± 0.08 % vs 0.39 ± 0.06 %, $p < 0.01$). Nuclear staining of β-catenin was observed in 38/40 of LT adenomas compared to 20/40 sporadic adenomas ($p < 0.0001$) and in none of the normal colon tissue samples.
In conclusion, the differences in proliferation, apoptosis and β-catenin expression in adenomas between LT recipients and controls support an accelerated course of the adenoma-carcinoma sequence in LT recipients.

MRP1 differentially modulates T lymphocyte and intestinal epithelial cell apoptosis

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Background: Multidrug Resistance-associated Proteins (MRPs) are known to cause multidrug resistance in cancer cells. Additionally, MRP1 is upregulated in intestinal epithelial cells and mononuclear cells during severe inflammation in patients with IBD. Recently, we have shown that MRP1 protects intestinal epithelial cells against cytokine and anti-Fas induced apoptosis (Blokzijl *et al.*, submitted). However, the role of MRP1 in modulating apoptosis of T-lymphocytes is unknown. Therefore, we investigated the effect of pharmacological inhibition of MRP function on T-lymphocyte apoptosis.
Methods: The human leukemia derived T-cell line Jurkat was used as a model for human T-cells and the colon carcinoma cell line DLD-1 as a model for intestinal epithelial cells. MRP1 expression was determined by quantitative(Q)-PCR (mRNA) and Western blotting (protein). MRP1 activity was assessed by efflux of the fluorescent substrate 5-carboxyfluorescein (5-CF). Jurkat and DLD-1 cells were treated with anti-FAS to induce apoptosis. MRP function was inhibited by the synthetic leukotriene D4 antagonist MK571 or the plant derived triterpene Oleanolic acid (OA). Cell death was determined by flow cytometry using Annexin V and propidium iodide staining or by caspase-3 activity assay.
Results: mRNA levels of MRP1 were approximately 8-fold higher in Jurkat cells compared to DLD-1 cells. Both MK571 and OA inhibit MRP(1) dependent efflux of 5-CF from Jurkat and DLD-1 cells. Maximum inhibition in Jurkat cells was obtained with 100 µM MK571 or 10 µg/ml OA. Inhibiting MRP1 function with both MK571 or OA reduces anti-FAS induced cell death in Jurkat cells while increasing apoptosis in DLD-1 cells.
Conclusions: In contrast to intestinal epithelial cells, MRP1 inhibition protects T-lymphocytes from anti-FAS induced apoptosis. Currently, we are analyzing whether therapy-resistance of Crohn's disease patients is related to MRP1 expression in T-lymphocytes.

High fat nutrition; a physiologic way to attenuate inflammation

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Attenuation of the inflammatory response is regarded to be fundamental in the treatment of systemic inflammatory response syndrome and sepsis. Previously, we demonstrated that a nutritional intervention with high fat feeding strongly reduces systemic inflammation and preserves gut barrier function following hemorrhagic shock. High fat feeding releases cholecystokinin (CCK) in the gut, which stimulates the autonomous nervous system (ANS) and subsequently inhibits inflammation via vagal efferents. This study investigates how CCK activates the ANS and thereby triggers the anti-inflammatory pathway. Rats were subjected to non-lethal hemorrhagic shock. Before shock, animals were fed high fat nutrition at 18 hrs, 2 hrs and 45 min. CCK mediated activation of the ANS was assessed by administering CCK-A or CCK-B receptor (r) antagonists prior to shock or vagal deafferentation with capsaicin. Plasma and tissue samples were collected 90 minutes after shock. TNF-alpha concentration was measured as inflammatory marker. Gut barrier function was assessed as gut permeability to horseradisch peroxidase (HRP). Administration of CCK-Ar antagonists significantly attenuates the effect of high fat feeding on TNF-alpha compared to vehicle (125.2 ± 5.9 vs 28.0 ± 2.0 pg/ml; $p<0.01$) and to blocking CCK-Br (96.4 ± 8.2 pg/ml; $p<0.05$). Preservation of gut permeability was abrogated by CCK-Ar antagonists compared to vehicle (7.2 ± 2.9 vs 1.9 ± 0.8 ng/ml; $p<0.01$) and to CCK-Br blocking (5.1 ± 2.1 ng/ml; $p<0.01$). Deafferentation significantly inhibited the effect of high fat feeding on TNF-alpha (133.7 ± 31.6 vs sham 45.3 ± 12.9 pg/ml; $p<0.01$) and preservation of gut permeability (6.1 ± 1.0 vs sham 2.7 ± 0.8 ng/ml; $p<0.01$).
In conclusion, these data suggest that by releasing CCK in the gut, high fat feeding activates a potent physiologic nutritional reflex, which stimulates the ANS primarily via vagal afferents and reduces the inflammatory response via vagal efferents.

