Programma najaarsvergadering 7 en 8 oktober 2010

NEDERLANDSE VERENIGING VOOR GASTROENTEROLOGIE

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

NEDERLANDSE VERENIGING VOOR HEPATOLOGIE

NEDERLANDSE VERENIGING VOOR GASTROINTESTINALE CHIRURGIE

NEDERLANDSE VERENIGING VAN MAAG-DARM-LEVERARTSEN

Locatie:

NH KONINGSHOF VELDHOVEN

INHOUDSOPGAVE **pag**

Tijdstippen diverse ledenvergaderingen donderdag

Nederlandse Vereniging voor Gastroenterologie	7 oktober, 11.30 uur – Brabantzaal
NVMDL i.o.	7 oktober, 12.00 uur – Zaal 81 / 82
Nederlandse Vereniging voor Hepatologie	7 oktober, 15.30 uur – Baroniezaal

INHOUDSOPGAVE **pag**

Tijdstippen diverse ledenvergaderingen vrijdag:
Sectie Endoscopie Verpleegkundigen en Assistenten 8 oktober, 11.45 uur - Diezezaal
Nederlandse Vereniging van Maag-Darm-Leverartsen 8 oktober, 12.00 uur - Genderzaal

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

VOORWOORD

Hierbij treft u het programma aan van de najaarsvergadering die gehouden wordt op 7 en 8 oktober a.s. in Congrescentrum NH Koningshof te Veldhoven.
Ook dit keer worden deze dagen vooraf gegaan door het cursorisch onderwijs in maag-darm-leverziekten, waarvan u het programma aantreft op bladzijde 6-7.

Het programma zal donderdag 8 oktober **om 10.00 uur** van start gaan met het eerste symposium van de nieuw opgerichte IBD-werkgroep, getiteld: 'Optimale inzet van medicatie bij IBD'. Parallel aan dit symposium kunnen in respectievelijk de Baroniezaal en het Auditorium de presentaties van de Nederlandse Vereniging voor Hepatologie en Nederlandse Vereniging voor Gastro Enterologie worden gevolgd. Na de lunch in de expositiehal, vindt in de middag onder andere een symposium over de dysmotore slokdarm plaats, een symposium van de NVH over leverfalen en hypertensie en een workshop Landelijke Colonstent database. Aan het einde van de middag zal in de Brabantzaal de 'Tytgat Lecture' worden gegeven, ditmaal door prof. dr. E. Van Cutsem uit Leuven met een voordracht getiteld: 'Op weg naar een meer gepersonaliseerde therapie voor colorectale kanker'. Om 17.00 volgt de President Select en om 18.00 uur aansluitend de uitreiking van de Janssen Cilag Gastrointestinale Research Award 2010. De eerste prijswinnaar zal na de uitreiking een erevoordracht houden. Met deze lezing wordt het programma van de donderdag afgesloten.
In de avond is er geen programma ingepland. Het diner vindt plaats in de Genderzaal, daarna, vanaf omstreeks 22.30 uur, is er muziek in de Baroniezaal en de gebruikelijke congresborrel in de Limburgfoyer.

Op vrijdagochtend starten de abstractpresentaties in verschillende zalen alweer om 08.30 uur. In de Brabantzaal wordt het 30-jarig bestaan van de Sectie Gastrointestinale Endoscopie gevierd met een groot symposium getiteld 'Choices in Endoscopy'. In de middag vindt er eveneens een jubileumsymposium plaats in de Brabantzaal in verband met het 25-jarig bestaan van de Stichting Opsporing Erfelijke Tumoren. Parallel daaraan in de Baroniezaal de richtlijnbijeenkomst Bloedingen. In de Diezezaal tenslotte, worden door Verpleegkundigen & Verzorgenden MDL (SEVA / VMDLV) een eigen programma met lezingen verzorgd.

Graag tot ziens in Veldhoven!

Dr. R.J.F. Felt-Bersma, secretaris
Nederlandse Vereniging voor Gastroenterologie

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

Belangrijke mededeling

over de aanwezigheid van farmaceutische industrieën

Aan alle deelnemers aan de najaarsvergadering

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

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

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

Het bestuur van de NVGE

Cursuscommissie: Prof. dr. P.D. Siersema (voorzitter) (MDL-arts, UMCU)
Dr. B.B. van Elzen (aios MDL, AMC)
Dr. E. van der Harst (chirurg, Maasstad Ziekenhuis)
Dr. D.J. de Jong (MDL-arts, UMCN)
Prof. dr. J.H. Kleibeuker (MDL-arts, UMCG)
Drs. A.D. Koch (aios MDL, Erasmus MC)
Dr. R. Timmer (MDL-arts, Antonius Nieuwegein)

Onderwerp: Oncologie (premaligne afwijkingen)

Voorzitter: *Dr. D.J. de Jong, MDL-arts, UMC St. Radboud, Nijmegen*

14.45 – 15.00	Evaluatie toets
15.00 – 15.30	Intestinale metaplasie van de maag *Dr. A.C. de Vries, aios MDL, Erasmus MC, Rotterdam*
15.30 – 16.00	Screening op HCC *Dr. R.J. de Knegt, maag-darm-leverarts, Erasmus MC, Rotterdam.*
16.00 – 16.30	Nieuwe endoscopische technieken voor detectie van colorectale poliepen *Dr. E. Dekker, maag-darm-leverarts,* *Academisch Medisch Centrum, Amsterdam*
16.30 – 17.00	Pauze
17.00 – 17.30	Non-adenomateuze polyposis *Prof. dr. A.A.M. Masclee, maag-darm-leverarts,* *Maastricht Universitair Medisch Centrum*
17.30 – 18.00	Syndroom van Lynch *Dr. J.J. Koornstra, maag-darm-leverarts,* *Universitair Medisch Centrum Groningen*
18.00 – 18.30	Adenomateuze polyposis *Prof. dr. H.F.A. Vasen, internist, Leids Universitair Medisch Centrum*
18.30 – 19.30	Dinerbuffet

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

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

19.30 – 20.00	Barrett-oesofagus vanuit de optiek van de MDL-arts *Dr. B.L.A.M. Weusten, maag-darm-leverarts,* *St. Antonius Ziekenhuis, Nieuwegein*
20.00 – 20.30	Barrett-oesofagus vanuit de optiek van de chirurg *Dr. B.P.L. Wijnhoven, chirurg, Erasmus MC, Rotterdam*
20.30 – 21.00	Premaligne cysteuze afwijkingen van de pancreas *Dr. E .van der Harst,chirurg, Maasstad Ziekenhuis, Rotterdam*
21.00 – 22.00	Paneldiscussie met B.L.A.M. Weusten, B.P.L. Wijnhoven, H.F.A. Vasen, aan de hand van casuïstiek *1. Premaligne cysteuze afwijking pancreas,* *2. Vroegcarcinoom Barrett-oesofagus,* *3. Duodenale polyposis,*
22.00 – 22.15	Afsluitende kennistoets

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

Programma donderdag 7 oktober 2010

DONDERDAG	BRABANTZAAL	BARONIEZAAL	PARKZAAL	AUDITORIUM
10.00 - 11.30	**IBD-symposium**: 'Optimale inzet van medicatie bij IBD' p. 28	Vrije voordrachten Nederlandse Vereniging voor Hepatologie p. 10		Vrije voordrachten Ned. Ver. voor Gastrointestinale Chirurgie p. 13
11.30 - 12.00	**Ledenvergadering NVGE**	Geen programma i.v.m. ALV		Geen programma i.v.m. ALV
12.00 - 13.00	Lunch in expositiehal	Lunch in expositiehal		Lunch in expositiehal
13.00 - 15.30	Vrije voordrachten NVGE gevolgd door **Symposium: 'De dysmotore slokdarm'** p. 29	Vrije voordrachten NVH, gevolgd door **Symposium: 'Portale hypertensie en Leverfalen'** p.18		Vrije voordrachten NVGIC en **Minisymposium: 'Diagnostiek en behandeling van cysteuze pancreaslaesies in de praktijk'** p. 23
15.30 - 16.00	Theepauze expositiehallen	Theepauze + ALV NVH		Theepauze
16.00 - 16.30	Vrije voordrachten NVGE p. 16	Vrije voordrachten NVH p. 20	**Workshop Landelijke** p. 22 **Colonstent database tot 17.30**	Vrije voordrachten NVGIC p. 25
16.30 - 17.00	**Tytgat lecture**: Prof. dr. E. van Cutsem, Leuven p. 17	Vrije voordrachten NVH p. 20	Parallel in zaal 8: **De rol van de NP in hepatitis behandeling** tot 19.00, zie p. 26	Vrije voordrachten NVGIC p. 25
17.00 - 18.00	**Presiden**t Select p. 17	Geen programma in deze zaal		Geen programma
18.00 - 18.30	**Uitreiking Jansen-Cilagprijs**	Geen programma in deze zaal		Geen programma
18.30 - 19.30	Borrel in expositiehal	Borrel in expositiehal		Borrel in expositiehal
19.30 - 22.00	Diner Genderzaal			
22.00 - 01.00	Borrel / Muziek in foyer			