High expression of p53 and KI67 and aneuploidy predict neoplastic progression in Barrett Esophagus

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Esophageal adenocarcinoma (EAC) carries a poor prognosis, unless detected at an early and therefore curable stage. Biomarkers, which are able to detect neoplastic progression in Barrett esophagus (BE), may improve the early identification of patients at risk for subsequent progression to EAC. In this study we examined expression of p53 and Ki67, and DNA ploidy status in the various steps of progression from BE towards EAC in a group of BE patients who ultimately developed high grade dysplasia (HGD) or EAC and matched these with a group of BE patients without neoplastic progression. Dysplasia grade was determined in 212 biopsy specimens obtained during follow-up endoscopies from 27 patients in whom ultimately HGD or EAC was detected (cases) and in 231 biopsy specimens from 26 patients without progression (controls). Ploidy status was determined by flow cytometry, whereas Ki67 and p53 expression were determined by immunohistochemistry (categories: 0=normal, 1=moderate, 2=strong). Odds ratios (OR) were calculated by logistic regression with multivariate adjustment for the potentially confounding variables sex, age and follow-up period. A total of 27 cases (89% men: mean age 59 ± 10 yr) and 26 controls (70%; 55 ± 12 yr) (p=0.173) were included. Mean duration of follow-up was similar in both groups (cases: 6.9 yr vs. controls: 7.5 yr, p=0.62). Biopsies of cases showed no dysplasia (ND), low grade dysplasia (LGD), HGD and EAC in 47 %, 32 %, 15 % and 6 % of biopsy specimens, respectively, whereas ND was present in 92 % and LGD in 8 % of controls. Moderate Ki67 expression in BE increased the risk of developing EAC (OR 3.0 (95% CI: 1.9-4.8) and was even stronger associated with an increased risk when strong expression was detected (OR15.4 (95% CI: 7.2-33.1). Moderate p53 expression was also associated with an increased risk of developing EAC (OR 14.1 (95% CI: 5.1-39.1), and even stronger when a strong p53 expression was found (OR 302.6 (95% CI: 40.0-2300). Similarly, aneuploidy was associated with an increased risk of developing neoplastic progression (OR 12.9 (95% CI: 2.9-56.8).

Conclusion: Our results show that biomarkers are strongly associated with neoplastic progression in patients with BE. This indicates that these markers may be useful in identifying patients at high risk for developing EAC, however this needs to be confirmed in a longitudinal follow-up study.

Essential fatty acid deficiency in mice impairs intestinal function as reflected by fat malabsorption and reduced lactose digestion

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Essential fatty acid deficiency (EFAD) induces fat malabsorption. Previous studies indicate that the underlying mechanism is located at the intestinal mucosa. In the present study we aimed to delineate the role of the intestinal mucosa in EFAD-induced fat malabsorption. For this purpose, we characterized in mice the effects of EFAD on small intestinal function by determining the digestive and absorptive capacity of another macronutrient, carbohydrates, as well as the intestinal histology. FVB mice were fed an essential fatty acid (EFA)-deficient diet or an EFA-sufficient (control) diet for 8 weeks. To assess EFA-deficiency, we determined triene/tetraene ratio (T/T ratio) in erythrocytes and intestinal fat absorption by a 72h-fat balance. After 8 weeks, we administered an intragastric bolus of U-^{13}C-glucose and 1-^{13}C-lactose, after which the blood appearance of these labels was determined by mass spectrometry. Lactase activity and expression (mRNA), and villus morphology were measured in proximal, mid and distal small intestine. After 8 weeks, mice fed the EFA-deficient diet were markedly deficient, compared to controls (T/T ratio, 0.23 vs. 0.01, resp., $p<0.01$), and malabsorbed their dietary fat (81% vs. 99% of amount ingested, resp., $p<0.01$). After administration of the lactose/glucose bolus, the total blood glucose concentrations and the blood U-^{13}C-glucose appearance were similar in EFAD and control mice, with peaks for blood glucose and blood U-^{13}C-glucose in 30-60 min. in both groups. In contrast, plasma appearance of ^{13}C-lactose was delayed in EFAD mice compared with controls (peak at 45 and 60 min., resp., $p<0.05$), indicating decreased lactose digestion. EFAD was associated with decreased enzyme activity and mRNA expression of lactase in mid small intestine (-55% and -57%, resp., $p<0.01$), but did not affect small intestinal morphology or proliferative capacity. Thus, EFA-deficiency in mice inhibits the capacity to digest carbohydrates without affecting small intestinal histology. Our results indicate that EFAD in mice profoundly impairs intestinal function as reflected by fat malabsorption and reduced lactose digestion.

Molecular mechanisms of microvillous inclusion disease

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Microvillus inclusion disease (MID) is a rare congenital enteropathy, presenting with severe, intractable secretory diarrhea shortly after birth. The complete inability of the intestine to absorb nutrients demands total parenteral nutrition and, eventually, transplantation of the small intestine. MID enterocytes display variable brush border atrophy and accumulate brush border proteins, lysosomal granules, and microvillous inclusions in the apical cytoplasm. While it has been proposed that MID results from a defect in apical membrane trafficking, the nature of such a trafficking defect is not known. Because our lab has previously shown that the apical recycling endosome system in cultured epithelial cells is important for the biogenesis and maintenance of structural and functional apical surfaces, we have investigated the hypothesis that MID enterocytes suffer from a defective apical recycling endosome system.For this, small intestine biopsies of two patients diagnosed with MID were taken. The expression and subcellular distribution of apical recycling endosome-associated proteins (rab11a, rip11, RCP, rabphilin-11 and EEA-1) in the villi and the crypts was investigated by immuno-histochemistry and compared to control patient material. Our data show that in the small intestine of control patient biopsies all apical recycling endosome-associated proteins are expressed close to the brush border in enterocytes of the villi. In the crypts, only rab11a is expressed close to the apical surface, while rip11 and RCP are diffusely expressed. Rabphilin-11 and EEA-1 are not expressed in the crypts and thus can be considered as novel differentiation markers. In striking contrast to the control patients, none of the apical recycling endosome-associated proteins are expressed in the apical cytoplasm of the villi enterocytes of either MID patient. In addition, while rip11 and RCP are likewise not expressed in the crypts, rabphilin-11 and EEA-1 are strongly expressed in the crypts. We conclude that MID enterocytes display an abnormal expression of apical recycling endosome markers and an improper expression of two novel endosome-associated differentiation markers in the crypts. This suggests that endosomal defects and premature intestinal epithelial cell differentiation may underlie MID.

Depletion of the colonic stem cell compartment upon conditional activation of the Hedgehog pathway

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Members of the Hedgehog family of morphogens are expressed throughout the epithelium of the gastrointestinal tract. The study on the role of Hedgehog signaling in the adult gut has been hampered by the embryological phenotype of Hedgehog mutant mice. Here we examined the role of Hedgehog signaling in the colon of adult mice with a conditional deletion of the Hedgehog receptor and transcriptional target Patched (Ptc).
We used tamoxifen-inducible conditional knock-out mice in which exon 8 and 9 of the Hedgehog-receptor Ptc was deleted. Loss of Ptc leads to loss of inhibition of the Hedgehog signaling receptor Smoothened and a constitutively active Hedgehog-signaling pathway. We collected the colons of the adult mice and performed in situ hybridization for Hedgehogs and transcriptional targets Gli1 and Ptc. The phenotype of Ptc mutant mice was examined using routine histological techniques, electron microscopy and by immunohistochemical analysis of cellular proliferation, differentiation markers and Wnt signaling activity.
The in situ hybridizations show that Indian Hedgehog is expressed in the colonic epithelial cells and the Hedgehog-target genes Ptc and Gli1 are expressed in the mesenchyme. Conditional deletion of Ptc increased the activity of of Hedgehog signaling in the mesenchyme. Ptc mutant mice showed large areas of colonic crypt hypoplasia. No gross differences were observed in the presence of the different epithelial cellular lineages, Deletion of Ptc resulted in depletion of cycling precursor cells in the colonic stem cell compartment and electron microscopic imaging showed that the base of the colonic crypts filled with immature cells of the enterocyte lineage. This loss of epithelial precursor cells was associated with inhibition of Wnt signaling as we observed nuclear exclusion of beta-catenin and loss of expression of Wnt-targets EphB2 and EphB3.
Our results show that Indian Hedgehog signals from the epithelium to the mesenchyme in the adult colon. Conditional deletion of the Hedgehog receptor Ptc results in colonic crypt hypoplasia, inhibition of Wnt signaling and depletion of the colonic stem cell compartment. Our results provide the first genetic evidence that Hedgehog signaling acts as a negative feedback loop from the differentiated cells to the stem cell compartment, via the regulation of an as yet unidentified factor in the mesenchyme.

Early presence of intestinal tissue damage in multiple trauma patients

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In trauma patients, the development of sepsis and organ failure are important factors of clinical outcome. Previously, we have shown in a model study for human trauma using hemorrhagic shock in rats that the inflammatory response is accompanied by early intestinal damage. The presence of intestinal damage in trauma patients however remains to be clarified. In this study early intestinal tissue damage is explored in multiple trauma patients. Adult trauma patients (n=67) admitted to the Emergency Room were divided into 4 groups regarding the Injury Severity Score (ISS) and presence of abdominal injury: ISS<25 with (w) abdominal injury (AI) (n=13); ISS>25 w AI (n=16); ISS<25 without (wo) AI (n=25) and ISS>25 wo AI (n=13). Plasma was obtained directly after admittance to the emergency room and on the following two days. Intestinal Fatty Acid Binding Protein (I-FABP), a small cytosolic protein constitutively present in mature enterocytes and released after cellular damage, was measured by ELISA. PCT levels were assessed by Kryptor-Assay. Data are presented as mean values ± SEM. Wilcoxon-test is used for statistic evaluation. On admission, plasma concentrations of I-FABP (1395±438 pg/ml) were significantly elevated in patients with ISS>25 w AI compared to all other groups on admission (ISS>25 wo AI: 309±67; ISS<25 w AI: 531±202; ISS<25 wo AI: 221±46 pg/ml). I-FABP values declined on the following 2 days. PCT values were not elevated at admittance, however PCT values were significantly increased on the first (3.4±0.9 ng/ml) and the second day after admittance in the ISS>25 w AI group compared to all other groups (day 1: ISS>25 wo AI: 0.8±0.3; ISS<25 w AI: 1.4±0.9; ISS<25 wo AI: 0.2±0.1 ng/ml).
In conclusion, this study shows early intestinal tissue damage in multiple trauma patients. Furthermore, these findings demonstrate a connection between early tissue damage and the inflammatory response, both in relation to severity and localization of injury. Since intestinal tissue damage develops early during human multiple trauma, interventions aimed at reducing tissue damage should be started as early as possible.