Programma vrijdag 8 oktober 2010

VRIJDAG	BRABANTZAAL	BARONIEZAAL	PARKZAAL	DIEZEZAAL
08.30 - 09.00	Vrije voordrachten Sectie Gastrointestinale Endoscopie p. 28	Vrije voordrachten Nederlandse Vereniging voor Gastroenterologie p. 30	Vrije voordrachten Nederlandse Vereniging voor Gastroenterologie p. 34	
09.00 - 10.30	Symposium 30-jaar SGE '**Choices in Endoscopy'** p. 29	Vrije voordrachten Nederlandse Vereniging voor Gastroenterologie p. 31	Vrije voordrachten Nederlandse Vereniging voor Gastroenterologie p. 35	V&VN MDL programma p.41
10.30 - 11.00	Koffiepauze	Koffiepauze	Koffiepauze	Koffiepauze
11.00 - 12.00	Symposium 30-jaar SGE '**Choices in Endoscopy'** p. 29	Vrije voordrachten Nederlandse Vereniging voor Gastroenterologie p. 33	Vrije voordrachten Nederlandse Vereniging voor Gastro-enterologie en NESPEN p. 37	Vervolg V&VN MDL programma p.41
12.00 - 13.30	ALV NVMDL Genderzaal	Lunch in expositiehal	Lunch in expositiehal	Na lunch V&VN MDL programma
13.30 - 15.00	**Symposium:** **'25 jaar Stichting Opsporing Erfelijke Tumoren'** p. 38	**Minisymposium 'Richtlijn acute bloedingen tractus digestivus'** p. 40	Geen programma in deze zaal	Einde programma ca. 15.00
15.00 - 15.30	Afsluiting met hapje en drankje	Afsluiting met hapje en drankje		

Donderdag 7 oktober 2010

IBD Symposium "Optimale inzet van medicatie bij IBD" — Brabantzaal

Voorzitters: D. de Jong en B. Oldenburg

10.00 Opening
Dr. B. Oldenburg, UMC Utrecht

10.05 Conventionele medicatie volgens de richtlijn
Dr. D.J. de Jong, UMC St Radboud Nijmegen

10.30 Biologicals volgens het boekje
Dr. G. Dijkstra, UMC Groningen

11.00 Vroege intensieve behandeling en "tight control"
Prof. dr. G. d'Haens, Imeldaziekenhuis, Bonheiden, Belgie

11.30 Einde symposium, aansluitend ledenvergadering NVGE in deze zaal.

Nederlandse Vereniging voor Hepatologie — Baroniezaal

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

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

10.00 The value of liver biopsy as a diagnostic tool in the evaluation of abnormal liver enzyme tests
P. de Boer, F. Ter Borg, M.E. Bartelink, Deventer Ziekenhuis, The Netherlands

10.10 IL28B polymorphisms are associated with histologicalrecurrence and treatment response following livertransplantation in patients with HCV Infection
B.J. Veldt[1,4], M.R. Charlton[1], A. Thompson[2], K. Watt[1], H. Tillman[2], J.J. Poterucha[1], J.K. Heimbach[3], D. Goldstein[2], J. McHutchison[2], Mayo Clinic, [1]Division of Gastroenterology and Hepatology, [3]Division of Transplantation Surgery, Rochester MN, USA, [2]Duke Clinical Research Institute, [4]Duke University Medical Centre, Durham, North Carolina, USA, Erasmus MC

University Medical Centre, Dept. of Gastroenterology and Hepatology, Rotterdam, The Netherlands

10.20 The potent bile acid sequestrant Colesevelam is not effective in cholestatic pruritus: Results of a double-blind, randomized, placebo-controlled trial

E.M.M. Kuiper[1], K.J. van Erpecum[2], U.H.W. Beuers[3], B.E. Hansen[1,4], H.B. Thio[5], R.A. de Man[1], H.L.A. Janssen[1], H.R. van Buuren[1], [1]Dept of Gastroenterology and Hepatology, [4]Biostatistics, [5]Dermatology, Erasmus University Medical Centre, Rotterdam, [2]Dept. of Gastroenterology and Hepatology, University Medical Centre Utrecht, [3]Dept. of Gastroenterology and Hepatology, Academic Medical Centre, Amsterdam, The Netherlands

10.30 Donor Mannose-binding lectin and Ficolin-2 gene polymorphisms compromise orthotopic liver transplant recipients with an increased risk for HCMV infection

B.F. de Rooij[1], M.T. van der Beek[2], B. van Hoek[1], A.C.T.M. Vossen[2], W.R. ten Hove[1], A. Roos[3,4], A.F. Schaapherder[5], R.J. Porte[6], J.J. van der Reijden[1], M.J. Coenraad[1], D.W. Hommes[1], H.W. Verspaget[1], [1]Dept. of Gastroenterology and Hepatology, [2]Dept. of Medical Microbiology, [3]Dept. of Clinical Chemistry, [4]Dept. of Nephrology, [5]Dept. of Surgery, Leiden University Medical Centre, Leiden, [6]Dept. of Hepatobiliary Surgery and Liver Transplantation, University Medical Centre Groningen, The Netherlands

10.40 Etiologic Factors Underlying Budd-Chiari Syndrome and Portal Vein Thrombosis: the Role of Site-specific Thrombosis

J. Hoekstra[1], A. Plessier[2], J.C. Garcia-Pagan[3], F. Fabris[4], S. Darwish Murad[1], J. Trebicka[5], M. Primignani[4], S. Seijo[3], D.C Valla[2], F.W.G. Leebeek[6], H.L.A. Janssen[1], For the EN-Vie Study Group, [1]Dept. of Gastroenterology and Hepatology, Erasmus University Medical Centre, Rotterdam, [2]Dept. of Hepatology, Hôpital Beaujon, University Paris-7, Clichy, France, [3]Hepatic Hemodynamic Laboratory, Liver Unit, Hospital Clinic, IDIBAPS and CIBERehd, Barcelona, Spain, [4]Gastroenterology and Gastrointestinal Endoscopy Unit, Ospedale Poli-clinico, Maggiagalli and Regina Elena Foundation, Milan, Italy, [5]Dept. of Internal Medicine I, University Hospital of Bonn, Bonn, Germany, [6]Dept. of Hematology, Erasmus University Medical Centre, Rotterdam, The Netherlands

10.50 Week 24 HCV RNA determination during treatment with peginterferon alfa and ribavirin for chronic hepatitis C using the most sensitive HCV RNA assay prevents unnecessary treatment

R. Roomer[1], A.J. van Vuuren[1], M. Schutten[2], A. Heijens[1], H.L.A. Janssen[1], R.J. de Knegt[1], [1]Dept. of Gastroenterology and Hepatology, Erasmus University Medical Centre, Rotterdam, [2]Dept. of Virology, Erasmus University Medical Centre, Rotterdam, The Netherlands

11.00 Quantitative HBV-DNA and AST are strong predictors for survival after detection of hepatocellular carcinoma

C.D.M. Witjes[1], J.N.M. IJzermans[1], A.A. van der Eijk[2], B.E. Hansen[3,4], C. Verhoef[5], R.A. de Man[4], [1]Hepatobiliary and Transplantation Surgery, [2]Virology, [3]Biostatistics, [4]Gastroenterology & Hepatology, [5]Surgical Oncology, Erasmus MC, University Medical Centre Rotterdam, The Netherlands

11.10 Viral kinetics and immunological response with continuous subcutaneous admini-stration of high-dose interferon alfa-2b in treatment-experienced chronic hepatitis C patients

J.F. Bergmann[1], R. Roomer[1], B.L. Haagmans[2], B.E. Hansen[1], R.J. de Knegt[1], H.L.A. Janssen[1], A. Boonstra[1], [1]Erasmus MC University Hospital, Dept. of Gastroenterology and Hepatology, Rotterdam, [2]Erasmus MC University Hospital, Dept. of Virology, Rotterdam, The Netherlands