Performance characteristics of faecal occult blood tests: which test to use for colorectal cancer screening

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Guaiac-based faecal occult blood tests (FOBT's) in a colorectal cancer screening setting are commonly hampered by a poor specificity and positive predictive value, resulting in many (futile) follow-up colonoscopies. Hence, immunochemical FOBT's with apparently better clinical performance, absence of dietary restrictions and only one faecal sample required, have been proposed as a more efficient screening tool.
The aim of the project was to compare an immunology-based (OC sensor®, Eiken chemical Co, Japan) and a guaiac-based (hemoccult®, Beckman Coulter, Inc.USA) FOBT in consecutive patients undergoing colonoscopy in terms of clinical yield of colorectal cancer and advanced adenomas.
All patients aged ≥18 years and scheduled for a colonoscopy in participating hospitals (N=5) were asked to perform both FOBT's in the week prior to colonoscopy. A haemoglobin concentration of ≥100ng/ml in the test sample was considered a positive result. Patients in whom the caecum was not visualized and/or bowel cleansing was insufficient (n=78) were excluded, leaving 962 eligible patients. McNemar's test was used for the comparison of correlated proportions. P≤0,05 was considered statistically significant.
Colorectal carcinoma and advanced adenomas (i.e. ≥1cm in diameter and/or villous architecture and/or high-grade dysplasia) were found in 3,0% and 8,7% of the patients, respectively. Small adenomas, colitis and other lesions were identified in 38,0% of the patients. No lesions were found in 50,2% of the patients. The hemoccult® test and OC sensor® test showed positive outcome in 7,8% and 11,5%, respectively. None of the differences between the tests were statistically significant.
In conclusion, although the sensitivity and specificity of both tests in detecting colorectal cancer were high in this patient group, the sensitivity to detect high-risk, pre-cancerous lesions was disappointing. The low positive predictive value in these pre-cancerous patients might hamper the introduction of either one of these tests in a screening setting. A larger cohort is currently being investigated to corroborate these preliminary findings and compare both types of tests.

Primary colonoscopy screening for colorectal cancer in a workplace-based community: first results of participation and acceptance

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Colonoscopy is considered as the gold standard for colorectal cancer(CRC) screening and as rather invasive. The feasibility of this screening method depends on participation and acceptance. Presently we study colonoscopy screening in workplace-based communities in the Netherlands. Data of the first community (hospital setting) on participation and acceptance will be presented.
After announcement by the employer, employees aged 50-65 yrs were invited by letter including an information brochure and answer form. Then, 9 open information sessions were held. Colonoscopies under conscious sedation were performed by experienced endoscopists (subjects with severe co-morbidity, prior colonoscopy ≤5 yrs and recent GI symptoms were excluded). Participation and acceptance were evaluated by questionnaires.
987 employees were invited (58.7% f, 41.3% m).The information sessions were attended by 180 employees (18.2%). After the information campaign, 547 employees (55.4%) returned the answer form. In total, 38.5% (380) confirmed their participation to colonoscopy: 27.6% before, and an additional 6.7% after the information sessions; further 4.2% applied when colonoscopies had started. Participation was equal for men and women. Reasons for participation (multiple answers possible) were: 21.2% family history of CRC; 10.3% GI symptoms; 67.0% health reassurance; 14.3% family support; 41.9% “obvious to accept screening”; 12.8% other reasons. Only 167 of 607 non-participants returned the answer form. In these, reasons of non-participation were: 16.5% co-morbidity or previous colon examination; 15.9% invasiveness of colonoscopy; 4.2% other; remainder without specification. So far 203 colonoscopies have been performed. Participants reported “no physical or mental complaints” in 23.4%, “some” in 65.0% and “many” in 11.6% during colonoscopy. One month later, bowel preparation and colonoscopy were rated as “somewhat uncomfortable” by 60.7% and 31.9%, and “very uncomfortable” by 17.0% and 0.7%, respectively. However, 99.3% was prepared to repeat the colonoscopy in future.
Initial compliance in this workplace-based colonoscopy screening was high and increased after diffusion of information within the community. Bowel preparation was perceived as more uncomfortable than colonoscopy. Our present conclusion is that colonoscopy screening using an extensive information campaign in a workplace setting has a good participation rate and is subsequently well-accepted.

Risk stratification among individuals attending population-based sigmoidoscopy screening

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Background: Screening for colorectal cancer (CRC) is widely accepted in the Western world. The AGA guidelines recommend determining the individual risk status on CRC before screening is initiated. Individuals with a high-risk status on CRC (high-risk individuals) should be offered more intensive colonoscopic surveillance and therefore not enter a mass screening program. In our sigmoidoscopy screening program high-risk individuals were advised to go to their general practitioner. However, unidentified high-risk participants of sigmoidoscopy screening, may lack sufficient screening (reassurance by negative sigmoidoscopy instead of full colonoscopy) or have the burden of an unnecessary sigmoidoscopy (positive sigmoidoscopy followed by colonoscopy). Aim: To identify high-risk individuals among participants of a sigmoidoscopy screening program. Methods: Three relevant categories to accomplish risk stratification were derived from literature: (i) history of colon polyps or CRC; (ii) history of inflammatory bowel disease (IBD); and (iii) positive family history of CRC (one first-degree relative with CRC < 50 yr, one first degree relative and one first- or second-degree relative with CRC). The three categories were incorporated in a risk stratification questionnaire (RSQ). All participants were asked to complete the RSQ prior to undergoing the sigmoidoscopy screening. Results: The individual RSQ was assessed in 566 (male=306; female=260; mean age 60.4, range 50-75 yrs). The response rate was 95.1%. One participant reported a history of CRC (0.2%), 18 of colon polyps (2.7%) and two of IBD (0.4%). Twelve participants had a positive family history (2.2%), of whom one participant also had a history of colon polyps. The participants with a history of CRC, as well as two out of seventeen participants with colon polyps were already under colonoscopic surveillance. Twenty-seven high-risk participants were not under colonoscopic surveillance (5.0%).
Conclusion: The percentage of unidentified high-risk individuals in our sigmoidoscopy program was rather low, however this group may account for a relatively high number of CRC. Thus, risk stratification prior to a population based screening program by using a RSQ may further optimize a population-based screening program. Participants who fulfill high-risk criteria should enter an intensive surveillance program instead of undergoing a sigmoidoscopy.

First Report: Triage for colorectal cancer with CT colonography with limited bowel preparation in a FOBT positive screening population

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In a first screening program for colorectal cancer (CRC) in the Netherlands a total of 10.000 individuals between 50 and 75 years are invited for a FOBT, either guiac or immunochemical. Earlier studies showed that FOBT might be false positive in approx. 60%. CT Colonography with limited bowel preparation (CTC) is a less burdensome technique than colonoscopy. CTC could be used as triage method after a positive FOBT. The aim of this study was to determine whether CTC is an accurate triage method for the detection of CRC and polyps ≥10 mm and polyps ≥6mm after a positive FOBT, to decrease the number of colonoscopies. The results of the first 100 FOBT positive individuals (22 Hemoccult, 78 OC-Sensor) participating in the CTC triage study between May 2006 and December 2006 were analysed. All participants underwent a CTC with limited bowel preparation, which was interpreted by two independent observers. Reference standard was colonoscopy with segmental unblinding. PPV and NPV were calculated on a per patient basis with two cut-off points: patients with a CRC and/or at least one polyp ≥10 mm (category 1) and patients with a CRC and/or at least one polyp ≥6mm (category 2).

In total 6% of FOBT positive patients had a carcinoma which were all identified at CTC, no false positive CRC finding (PPV and NPV:100%). 50% of FOBT positives had a category 1 lesion (OC Sensor PPV 47%; Hemoccult PPV 64%) and 70% a category 2 lesion (OC-Sensor PPV 68%; Hemoccult PPV 82%).

In category 1, CTC was positive in 47 patients (PPV 87%) and negative in 53 patients (NPV 83%). However, of the 9 false negative patients, 7 patients had a matched polyp between 6,5 mm and 9,9 mm on CTC. In category 1 for patients with a positive OC-sensor CTC had a PPV of 88% and a NPV of 86%. For Hemoccult for category 1 CTC had a PPV of 85% and a NPV of 67%.

In category 2 CTC was positive in 72 patients (PPV 92%) and negative in 28 patients (NPV 86%). In category 2 CTC had for patients with a positive OC-Sensor a PPV of 89% and a NPV of 90%. For Hemoccult for category 2 CTC had a PPV of 100% and a NPV of 67%.

CTC is an accurate triage technique for CRC in a FOBT positive population. In this cohort the number of patients with polyps ≥ 6mm was very high and CTC was less accurate in triage of patients with such lesions. CTC can be used as triage technique to reduce the number of colonoscopies, but might be more useful in triage for OC-sensor test positives, than for Hemoccult test positives.

How safe are Dutch guidelines for endoscopic follow-up of colonic adenomas?

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In the Netherlands in 2001 guidelines for endoscopic follow-up of colonic adenomas were revised. Standards for follow-up intervals of sporadic colonic adenomas were based on the number of identified adenomas and on age of the patient. To our knowledge there are no data yet on the incidence of colonic adenocarcinoma in patients treated according to these guidelines.In our department we register, schedule and call patients for postpolypectomy surveillance. In 2002 all patients were rescheduled according to current guidelines. All endoscopies as well as clinical and histology data are stored in an electronic database.Patients undergoing colonoscopy between June 2000 and June 2002 were identified. This cohort was followed until 2007. Clinical and endoscopic characteristics were analysed. Secondly, the pathology PALGA database was searched for colonic carcinomas and these data were matched with the colonoscopy cohort. Patients with Inflammatory Bowel Disease (IBD), HNPCC, Familial Adenomatous Polyposis (FAP) and colon carcinoma were excluded.During this period 3230 patients underwent colonoscopy, 170 patients were found to have colon cancer, 451 patients were excluded for IBD, FAP or HNPCC, 44 had only hyperplastic polyps.In 701 (M/F= 388/313) of the remaining 2565 patients (27%), colonic polyps were found and treated. Mean age was 61yr (range 22-88). Cecal intubation, as recorded by photography was established in 94%. Histology was obtained in 411 patients: 42 had adenomas with severe dysplasia , 369 had mild or moderate dysplasia. If no histology was obtained patients were treated according tot guidelines as if they had adenomas. We identified 5 patients of our cohort of 701 (0,7%) who developed subsequent colonic carcinoma: One patient (age 86) was found to have a cecal carcinoma 9 months after initial endoscopy. Four other patients developed colonic cancer 24-59 months after colonoscopy. Three of these patients had their colon cancer before scheduled surveillance and one after cessation of surveillance because of advanced age. The incidence of colon carcinoma in our cohort is 1,6 cases per 1000 person years.
In conclusion, these results are within the expected range and confirm the safety of current guidelines.

Autofluorescence endoscopy improves the detection of colorectal adenomas in subjects with hereditary non polyposis colorectal cancer or familial colorectal cancer; a back-to-back colonoscopy study