11.20 Analysis of resistance-associated mutations in chronic hepatitis C patients treated with narlaprevir and standard of care

J. de Bruijne[1] , X.V. Thomas[2] , H.W. Reesink[1], C.J. Weegink[1], M.A. Treitel[3] , E.A. Hughes[3], R.J. de Knegt[4] A. van Vliet[5], H.L.A. Janssen[4] , R. Molenkamp[2] , J. Schinkel[2] , [1]Academic Medical Centre, Dept. of Gastroenterology and Hepatology, Amsterdam, [2]Academic Medical Centre, Dept. of Medical Microbiology, Section of Clinical Virology, Amsterdam, The Netherlands, [3]Merck Research Laboratories, Kenilworth, New Jersey, USA, [4]Erasmus MC University Hospital, Dept. of Gastroenterology and Hepatology, Rotterdam, [5]PRA International, Zuidlaren, The Netherlands

11.30 **Ledenvergadering NVGE in Brabantzaal**

12.00 Lunchbuffet in expositiehal

Nederlandse Vereniging voor Gastrointestinale Chirurgie **Auditorium**

Voorzitters: S. Gisbertz en T. Karsten

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

10.00 Surgical randomised trials in PubMed journals in 1999 and 2009: systematic review of volume and methodology
U. Ahmed Ali[1], P.C. van der Sluis[1], Y. Issa[2], H.G. Gooszen[3], A. Agra[4], M.G. Besselink[1], [1]Dept. of Surgery, University Medical Centre Utrecht, Utrecht, [2]Dept. of Surgery, [3]OR/Evidence Based Surgery, Radboud University Nijmegen Medical Centre, Nijmegen, [4]Julius Centre for Health Sciences and Primary Care, University Medical Centre Utrecht, Utrecht, The Netherlands

10.10 Cyclooxygenase isoenzyme-2 and vascular endothelial growth factor expression are significantly associated with prognosis in esophageal adenocarcinoma
M.J.D Prins[1], R.J.J. Verhage[1], F.J.W. ten Kate[2], R. van Hillegersberg[1], [1]Dept. of Surgery, University Medical Centre Utrecht, Utrecht, [2]Dept. of Pathology, University Medical Centre Utrecht, Utrecht, The Netherlands

10.20 Second PET-CT in the detection of metastatic disease after neoadjuvant therapy in esophageal carcinoma
R.L.G.M. Blom[1], W.M.J. Schreurs[2], H.J. Belgers[1], R.F.A. Vliegen[3], L.E. Oostenbrug[4], M.N. Sosef[1], [1]Dept. of Surgery, [2]Dept. of Nuclear Medicine, [3]Dept. of Radiology, [4]Dept. of Internal Medicine and Gastroenterology, Atrium Medical Centre, Heerlen, The Netherlands

10.30 Surveillance and Follow-up Characteristics of Patients with High Grade Dysplasia in Barrett's Esophagus: a Dutch Population-Based Study
R.E. Verbeek[1], F. J. ten Kate[2], F.P. Vleggaar[1], M.E.I. Schipper[2], M.K. Casparie[3], M.G.H. van Oijen[1], J.W.P.M. van Baal , P.D. Siersema[1], [1]Dept. of Gastroenterology and Hepatology, [2]Dept. of Pathology, University Medical Centre Utrecht, [3]Stichting PALGA, Utrecht, The Netherlands

10.40 Validation and reproducibility of tumour-stroma ratio scoring on oesophageal adeno-carcinoma biopsies
E.F.W. Courrech Staal[1], V.T.H.B.M. Smit[2], M.F. van Velthuysen[3], J.M.J. Spitzer-Naaykens[4], W.E. Mesker[5], R.A.E.M. Tollenaar[5], J.W. van Sandick[1],

[1]Dept. of Surgical Oncology, the Netherlands Cancer Institute / Antoni van Leeuwenhoek Hospital, [2]Dept. of Pathology, Leiden University Medical Centre, [3]Dept. of Pathology, Cancer Institute / Antoni van Leeuwenhoek Hospital, [4]Dept. of Pathology, Reinier de Graaf Gasthuis, [5]Dept. of Surgical Oncology, Leiden University Medical Centre, The Netherlands

10.50 How to define a positive circumferential resection margin in patients with T3 adeno-carcinoma of the esophagus.
R.J.J. Verhage[1], H.J.A. Zandvoort[1], F.J.W. ten Kate[2], R. van Hillegersberg[1], [1]Dept. of Surgery, [2]Dept. of Pathology, University Medical Centre Utrecht, The Netherlands

11.00 Removable and repositionable covered metal self-expandable stents for post-surgical leaks in the upper gastro-intestinal tract. Experiences in a tertiary referral hospital
B.J.M. Leenders[1], A. Stronkhorst[1], J. Smulders[2], G.A.P. Nieuwenhuizen[2], L.P.L. Gilissen[1], [1]Depts. of Gastroenterology and Hepatology and [2]Surgery, Catharina Hospital Eindhoven, The Netherlands

11.10 The effect of patient characteristics, with special reference to socioeconomic status, on treatment choice in esophageal cancer
P. Bus[1], V.E.P.P. Lemmens[2] , G.J. Creemers[3] , G.A.P. Nieuwenhuijzen[3] , J.W.P.M. van Baal[1] , P.D. Siersema[1], [1]Dept. of Gastroenterology and Hepatology, University Medical Center Utrecht, [2]Comprehensive Cancer Centre South (CCCS), Eindhoven, [3]Catharina Hospital, Eindhoven, The Netherlands

11.20 Effect of centralization on morbidity and mortality after surgical treatment of esopha-geal cancer
D. Faraj[1], B.S. Langenhoff [2], F.V. Workum[1], J. J. Bonenkamp[3] , J.H.W. de Wilt[3] , C. Rosman[1], [1]Dept. of Surgery, Canisius-Wilhelmina Hospital, Nijmegen, [2]Dept. of Surgery, Rijnstate Hospital, Arnhem, [3]Dept.of Surgery, Radboud University Nijmegen Medical Centre, The Netherlands

11.30 - 12.00 Ledenvergadering NVGE in Brabantzaal

12.00 - 13.00 Lunch

Nederlandse Vereniging voor Gastroenterologie **Brabantzaal**

Voorzitters*:* A.J.P.M. Smout en M.A. Benninga

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

13.00 Efficacy of an integrated multidisciplinary approach of patients with severe functional gastrointestinal disorders
R. Dellink[1], J. Kruimel[1], C. Leue[2], J. Strik[2], J. van Os[2], A. Masclee[1], [1]Dept. of Internal Medicine, Division of Gastroenterology , and [2]Dept. of Psychiatry, University Hospital Maastricht, Maastricht University, The Netherlands

13.10 Clinical trial on the short and long term effect of two psychological interventions for irritable bowel syndrome
M. Vidakovic-Vukic[1], S. Ludidi[2], M. Groenteman[3], A. Thijssen[2], S. Fischer[3], A. Masclee[2], [1,2]Depts. of Internal Medicine and Gastroenterology-Hepatology, [3]Dept. of Clinical Psychology, Sint Lucas Andreas Hospital, [3]Slotervaart Hospital, Amsterdam and Maastricht University Medical Center[2], Maastricht, The Netherlands

13.20 Anorectal function evaluation and predictive factors for fecal incontinence in 600 patients
T.J. Lam[1], D.J. Kuik[2], C.J.J. Mulder[1], R.J.F. Felt-Bersma[1], [1]Dept. of Gastro-enterology and Hepatology, VU University Medical Centre, Amsterdam, [2]Dept. of Epidemiology and Biostatistics, VU University Medical Centre, Amsterdam, The Netherlands

Sectie Neurogastroenterologie en Motiliteit **Brabantzaal**

Voorzitters*:* A.J.P.M. Smout en M.A. Benninga

Symposium : "De dysmotore slokdarm"

13.30 De klassieke slokdarmmotoriekstoornissen
Dr. J.M. Conchillo, mdl-arts, Maastricht Universitair Medisch Centrum

13.50 Achalasie: nieuwe ontwikkelingen
Prof.dr. G.E.E. Boeckxstaens, mdl-arts, Katholieke Universiteit Leuven

Donderdag 7 oktober 2010

14.15 Aerofagie en boeren
Dr. A.J. Bredenoord, mdl-arts i.o., Academisch Medisch Centrum, Amsterdam

14.40 Eosinofiele oesofagitis
Dr. F. ter Borg, mdl-arts, Deventer Ziekenhuis

15.05 Hoge-resolutie manometrie: wat en 'so-what?'
Prof. dr. A.J.P.M. Smout, maag-darm-leverarts, Academisch Medisch Centrum, Amsterdam