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Surveillance colonoscopy is advised in familial colorectal cancer (CRC) syndromes. Especially in hereditary non-polyposis colorectal cancer (HNPCC) small or flat neoplastic lesions are prone to progress rapidly into colorectal cancer. These lesions can easily be missed on standard flexible white light endoscopy (WLE). Autofluorescence endoscopy (AFE) might be capable of detecting adenomatous lesions that are not recognized using WLE. The aim of the present study was to compare the sensitivity of autofluorescence endoscopy and white light endoscopy in diagnosing colorectal adenomas in patients belonging to HNPCC or familial CRC families.Fifty-one consecutive asymptomatic patients (mean age 48 ± 11 years) belonging to HNPCC or familial CRC families were recruited for examination with both WLE and AFE. First, standard WLE was performed using a standard video endoscope (CF160, Olympus, Japan). Immediately after the WLE procedure a second endoscopist, unaware of the results of the previous WLE, performed AFE with an autofluorescence endoscopy system (Onco-LIFE, Xillix, Canada). During both procedures all lesions were photographed and videotaped, and graded according to size, morphology, and location. All lesions were judged to be either non-dysplastic or suspicious using both techniques and were removed and collected during AFE. Lesions missed on second endoscopy by AFE were identified and removed on third endoscopy by WLE again. Sensitivity was calculated by correlating positive and negative findings to the pathology results.A total of 65 adenomas were detected in 31 patients. White light endoscopy identified 43 adenomas in 20 patients. All these lesions except for three were also found by AFE. This method however identified an additional number of 22 adenomas in 11 patients. The 22 additionally detected adenomas had a significantly smaller mean size compared to the adenomas detected by WLE (3.0 mm vs. 5.0 mm, $p < 0.01$). The sensitivity of AFE for the detection of adenomas was significantly higher than the sensitivity of WLE (95% vs. 66%; $p < 0.001$).
Conclusions: Autofluorescence endoscopy significantly improves the detection of colorectal neoplasia in patients with HNPCC or familial colorectal cancer. For this high risk population autofluorescence endoscopy has a clear additional value in the detection of small and flat adenomas.

Proton pump inhibitors and the risk of colorectal cancer

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Proton pump inhibitor (PPIs) use is associated with increased serum gastrin levels and bacterial overgrowth resulting in more toxic bile salt formation. Concern has risen that these factors may increase the risk of colorectal neoplasia. We conducted a population-based case-control study within the Dutch Primary Care Information (IPCI) database during the period 1996-2005 to investigate the association between the use of PPIs and the risk of colorectal cancer. Cases with colorectal cancer were matched with up to 20 controls on age, gender, calendar time and duration of follow-up prior to diagnosis. Cumulative exposure to PPIs was assessed in the five years prior to diagnosis with a one-year lag time analysis. The relative risk of colorectal cancer, overall and separately for the right and left hemicolon, was estimated by adjusted odds ratios (OR) with 95% confidence intervals (95% CI) using multivariate conditional logistic regression analysis. Within the source population of 457,024 persons, we identified 595 colorectal cancer cases. Thirty percent of the tumours were located in the right hemicolon and 66% in the left hemicolon. Fifty-three cases (8.9%) and 725 controls (9.3%) used PPIs prior to the index date. Patients ever using PPIs were not at an increased risk of colorectal cancer compared to patients who never used PPIs (OR: 0.85, 95%CI: 0.63-1.16). Also patients using PPIs for 30-365 days or for >365 days were not at an increased risk of colorectal cancer compared to patients who did not use PPIs (OR: 0.77, 95%CI: 0.49-1.22 and OR: 0.79, 95%CI: 0.44-1.41 respectively). The risk of cancer in both the right and left hemicolon was not increased in patients using PPIs.
Conclusion: The present study shows no increased risk of colorectal cancer among PPI users.

Efficacy of colonoscopy, sigmoidoscopy and barium enema in reducing the incidence of CRC

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Colorectal cancer (CRC) screening programs have been implemented in many countries. The efficacy of different screening methods in reducing the incidence of CRC is however much debated. We therefore investigated the uptake of colorectal examinations (colonoscopy, sigmoidoscopy and barium enema (BE)) prior to diagnosis in CRC patients, compared with a matched control group to estimate the effect of these examinations on the incidence of CRC.
We conducted a case-control study using the Integrated Primary Care Information database, a general practice research database containing the complete, longitudinal electronic medical records of more than 500.000 persons throughout the Netherlands. All incident CRC cases during the study period were identified. The mean time prior to diagnosis was 4 yrs (range 0.5-5 yrs). For each CRC case, up to 20 controls (mean 13 per case) were identified, matched for age, sex, indexdate (date of CRC diagnosis) and time prior to diagnosis. All colorectal examinations performed >0.5 to max. 5 yrs prior to the index date in CRC cases and their controls were considered in the analysis. The influence of several covariates (obesity, smoking, NSAID use, IBD etc) were tested.
In total, 594 incident cases of CRC (M/F 301/293, mean age 69 yrs, range 25-99) were identified. In the period 0.5 to max. 5 yr prior to indexdate, 2.9% (17/594) of the CRC cases had undergone a colorectal examination, compared with 4.4% (345/7790) in the control population (p=0.029, OR 0.56, 95% CI 0.33 to 0.94, multivariate analysis). IBD was found to be the only confounder (OR 3.0, 95% CI 1.38-6.6).
One percent of the cases had undergone at least one colonoscopy, 0.5% a sigmoidoscopy, and 1.3% a BE. In the control group 2.2% had undergone a colonoscopy, 1.1% a sigmoidoscopy and 1.6% a BE.
Significantly more controls were examined for the purpose of surveillance after polypectomy (0.5% vs 7%, p<0.01). Change of bowel habits and abdominal pain was the main indications in the control group, resp. 28% vs 20% and 25% vs 13% compared to CRC patients (p<0.01), rectal blood loss was the main indication in CRC patients (36% vs 21% in controls, p<0.01).
In conclusion, significantly more controls have previously undergone colorectal examinations than CRC patients. This supports the concept that colorectal examination by various modalities exerts a long-term preventive effect on the incidence of CRC. This effect is of considerable magnitude, even after a single investigation.

Association between JC virus and the development of colorectal neoplasia after liver transplantation

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Liver transplant (LT) recipients have an increased risk of colorectal neoplasia. The mechanism responsible for this is unknown. JC virus (JCV) has been implicated in colorectal carcinogenesis by encoding a transforming gene, T-antigen (T-Ag). We hypothesized that the use of immunosuppression in LT recipients facilitates reactivation of the oncogenic JCV. Using a gene specific PCR and real-time PCR, JCV T-Ag DNA and viral copy number were determined in normal colonic epithelium (n=15), adenomatous polyps (n=33) and carcinomas (n = 3) from LT recipients on long term immunosuppressive therapy and compared with normal epithelium (n = 21) and adenomas (n=33) from control patients.JCV T-Ag DNA sequences were found in normal mucosa of 10/15 (66.7 %) LT recipients, compared to 5/21 (23.8 %) in control normal mucosa samples ($p = 0.025$). JCV T-Ag DNA sequences were detected in 17/33 (51.5 %) LT adenomas and in 2/3 (66.7 %) LT carcinomas compared to 16/33 (48 %) control adenomas. The average JC viral copy number per cell in the normal LT samples was 16 times higher than in the normal control samples ($p < 0.005$). The viral copy number in the LT adenoma samples was 3.2 times higher than in the control adenoma samples ($p < 0.05$).
In conclusion, the more frequent detection of JCV T-Ag sequences in LT normal mucosa and the presence of higher copy numbers of JCV in LT colorectal mucosa and adenomas compared with controls suggest that JCV contributes to the increased risk of colorectal neoplasia in LT recipients.

Sequential versus combination chemotherapy with capecitabine, irinotecan, and oxaliplatin in advanced colorectal cancer (ACC). A Dutch Colorectal Cancer Group (DCCG) phase III study.

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Overall survival (OS) in phase III studies with 1st line combination therapy in ACC may be influenced by imbalances in salvage treatments. This is the first study that prospectively investigates the sequential vs the combined use of all available effective cytotoxic drugs.
Previously untreated patients (pts), WHO PS 0-2 were randomized between 1st line capecitabine (Cap), 2nd line irinotecan (Iri), and 3rd line Cap + oxaliplatin (CapOx) (Arm A, sequential) vs 1st line CapIri and 2nd line CapOx (Arm B, combination). The dose of Cap was 1250 mg/m^2 (mono) or 1000 mg/m^2 (combination) b.i.d. day 1-14, Iri 350 mg/m^2 (mono) or 250 mg/m^2 (combination), and Ox 130 mg/m^2. All cycles were q 3 weeks with Iri/Ox given i.v. on day 1. Response was assessed q 3 cycles. Primary endpoint was OS. The study was designed to detect a 20% reduction in the hazard of death (HR=0.80) for an increase in median OS from 14 to 17.5 months (α=0.05, 2-tailed test).
820 pts were randomized between jan '03 and dec '04 in 74 Dutch hospitals. Of 804 eligible pts, 796 received $\geq$ 1 cycle. Median age was 63 (27-84) yrs, median WHO PS 0 (0-2), median follow-up 32 m. Pts (n) in arm A: 398 (1st line), 248 (2nd line), 141 (3rd line); arm B: 398 (1st line), 210 (2nd line). Median OS in arm A was 16.3 months (95%CI 14.3-18.2) and in arm B 17.7 months (95%CI 15.2-19.4), logrank p=0.2. Overall gr 3-4 toxicity over all lines did not differ significantly except for gr 3 hand-foot syndrome (HFS) (13% in A and 6% in B, p=0.0009). Death was probably related to treatment in 11 pts (neutropenic sepsis and/or diarrhea, 8 arm A, 3 arm B) and involved protocol violations in some. In 1st line significant differences in gr 3-4 toxicity in arm A vs arm B were diarrhea (10% vs 25%, p<0.0001), febrile neutropenia (1% vs 6%, p=0.0001) and HFS (12% vs 5%, p=0.0004). All-cause 60-day mortality was 3.0% (n=12) in arm A and 4.5% (n=18) in arm B. Updated results will be presented at the meeting, including data on QoL (EORTC QLQ C30).
Conclusions: Combination therapy does not significantly improve OS compared with sequential therapy. Both treatment strategies are valid options for pts with ACC.

Alfabetische lijst van standhouders

B = Beneluxhal K = Kempenhal	***Standnr.***
Abbott B.V.	B18
Allergan B.V.	B6
Alvleesklliervereniging	K21
AstraZeneca B.V.	B19
B. Braun Medical B.V.	B22
Bipharma Diagnostics B.V.	B26, K7
Boston Scientific Benelux B.V.	B24
Bristol Myers Squibb	B7
Campro Scientific GMBH	B27
C-MEX	K18
Cobra Medical B.V.	K5
Crohn en Colitis Ulcerosa Vereniging Nederland	K14
Danica Nederland B.V.	B21
Dyped B.V.	B4
Endomed B.V.	B30
Endotechniek	B20
Ferring B.V.	B1
FMH Medical B.V.	K8
Fresenius Kabi Nederland B.V.	B29
Getinge B.V.	B25
Gullimex B.V.	B14
Hitachi Medical Systems	B11
Jansen Medicars B.V.	B10
Janssen-Cilag B.V.	B16
Lans Medical	B9
Medical Measurements Systems B.V.	B17
Medicor	B5
Mediphos Medical Supplies B.V.	B8
Medtronic Trading NL BV	B28
MTW-Endoskopie	B12
Nationaal Hepatitis Centrum	K22
Nederlandse Coeliakie Vereniging	K3
Norgine B.V.	B23
Novartis Pharma B.V. (infectieziekten)	K16
Nycomed bv (voorheen ALTANA Pharma bv)	K13, K15
Olympus Nederland B.V.	K10, K17
Roche Nederland B.V.	K6
RVC B.V.	B17a
Schering-Plough B.V.	K23
Solvay Pharma B.V.	K11
Stichting Opsporing Erfelijke Tumoren	K20
Stichting Vreemde Kronkels	K4
Surgical Technologies B.V.	B13
Tramedico B.V.	K1
UCB Pharma B.V. Afd. Inflammation	K12
UCB Pharma B.V. Afd. Infectious Diseases	B3
Vandeputte Medical	B2
Vereniging Ziekte van Hirschsprung	K19
Wassenburg Medical Devices B.V.	K9
Zambon Nederland B.V.	K2