15.30 Theepauze

Nederlandse Vereniging voor Gastroenterologie **Brabantzaal**

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

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

16.00 The association between proton pump inhibitors and bone fractures re-visited: results of a systematic review
M.G.H. van Oijen[1], R.J.F. Laheij[1], P.J. Lestrade[2] , P.D. Siersema[1], [1]Dept. of Gastroenterology and Hepatology, University Medical Centre Utrecht, Utrecht, [2]Dept. of Internal Medicine, Jeroen Bosch Hospital, 's-Hertogen-bosch, The Netherlands

16.10 Use of proton ump inhibitors (PPI) may cause false positive tumour marker elevation of chromogranin A: a potential pitfall in the evaluation of neuro-endocrine tumours
M. Muller[1], C.M. Korse[2], J.M.G.Bonfrer[2], B.G.Taal[1], [1]Dept. of Gastro-enterology, [2]Clinical Chemistry; The Netherlands Cancer Institute-Antoni van Leeuwenhoek Hospital, Amsterdam, The Netherlands

16.20 Glasgow Blatchford bleeding scale identifies patients who do not need in hospital treatment in a Dutch Emergency Department
L.M. Jansen[1,3], P. Leffers[2] , M.A.W. Hermans[1], P.M. Stassen[1], A.A.M. Masclee[3], Y.C. Keulemans[3], [1]Dept. of Internal Medicine, Division Emergency Medicine, Maastricht University Medical Centre, [2]Dept. of Epidemiology, School CAPHRI, Maastricht University, [3]Dept. of Internal Medicine, division Gastroenterology, Maastricht University Medical Centre, The Netherlands

Tytgat Lecture — Brabantzaal

Voorzitter: C.J.J. Mulder

16.30 'Op weg naar een meer gepersonaliseerde therapie voor colorectale kanker'
Prof. dr. Eric Van Cutsem, MD, PhD, Digestive Oncology Unit, University Hospital Gasthuisberg, Leuven, Belgium

President Select — Brabantzaal

Voorzitter: C.J.J. Mulder

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

17.00 In-hospital costs of laparoscopy and/or fast track multimodal management versus open and/or standard care in colonic surgery (LAFA-trial)
S.A.L. Bartels[1], M.S. Vlug[1], J. Wind[1], B.A. van Wagensveld[2], F.F. Asselman[3], M.W. Hollmann[4], W.A.Bemelman[1], [1]Dept. of Surgery, Academic Medical Centre, Amsterdam, [2]Dept. of Surgery, St. Lucas Andreas Hospital, Amsterdam, [3]Dept. of Finance, Academic Medical Centre, Amsterdam, [4]Dept. of Anesthesiology, Amsterdam, The Netherlands

17.15 High diagnostic yield of direct endoscopic mucosal oxygen saturation measurements in patients suspected for chronic upper gastrointestinal ischemia
L.M.G. Moons[1], A. Sana[1], D. van Noord[1], T.C. Leertouwer[3], H.J.M. Verhagen[2] , E.V. Rouwet[2], S.F.M. Jenniskens[3], E.J. Kuipers[1], P.B.F. Mensink[1], [1]Dept. of Gastroenterology & Hepatology, [2]Vascular Surgery and [3]Intervention Radiology, Erasmus MC University Medical Centre Rotterdam, The Netherlands

17.30 Symptomatic Wilson disease during long-term zinc maintenance mono-therapy after initial penicillamine decoppering: Experience in 30 patients.
J. Ras[1,2], R.H.J. Houwen[2], F.H.H. Linn[3-5], K.J. van Erpecum[1], Depts. of [1]Gastroenterology, [2]Pediatrics, [3]Neurology of the University Medical Centre Utrecht, [4]Rudolf Magnus Institute of Neuroscience Utrecht, [5]Central Military Hospital Utrecht, The Netherlands

17.45 Post-ERCP Cholecystitis - incidence and risk factors
A-L.W. Westenburg[1], G.A. Patijn[2], A.C. Poen[1], H. Klip[3], E-J. van der Wouden[1], J.Vecht[1], [1]Dept. of Gastro-Enterology, [2]Dept. of Surgery, [3]Dept. of Epidemiology, Isala clinics, Zwolle, The Netherlands

Prijsuitreiking **Brabantzaal**

18.00 **Uitreiking van de**
Janssen-Cilag Gastrointestinale Researchprijs 2010
door de voorzitter van de jury: Prof. dr. C.H.C. Dejong

18.30 Congresborrel in expositiehal

19.30 Diner in Genderzaal

Nederlandse Vereniging voor Hepatologie **Baroniezaal**

Voorzitters: H. van Buuren en S.W.M. Olde Damink

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

13.00 High prevalence of common bile duct dilatation among hepatitis C infected metha-done users
D.M. Hotho[1], B.E. Hansen[1,2], J.N.L. Schouten[1], P. Taimr[1], H.L.A. Janssen[1], R. J. de Knegt[1] Depts. of Gastroenterology and Hepatology, [2]Biostatistics, Erasmus MC University Medical Centre, Rotterdam, The Netherlands

13.10 Maintenance treatment is necessary even when auto immune hepatitis is in remission
N.M.F. van Gerven, C.M.J van Nieuwkerk, J.P. Kuyvenhoven, B.J. Verwer, M Klemt-Kropp, C.J.J. Mulder, G. Bouma, VU Medical Centre, Medical Centre Alkmaar, Kennemer Gasthuis Haarlem, The Netherlands

13.20 Sperm DNA integrity is not affected by treatment with peginterferon alfa and ribavirin for chronic hepatitis C
R. Roomer[1], G. Bezemer[1], J. van Brakel[2], J.C. Romijn[2], B.E. Hansen[1,3], G. Dohle[2], H.L.A. Janssen[1], R.J. de Knegt[1], [1]Dept. of Gastroenterology and Hepatology, [2]Dept. of Urology, [3]Dept. of Biostatistics, Erasmus University Medical Centre Rotterdam, Rotterdam, The Netherlands

13.30 Assessment of hepatic involvement in sarcoidosis
J.P. Cremers[1,2,3] , M. Drent[1,4], A.L.C. Driessen[2], F.M. Nieman[5], G.H. Koek[1,3], [1]Maastricht University Medical Centre (MUMC), [2]Dept. of Pathology, MUMC, [3]Division of Gastro-enterology and Hepatology, Dept. of Internal Medicine, MUMC, [4]Dept. of Respiratory Medicine, MUMC, [5]Clinical Epidemiology and Medical Technology Assessment (KEMTA), MUMC, The Netherlands

13.40 Prevalence and risk factors of hepatic steatosis in elderly: results of a population based study
E.M. Koehler[1], J.N.L. Schouten[1], B.E. Hansen[2], B.H. Stricker[2], H.L.A. Janssen[1], [1]Dept. of Gastroenterology and Hepatology, [2]Dept. of Epidemiology and Biostatistics, Erasmus MC University Hospital, Rotterdam, The Netherlands

13.50 Prediction of sustained response to peginterferon alfa-2b for HBeAg-positive chronic hepatitis B using on-treatment HBsAg decline
M.J. Sonneveld[1], V. Rijckborst[1] , C.A.B. Boucher[2], B.E. Hansen[1,3], H.L.A. Janssen[1], Depts. of [1]Gastroenterology and Hepatology, [2]Virology and [3]Biostatistics, Erasmus MC University Medical Centre, Rotterdam, The Netherlands

14.00 Einde abstractsessie

Nederlandse Vereniging voor Hepatologie **Baroniezaal**

Voorzitters: S.W.M. Olde Damink

Symposium: "Portale hypertensie en Leverfalen"

14.00 Endoscopic and other treatment modalities in variceal bleeding: the new Baveno Consensus Guidelines.
Prof. dr. F. Nevens, Leuven (B)

Donderdag 7 oktober 2010

14.20 Management of Budd-Chiari syndrome and Portal Vein Trombosis: the new Baveno Consensus Guidelines
Prof. dr H.L.A. Janssen, Rotterdam

14.40 Acute-on-chronic liver failure
Prof. dr. R. Jalan, Royal Free, London (UK)

15.00 Post-operative liver failure
Prof. dr. C.H.C. Dejong, Maastricht.

15.20 Discussion

15.30 Theepauze en Ledenvergadering NVH

Nederlandse Vereniging voor Hepatologie **Baroniezaal**

Voorzitters: H.L.A. Janssen en C.M.J. van Nieuwkerk

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

16.00 Biliary atresia in The Netherlands: outcome of 232 patients diagnosed between 1987-2008
W. de Vries[1], Z.J. de Langen[2], J.B.F. Hulscher[2], P. Jansen-Kalma[1], E. de Vries[1], H.J. Verkade[1] , also on behalf of NeSBAR (Netherlands Study group on Biliary Atresia Registry), Depts. of [1]Pediatric Gastroenterology and Hepatology and [2]Pediatric Surgery, Beatrix Children's Hospi-tal, University Medical Centre Groningen, The Netherlands

16.10 Suboptimal endogenous erythropoietin response in chronic hepatitis C patients during ribavirin and PEG-interferon treatment
L.G. van Vlerken[1], H. van Soest[1], M.P. Janssen[2], G.J. Boland[3], J.P.H. Drenth[4], D.M. Burger[5], P.D. Siersema[1], K.J. van Erpecum[1], [1]Dept. of Gastro-enterology and Hepatology, [2]Julius Centre for Health Sciences, [3]Primary Care and Dept. of Virology, University Medical Centre Utrecht, [4]Dept. of Gastroenterology and Hepatology and [5]Dept. of Clinical Pharmacy, Radboud University Nijmegen Medical Centre, The Netherlands

16.20 Lower serum ribavirin concentrations are associated with non-response to PEG-interferon and ribavirin therapy in naive chronic hepatitis C patients
L.G. van Vlerken[1], E.J. Huisman[1], H. van Soest[1], G.J. Boland[2], J.P.H. Drenth[3], P.D. Siersema[1], D.M. Burger[4], K.J. van Erpecum[1], [1]Dept. of Gastroenterology and Hepatology and [2]Dept. of Virology, University Medical Centre Utrecht, [3]Dept. of Gastroenterology and Hepatology and [4]Dept. of Clinical Pharmacy, Radboud University Nijmegen Medical Centre, The Netherlands

16.30 Bedside reagent strip analysis of ascites can reliably rule out spontaneous bacterial peritonitis and is a cost-effective strategy
J.J. Kuiper, H.R. van Buuren, R.A. de Man, Erasmus Medical Centre Rotterdam, Dept. of Gastroenterology and Hepatology, Rotterdam, The Netherlands

16.40 Serum HBsAg levels decrease through long-term follow-up in HBeAg-negative patients achieving a sustained response to peginterferon alfa-2a
V. Rijckborst[1], B.E. Hansen[1,2], B. Pinarbasi[3], M. Akdogan[4], M.J. ter Borg[1], P. Ferenci[5], K. Simon[6], R. Flisiak[7], U.S Akarca[8], M. Raptopoulou-Gigi[9], E. Verhey[1], A.J. van Vuuren[1], C.A.B. Boucher[10], H.L.A. Janssen[1], for the PARC Study Group, [1]Dept. of Gastroenterology and Hepatology, [2]Biostatistics and [10]Virology, Erasmus MC University Medical Centre, Rotterdam, The Netherlands; [3]Dept. of Gastroentero-hepatology, Istanbul University Medical School, Istanbul, Turkey, [4]Dept. of Gastroenterology, Turkiye Yuksek Ihtisas Hospital, Ankara, Turkey, [5]Dept. of Internal Medicine 3, Gastroenterology and Hepatology, Medical University of Vienna, Vienna, Austria, [6]Dept. and Clinic of Infectious Diseases, Hepatology and Acquired Immune Deficiences, Medical University Wroclaw, Wroclaw, Poland, [7]Dept. of Infectious Diseases and Hepatology, Medical University of Bialystok, Bialystok, Poland, [8]Dept. of Gastroenterology, Ege University Faculty of Medicine, Izmir, Turkey; [9]Second Medical Dept. Aristototle University of Thessaloniki, Thessaloniki, Greece

16.50 Performance of the Bordeaux criteria for liver adenoma classification in a large single centre study in the Netherlands
S.M. van Aalten[1], J. Verheij[3], T. Terkivatan[1], R.A. de Man[2], J.N.M. IJzermans[1], [1]Dept. of Surgery, [2]Dept. of Gastroenterology and Hepatology, [3]Dept. of Pathology, Erasmus Medical Centre, Rotterdam, The Netherlands

17.00 Einde abstractsessie

Donderdag 7 oktober 2010

Voor de plenaire sessie (President Select) en de uitreiking van de Janssen-Cilag Gastrointestinale Research prijs 2010 kunt u zich begeven naar de Brabantzaal

Workshop Landelijke Colonstent database — Parkzaal

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

Bridge to Surgery middels colonstents; een geprotocoleerde introductie met parallelle registratie van resultaten in de DSCA

16.00 Resultaten na 1 jaar colorectale registratie middels de DSCA, meer dan 11.000 behandelingen geincludeerd.
Prof. dr. R.A.E.M. Tollenaar, chirurg, Leids Universitair Medisch Centrum

16.15 Deventer resultaten na plaatsen colonstents, zowel palliatief als "bridge to surgery".
Dr. M. Ledeboer, MDL-arts, Deventer Ziekenhuis

16.30 De Stent-in I en II data.
J.E. van Hooft, MDL-arts, Academisch Medisch Centrum, Amsterdam

16.45 Mogelijkheden van de DSCA om implementatie van nieuwe behandelingen te monitoren.
Dr. E.H. Eddes, chirurg, Deventer Ziekenhuis

17.00 Een voorstel voor de geprotocoleerde implementatie van colonstents bij de behandeling van obstructies.
Dr. F. ter Borg, MDL-arts, Deventer Ziekenhuis

17.15 Paneldiscussie

17.30 Einde programma

Nederlandse Vereniging voor Gastrointestinale Chirurgie **Auditorium**

Voorzitters: M.I. van Berge Henegouwen en M.J. Bruno

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

13.00 Transoral incisionless fundoplicationfor treatment of gastroesophageal reflux disease in clinical practice Three year follow-up in 38 chronic GERD patients
B.P.L. Witteman[1], R. Strijkers[1], E. de Vries[1], L. Toemen[1], J.Conchillo[2], P. Dagnelie[3], G.H. Koek[2], N.D. Bouvy[1], [1]Dept. of General Surgery, Maastricht University Medical Centre, [2]Dept. of Gastroenterology, Maastricht University Medical Centre, [3]Dept. of Epidemiology, Maastricht University Medical Centre, The Netherlands

13.10 Laparoscopic Nissen Fundoplication after Failed Endoluminal EsophyX Fundoplication
E.J.B. Furnée[1], J.A.J.L. Broeders[1], W.A. Draaisma[2], M.P. Schwartz[3], E.J. Hazebroek[1], A.J.P.M. Smout[4], P.J.J. van Rijn[5], I.A.M.J. Broeders[2], [1]Dept. of Surgery, University Medical Centre Utrecht, [2]Dept. of Surgery, [3]Dept. of Gastroenterology, Meander Medical Centre, Amersfoort, [4]Dept. of Gastro-enterology, Academic Medical Centre, Amsterdam, [5]Dept. of Surgery, Lange Land Hospital, Zoetermeer, The Netherlands

13.20 Staging laparoscopy for hilar cholangiocarcinoma: is it still worthwhile?
A.T. Ruys, O.R. Busch, D.J. Gouma, T.M.van Gulik, Dept. of Surgery, Academic MedicalCentre, Amsterdam, The Netherlands

13.30 Randomized controlled trial analyzing the effect of 15 or 30 minutes intermittent Pringle manoeuvre on hepatocellular damage during liver surgery
M.A.J. van den Broek[1], J.G. Bloemen[1,2], S.A.W.G. Dello[1,2], M.C.G. van de Poll[1,2], M.H. Bemelmans[1], R.M. van Dam[1] , S.W.M. Olde Damink[1,2,3], C.H.C. Dejong[1,2], [1]Dept. of Surgery, Maastricht University Medical Centre, Maastricht, The Netherlands, [2]Nutrition and Toxicology Research Institute Maastricht, Maastricht University, The Netherlands, [3]University College London Hospitals and University College London, London, United Kingdom