plattegrond

AANMELDINGSFORMULIER VOOR HET LIDMAATSCHAP VAN DE NEDERLANDSE VERENIGING VOOR GASTROENTEROLOGIE

Naam : M/V*
Voorletters :
Geboortedatum :
Titel :
Specialisme :
BIG registratienummer :
Assistent in opleiding voor :
einde opleiding :

Werkadres
instituut :
afdeling :
straat :
postcode en plaats :
telefoon :
e-mail :

Huisadres
straat :
postcode en plaats :
telefoon :

Doctoraalexamen : ja/neen*; zo ja, welke studierichting:
Datum artsexamen : d.d. . . . . ./n.v.t.*
Inschrijving MSRC : ja/neen*, zo ja, welk:
Speciale interesses op GE-gebied :

geeft zich hierbij graag op als lid van de NVGE *(contributie € 35,- per jaar)*
Aanvullende lidmaatschappen van met *aangegeven secties zijn kosteloos

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)*
contributie, 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)

Toezending verenigingspost aan huis-/werkadres*.

Datum: Handtekening:

_____

Sturen aan de secretaris van de NVGE: Postbus 657, 2003 RR Haarlem
* doorhalen wat niet van toepassing is.

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

AANMELDINGSFORMULIER VOOR HET LIDMAATSCHAP VAN DE NEDERLANDSE VERENIGING VOOR HEPATOLOGIE

Nederlandse Vereniging voor Hepatologie

Naam : M / V*
Voorletters :
Geboortedatum :
Titel :
Specialisme :
BIG registratienummer :
Assistent in opleiding voor :

Werkadres
Instituut :
Afdeling :
Straat :
Postcode en plaats :
Telefoon :
e-mail :

Huisadres
Straat :
Postcode en plaats :
Telefoon :

Toezending verenigingspost aan : huis- / werkadres*.
Doctoraalexamen : ja/neen*; zo ja, welke studierichting
Datum artsexamen : d.d. /n.v.t.*
Inschrijving Specialistenregister : ja/neen*; zo ja, welk:
Speciale interesses op hepatologisch gebied :

Toezending verenigingspost aan huis-/werkadres*.

☐ Hierbij machtig ik de penningmeester van de Nederlandse Vereniging voor Hepatologie om de verschuldigde contributie, ad € 25,00 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 acceptgiro.
Het lidmaatschap loopt per kalenderjaar, eventuele opzeggingen derhalve vóór 1 november.

(Post)bankrekeningnummer

Datum: Handtekening,

_____

Sturen aan: Secretariaat NVH, Postbus 657, 2003 RR Haarlem

** Doorhalen wat niet van toepassing is.*

Nederlandse vereniging voor Gastro-Enterologie

SEVA Sectie endoscopie verpleegkundigen en assistenten

AANMELDINGSFORMULIER LIDMAATSCHAP NVGE / SEVA

Naam : M / V*
Evt. meisjesachternaam :
Voorletters :
Geboortedatum :

Werkadres

Instituut :
Afdeling :
Straat :
Postcode en plaats :
Telefoon :
e-mail :

Huisadres

Straat :
Postcode en plaats :
Telefoon :

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

U bent verpleegkundige / doktersassistent(e) anders, nl. ……*

Datum:…… Handtekening:……..

** aangeven wat van toepassing*

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

Bankrekeningnummer Handtekening

Indien u geen machtiging tot incasso geeft ontvangt u automatisch een acceptgiro.
N.B. Het lidmaatschap loopt per kalenderjaar. Opzeggen dient dus vóór 1 januari te gebeuren.

Dit formulier sturen naar:
Centraal Secretariaat NVGE (ledenadministratie SEVA) Postbus 657 - 2003 RR Haarlem

VERENIGING
MAAG
DARM
LEVER
VERPLEEGKUNDIGEN

VMDLV

AANMELDINGSFORMULIER
LIDMAATSCHAP NVGE/VMDLV

Naam : M / V*
Evt. meisjesachternaam :
Voorletters :
Geboortedatum :

Werkadres
Instituut :
Afdeling :
Straat :
Postcode en plaats :
Telefoon :
E-mail :

Huisadres
Straat :
Postcode en plaats :
Telefoon :

BIG registratienummer : _____ datum registratie:_____

geeft zich hierbij 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:…….

** aangeven wat van toepassing is.*

☐ 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 acceptgiro.

(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 formulier sturen naar:
Centraal Secretariaat NVGE (ledenadministratie VMDLV)
Postbus 657 - 2003 RR Haarlem