13.40 Preoperative infliximab therapy and postoperative complications after procto-colec-tomy with ileum pouch anal anastomosis
E.J. Eshuis[1,2], R. al Saady[1], P.C.F. Stokkers[2,3], W.A. Bemelman[1], [1]Dept. of Surgery, Academic Medical Centre, Amsterdam, [2]Dept. of Gastroenterology and Hepatology, Academic Medical Centre, Amsterdam, [3]Dept. of Gastro-enterology and Hepatology, St. Lucas Andreas Hospital, Amsterdam, The Netherlands

13.50 Viable tumor tissue adherent to needle applicators after local ablation: a risk factor for local tumor progression
N. Snoeren[1] , J. Huiskens[2] , M.C. Jansen[2] , A.M. Rijken[3] , R. van Hillegersberg[1], A.R. van Erkel[4], G. Slooter[5], J. Klaase[6], M.P. van den Tol[7], F.J.W. Ten Kate[2], T. M. van Gulik[2], [1]University Medical Centre Utrecht, Utrecht, [2]Academic Medical Centre, Amsterdam, [3]Amphia Hospital, Breda, [4]Leiden University Medical Centre, Leiden, [5]Maxima Medical Centre, Veldhoven, [6]Medisch Spectrum Twente, Enschede, [7]VU Medical Centre, Amsterdam, The Netherlands

14.00 Einde abstractsessie

Minisymposium NVGIC **Auditorium**

Voorzitters: M.I. van Berge Henegouwen en M.J. Bruno

Diagnostiek en behandeling van cysteuze pancreaslaesies in de praktijk.

14.00 *Waarde van cross sectionele beeldvorming bij cysteuze afwijkingen in het pancreas*
T.H.L. Bollen, radioloog, St. Antonius Ziekenhuis, Nieuwegein

14.30 *Waarde van EUS en FNA by cysteuze pancreaslaesies en follow-up schema's.*
M.J. Bruno, MDL-arts, Erasmus MC, Rotterdam

15.00 *Operatieve behandeling van cysteuze pancreaslaesies*
O.R. Busch, chirurg, Academisch Medisch Centrum, Amsterdam

15.30 uur Theepauze

Nederlandse Vereniging voor Gastrointestinale Chirurgie **Auditorium**

Voorzitters: W. Draaisma en M. Sosef

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

16.00 The C-seal; a biofragmentable drain protecting the stapled colorectal anastomosis from leakage
A.N. Morks[1], K. Havenga[1], H.O. ten Cate Hoedemaker[1], R.J. Ploeg[1], [1]University Medical Centre Groningen, Dept. of Surgery, Division of Abdominal Surgery, The Netherlands

16.10 C-reactive protein concentration is associated with prognosis in patients suffering from peritoneal carcinomatosis of colorectal origin
M.C.G. van de Poll[1], Y.L.B. Klaver[1], V.E.P.P. Lemmens[2], B. Leenders[1], S.W. Nienhuijs[1], I.H.J.T. de Hingh[1], [1]Catharina hospital Eindhoven, Dept. Of Surgery, [2]Integrale Kankerregistratie Zuid, The Netherlands

16.20 Can we identify high risk stage II colonic cancer patients?
B. Koebrugge[1], D.J. Lips[1], J.F. Pruijt[2], J.C. van der Linden[3], M.F. Ernst[1], K. Bosscha[1], [1]Jeroen Bosch Hospital, Dept. of Surgery, [2]Jeroen Bosch Hospital. Dept. of Internal Medicine, [3]Jeroen Bosch Hospital, Dept. of Pathology, The Netherlands

16.30 Evaluation of the IRIS scoring system in predicting in hospital mortality and morbidity after colorectal surgery
F. van der Sluis[1], A.F. Engel[1], [1]Dept. of Surgery of the Zaans Medical Centre, Zaandam, The Netherlands

16.40 Acute toxicity and surgical complications of preoperative chemoradiotherapy with capecitabine for locally advanced rectal cancer - in need of uniform definitions
H.A.M. Swellengrebel[1], C.A.M. Marijnen[2,3], V.J. Verwaal[4], A. Vincent[5], G Heuff[6], M.F. Gerhards[7], A.A.W. van Geloven[8], W.F. van Tets[9], M. Verheij[2], A. Cats[1], [1]Dept. of Gastroenterology,[2]Dept. of Radiation Oncology, the Netherlands Cancer Institute - Antoni van Leeuwenhoek Hospital,

Amsterdam, [3]Dept. of Clinical Oncology, Leiden University Medical Centre, Leiden, [4]Dept. of Surgical Oncology, the Netherlands Cancer Institute - Antoni van Leeuwenhoek Hospital, Amsterdam, [5]Department of Biometrics, the Netherlands Cancer Institute - Antoni van Leeuwenhoek Hospital, Amsterdam, [6]Dept. of Surgery, Spaarne Hospital, Hoofddorp, [7]Dept. of Surgery, Onze Lieve Vrouw Gasthuis, Amsterdam, [8]Dept. of Surgery, Tergooi Hospital, Hilversum and Blaricum, [9]Dept. of Surgery, Sint Lucas Andreas Hospital, Amsterdam, The Netherlands

16.50 Costs, short- and long-term results of open versus laparoscopic appendectomy
H.A. Swank, E.J. Eshuis, W.A. Bemelman, Dept. of Surgery, Academic Medical Centre Amsterdam, The Netherlands

17.00 Einde abstractsessie

Voor de plenaire sessie (President Select) en de uitreiking van de Janssen-Cilag Gastrointestinale Researchprijs 2010 kunt u zich om 17.00 uur begeven naar de Brabantzaal

Programma Hepatitis Verpleegkundigen — Zaal 008

Hoe vertaal jij de richtlijnen voor behandeling van hepatitis B en C naar de praktijk?

Voorzitter: A. Nijmeijer

16.00 Welkom
A.J. Nijmeijer-Hulsegge, verpleegkundige, Medisch Spectrum Twente

16.10 Bespreken richtlijnen hepatitis B
Dr. R.B. Takkenberg, mdl-arts i.o., Academisch Medisch Centrum Amsterdam

16.40 Casuïstiek / hepatitis B
A.W. van Lohuizen-Meulenbeek, mdl-verpleegkundige, Medisch Centrum de Veluwe

17.10 Pauze

17.30 Bespreken richtlijnen hepatitis C
Dr. G.H. Koek, mdl-arts, Maastricht Universitair Medisch Centrum

18.30 Casuïstiek casus (2x) hepatitis C
H. Huiskamp, mdl-verpleegkundige, Deventer Ziekenhuis

18.30 Vragen en discussie

18.45 Afsluiting
A.J. Nijmeijer-Hulsegge, verpleegkundige, Medisch Spectrum Twente

19.00 Congresborrel expositiehal

Sectie Gastrointestinale Endoscopie **Brabantzaal**

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

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

08.30 A retrograde-viewing auxiliary imaging device improves detection rates for adenomas and other polyps during colonoscopy

A.M. Leufkens[1], D.C. DeMarco[2], A. Rastogi[3], P.A. Akerman[4], K. Azzouzi[5], R.I. Rothstein[6], F.P. Vleggaar[1], A. Repici[7], G. Rando[7], P. Okolo[8], O. Dewit[5], A. Ignjatovic[9], E. Odstrcil[2], J.E. East[9], P.H. Deprez[5], B.P. Saunders[9], A.N. Kalloo[8], B. Creel[2], V. Singh[3], A.M. Lennon[8], P.D. Siersema[1], [1]Gastroenterology and Hepatology, University Medical Centre Utrecht, The Netherlands, [2]Baylor University Medical Centre, Dallas, TX, United States, [3]Kansas City Veterans Administration Medical Centre, Kansas City, MO, United States, [4]Bayside Endoscopy Centre, Providence, RI, United States, [5]Cliniques Universitaires Saint-Luc, Brussels, Belgium, [6]Dartmouth-Hitchcock Medical Centre, Lebanon, NH, United States, [7]Istituto Clinico Humanitas, Milan, Italy, [8]Johns Hopkins Hospital, Baltimore, MD, United States, [9]St. Mark's Hospital, London, United Kingdom

08.40 Can surveillance intervals be increased after a negative faecal immunochemical test in asymptomatic high risk patients?

J J.S. Terhaar sive Droste[1], S.T. van Turenhout[1], F.A. Oort[1], R.W.M. van der Hulst[2], V.M.H. Coupé[3], M.A. Blankenstein [4], G.A. Meijer[5], C.J.J. Mulder[1], [1] Gastroenterology and Hepatology, VU University Medical Centre, Amsterdam, [2]Gastroenterology and Hepatology, Kennemer Gasthuis, Haarlem, [3]Epidemiology and Biostatistics, VU University Medical Centre, Amsterdam, [4]Clinical Chemistry, VU University Medical Centre, Amsterdam, [5]Pathology, VU University Medical Centre, Amsterdam, The Netherlands

08.50 Developing competence in ERCP

V.E. Ekkelenkamp[1], A.D. Koch[1], J. Haringsma[1], R.A. de Man[1], [1]Dept. Gastroenterology and Hepatology, Erasmus MC – University Medical Center Rotterdam, The Netherlands

Symposium 30 jaar Sectie Gastrointestinale Endoscopie **Brabantzaal**

Choices in Endoscopy
An interactive symposium beyond evidence and guidelines

During the symposium all participants are invited to show their knowledge and skills with a voting system.

Chairman: J.J.G.H.M. Bergman and M.A.M.J. Jacobs

09.00 Proctology for dummies and the practising endoscopist
Prof. J. Bartelsman, Academic Medical Hospital, Amsterdam

09.30 Upper GI-bleeding: when and how should you treat acute GI bleeding
Prof. J. Sung, The Chinese University, Hong Kong

10.00 Quality in colonoscopy: are you the expert?
Prof. D. Lieberman, Oregon Health and Science University, Portland, U.S.A.

10.30 Coffee break

Chairman: J.W. Poley and B.L.A.M. Weusten

ERCP techniques: How to get to the papilla and do the job
Prof. L. Aabakken, Oslo University Hospital – Oslo, Norway

When or why not do an endoscopy?
Dr. W. Hameeteman, Maastricht University Medical Centre, Maastricht

12.00 Discussion and closure

12.00 Lunch in expositiehal (ledenvergadering NVMDL met lunch in Genderzaal)

Nederlandse Vereniging voor Gastroenterologie **Baroniezaal**

Voorzitters: M.J. Bruno en A.A.M. Masclee

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

08.30 Therapeutic delay and survival after surgery for cancer of the pancreatic head with or without preoperative biliary drainage

W.J. Eshuis[1] , N.A. van der Gaag[1], E.A.J. Rauws[2], C.H.J. van Eijck[3], M.J. Bruno[4], E.J. Kuipers[4], P.P. Coene[5], F.J.G.M. Kubben[6], J.J.G.M. Gerritsen[7], J.W. Greve[8], M.F. Gerhards[9], I.H.J.T. de Hingh[10], J.H. Klinkenbijl[11], C.Y. Nio[12], S.M.M. de Castro[1], O.R.C. Busch[1], T.M. van Gulik[1], P.M.M. Bossuyt[13], D.J. Gouma[1], [1]Dept. of Surgery, Academic Medical Centre, Amsterdam, [2]Dept. of Gastroenterology, Academic Medical Centre, Amsterdam, [3]Dept. of Surgery, Erasmus Medical Centre, Rotterdam, [4]Dept. of Gastroenterology, Erasmus Medical Centre, Rotterdam, [5]Dept. of Surgery, Maasstad Hospital, Rotterdam, [6]Dept. of Gastroenterology, Maasstad Hospital, Rotterdam, [7]Dept. of Surgery, Medical Spectrum Twente, Enschede, [8]Dept. of Surgery, University Hospital Maastricht, now Dept. of Surgery, Atrium MC, Heerlen, [9]Dept. of Surgery, Onze Lieve Vrouwe Gasthuis, Amsterdam, [10]Dept. of Surgery, Catharina Hospital, Eindhoven, [11]Department of Surgery, Rijnstaete Hospital, Arnhem, now Dept. of Surgery, Academic Medical Centre, Amsterdam, [12]Dept. of Radiology, [13]Dept. of Clinical Epidemiology and Biostatistics, Academic Medical Centre, Amsterdam, The Netherlands

08.40 Does erytromycin increase the completion rate of small bowel capsule endoscopy?

J. Westerhof, R.K. Weersma, R.A. Hoedemaker, J.J. Koornstra, University Medical Centre Groningen, Dept of Gastroenterology and hepatology, The Netherlands

08.50 Prevalence of benign disease and autoimmune pancreatico cholangitis in Whipple resections for presumed malignancy of the pancreatic head: are we doing better?

M.J. van Heerde[1], H.R. van Buuren[1], K. Biermann[2], C.H.J. van Eijck[3], G. Kazemier[3], E.J. Kuipers[1], [1]Dept. of Gastroenterology and Hepatology, Erasmus University Medical Centre, Rotterdam, [2]Dept. of Pathology, Erasmus University Medical Centre, Rotterdam, [3]Dept. of Surgery, Erasmus University Medical Centre, Rotterdam, The Netherlands

09.00 Serum intestinal fatty acid binding protein (I-FABP) levels accurately predict villous atrophy and mucosal healing in adult celiac disease

M.P.M. Adriaanse[1], G.J. Tack[2], W.A. Buurman[3], K. van Wijck[3], M.W.J. Schreurs[4], C.J.J. Mulder[2], A.C.E. Vreugdenhil[1], [1]Dept. of Pediatrics & Nutrition and Toxicology Research Institute Maastricht (NUTRIM), Maastricht University Medical Centre, Maastricht, [2]Dept. of Gastroenterology, VU University Medical Centre Amsterdam, [3]Dept. of Surgery, Maastricht University Medical Centre, Maastricht, [4]Dept. of Pathology, VU University Medical Centre Amsterdam, The Netherlands

09.10 Acute pancreatitis and concomitant use of pancreatitis-associated drugs

B.W.M. Spanier[1], H.A.R.E. Tuynman[2], R.W.M. van der Hulst[3], M.G.W. Dijkgraaf [4], M.J. Bruno[5], [1]Dept. of Gastroenterology and Hepatology, Rijnstate Hospital, Arnhem, [2]Dept. of Internal Medicine and Gastroenterology, Medical Centre Alkmaar, [3]Dept. of Gastro-enterology and Hepatology, Kennemer Gasthuis, Haarlem, [4]Dept. of Clinical Epidemiology & Biostatistics, Academic Medical Centre, Amsterdam, [5]Dept. of Gastroenterology and Hepatology, Erasmus University Medical Centre, Rotterdam, The Netherlands. On behalf of the other members of the EARL study group

09.20 The Prevalence of Coeliac Disease in Infertile Couples in The Netherlands is at the Level of the General Population

C.E. Hogen Esch[1], M.J.L. van Rijssen[1], F.M. Helmerhorst[2], A. Roos[3], F. Koning[4], M.L. Mearin[1], J.J. Schweizer[1], [1]Dept. of Paediatrics; [2]Dept. of Gynaecology; [3]Dept. of Clinical Chemistry; [4]Dept. of Immunohaematology and Blood Transfusion; Leiden University Medical Centre, Leiden, The Netherlands

09.30 The pathological incidence of duodenopancreatic neuroendocrine tumors in the Netherlands, a PALGA study

P. Kuiper[1], H.W. Verspaget[1], H.J. van Slooten[2], L. Overbeek[3], I. Biemond[1], C. B. Lamers[1], [1]Dept. of Gastroenterology and Hepatology, Leiden University Medical Centre, [2]Dept. of Pathology, Medical Centre Alkmaar, [3]PALGA, Utrecht, The Netherlands

09.40 Small intestinal alterations in severely obese hyperglycemic subjects - increased functional enterocyte mass and turnover is associated with chronic hyperglycemia

F.J. Verdam[1], J.W.M. Greve[1,2], S. Roosta[1], H. van Eijk[1], N. Bouvy[1], W.A. Buurman[1], S.S. Rensen[1], [1]Dept. of General Surgery, School for Nutrition, Toxicology and Metabolism Research Institute Maastricht (NUTRIM),

Maastricht University Medical Centre, Maastricht, [2]Dept. of Surgery, Atrium Medical Centre, Heerlen, The Netherlands

09.50 Comparison of a new flowcytometric method for diagnosing spontaneous bacte-rial peritonitis with other methods

M. van Gent[1], G.J.M. van de Geijn[1], M.H. Beunis[1], N. Bom[1], T.L. Njo[1], A.J.P. van Tilburg[2], [1]Dept. of Clinical Chemistry and Hematology, [2]Dept. of Gastroenterology, Sint Franciscus Gasthuis, Rotterdam, The Netherlands

10.00 Peutz-Jeghers syndrome and family planning: the attitude towards prenatal genetic testing

S.E. Korsse[1], M.G.F. van Lier[1], E.M.H. Mathus-Vliegen[2], E.J. Kuipers[1,3], K. Vanheusden[4,5], M.E. van Leerdam[1], A. Wagner[4], [1]Gastroenterology & Hepa-tology, Erasmus University Medi-cal Centre, Rotterdam, [2]Gastroenterology & Hepatology, Academic Medical Centre, Amsterdam, [3]Internal Medicine, [4]Clinical Genetics, [5]Psychology, Erasmus University Medical Centre, Rotterdam, The Netherlands

10.10 Increased prevalence of HLA DQ2 and DQ8 account for susceptibility to celiac disease in cystic fibrosis patients

M.P.M. Adriaanse[1], E.M.T. Mulkers[2], A.M. van den Neucker[1], M.G.J. Tilanus[2], A.C.E. Vreugdenhil[1], [1]Dept. of Pediatrics & Nutrition and Toxicology Research Institute Maastricht (NUTRIM), [2]Dept. of Tissue Typing, Maastricht University Medical Centre, Maastricht, The Netherlands

10.20 Loss of intestinal barrier function in human intestinal ischemia-reperfusion: the role of goblet cells

G.F. Paulus, J. Grootjans, K. Lenaerts, R.M. van Dam, C.H.C. Dejong, W.A. Buurman, School for Nutrition & Metabolism (NUTRIM) Maastricht University Medical Centre, The Netherlands

10.30 Koffiepauze

Voorzitters: G. Dijkstra en J.Ph. Kuijvenhoven

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

11.00 Malignant transformation of perianal- and enterocutaneous fistulas occurs rarely: Results of 17 years of follow-up from The Netherlands

J.E. Baars[1], E.J. Kuipers[1,2], G. Dijkstra[3], D.W. Hommes[4*], D.J. de Jong[5*], P.C.F. Stokkers[6*], B. Oldenburg[7*], M. Pierik[8*], P.J. Wahab[9*], A.A. van Bodegraven[10*], C.J. van der Woude[1*], the Initiative for Crohn and Colitis, [1]Depts of Gastroenterology and Hepatology and [2]Internal Medicine, Erasmus Medical Center, Rotterdam, [3]Depts of Gastroenterology and Hepatology, University Medical Center Groningen, Groningen, [4]Leiden University Medical Center, Leiden, [5]Radboud University Medical Center, Nijmegen, [6]Academic Medical Center Amsterdam, Amsterdam, [7]University Medical Center Utrecht, Utrecht, [8]Maastricht University Medical Center, Maastricht, [9]Rijnstate Hospital, Arnhem, [10]VU University Medical Center Amsterdam, Amsterdam, The Netherlands*

11.10 A short course of corticosteroids prior to surveillance colonoscopy to diminish mucosal inflammation in inflammatory bowel disease patients: results from a rando-mized controlled trial

J.E. Baars[1], L. Vogelaar[1], F. Wolfhagen[2], K. Biermann[3], E.J. Kuipers[1,4], C.J. van der Woude[1], [1]Depts of Gastroenterology and Hepatology, [3]Pathology, [4]Internal Medicine, Erasmus MC, Rotterdam, [2]Dept of Gastroenterology and Hepatology, Tweesteden Hospital, Tilburg, The Netherlands

11.20 HNF4α and CDH1 are associated with ulcerative colitis in a Dutch cohort

S. van Sommeren[1,2], M. Visschedijk[2,3], E.A.M. Festen[1,2], D.J. de Jong[4], C.Y. Ponsioen[5], C. Wijmenga[1], R.K. Weersma[2], [1]Dept. of Genetics, University Medical Centre Groningen and University of Groningen, [2]Dept. of Gastro-enterology and Hepatology, University Medical Centre Groningen, University of Groningen, [3]Dept. of Gastroenterology, Isala Klinieken, Zwolle, [4]Dept. of Gastroenterology and Hepatology, Radboud University Medical Centre, Nijmegen, [5]Dept. of Gastroenterology and Hepatology, Academic Medical Centre, Amsterdam, The Netherlands

11.30 Two third of patients with inflammatory bowel disease in clinical remission has asymptomatic mucosal inflammation
J.E. Baars[1], V. Nuij[1] , B. Oldenburg[2], E.J. Kuipers[1,3], C.J. van der Woude[1], [1]Depts of Gastro-enterology and Hepatology, and [3]Internal Medicine, Erasmus MC, Rotterdam, [2]Dept of Gastroenterology and Hepatology, University Medical Centre Utrecht, The Netherlands

11.40 Course of Life of Adolescents with an Inflammatory Bowel Disease
T.Z. Hummel[1], A.E. Tak[1], H. Stam[2], A. Kindermann[1], M.A. Grootenhuis[2], [1]Dept. of Pediatric Gastroenterology, Emma Children's Hospital AMC, Academic Medical Centre, University of Amsterdam, [2]Pediatric Psychosocial Dept., Emma Children's Hospital AMC, Academic Medical Centre, University of Amsterdam, The Netherlands

11.50 Presentation of inflammatory bowel disease flare during pregnancy
Z. Zelinkova[1], J. Dees[1], H.J.T. Smalbraak[2], C. Verveer[3], P.C.J. ter Borg[3], H.G. Vermeulen[4], van Kemenade[5], C.J. van der Woude[1], on behalf of the IBD Group South-West Netherlands, [1]Dept. of Gastroenterology and Hepatology, Erasmus MC, Rotterdam, [2]Lievensberg Ziekenhuis, Bergen op Zoom, [3]Ikazia Ziekenhuis, Rotterdam, [4]Ziekenhuis Walcheren, Vlissingen, [5]Van Weel-Bethesda Ziekenhuis, Dirksland, The Netherlands

12.00 Lunch in expositiehal
Ledenvergadering NVMDL in Genderzaal

Nederlandse Vereniging voor Gastroenterologie **Parkzaal**

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

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

08.30 Educational level and risk of colorectal cancer in the European Prospective Inves-tigation into Cancer and nutrition with specific reference to tumor location
A.M. Leufkens[1,2], H.B. Bueno-de-Mesquita[2,1], F.J.B. van Duijnhoven[2,3], H.C. Boshuizen[2], A. E. Kunst[4], P.D. Siersema[1], [1]Dept. of Gastroenterology and Hepatology, University Medical Centre, Utrecht, [2]National Institute for Public Health and the Environment (RIVM), Bilthoven, [3]Julius Center for Health Sciences and Primary Care, University Medical Centre Utrecht, [4]Dept. of

Public Health, Academic Medical Centre, University of Amsterdam, The Netherlands

08.40 Predictors of advanced colorectal neoplasia after polypectomy.
C.C.G. van Enckevort[1], A.P.J. de Graaf[1], H. Hollema[2], J.H. Kleibeuker[1], J.J. Koornstra[1], [1]Dept. of Gastroenterology, [2]Dept. of Pathology, University Medical Centre, Groningen, The Netherlands

08.50 No change in colorectal cancer stage 4 years after revision of the surveillance guidelines after polypectomy in The Netherlands
H.J.M. Pullens, M.G.H. van Oijen, R.J.F. Laheij, F.P. Vleggaar, P.D. Siersema, Dept. of Gastroenterology and Hepatology, University Medical Centre Utrecht, The Netherlands

09.00 Haemorrhoids are an infrequent cause of false positive results on faecal immunochemical tests
S.T. van Turenhout[1], F.A. Oort[1], J.S. Terhaar sive Droste[1], R.W.M. van der Hulst[2], V.M.H. Coupé[3], A.A. Bouman[4], L.G.M. van Rossum[5], G.A. Meijer[6], and C.J.J. Mulder[1], [1]Gastro-enterology and Hepatology, VU University Medical Centre, Amsterdam, [2]Gastroenterology and Hepatology, Kennemer Gasthuis, Haarlem, [3]Epidemiology and Biostatistics, [4]Clinical Chemistry, VU University Medical Centre, Amsterdam, [5]Epidemiology, Biostatistics and HTA, St. Radboud University Medical Centre, Nijmegen, [6]Pathology, VU University Medical Centre, Amsterdam, The Netherlands

09.10 Survival after colorectal cancer in young patients with a family history for this malignancy
N. de Groot[1,2], K. Kessels[1,2], J. Offerhaus[3], R. Timmer[2], B. Weusten[2], K. Seldenrijk[4], T. van Dalen[5], J. van Gorp[6], M. van Ooijen[1], P.D. Siersema[1], [1]Gastroenterology and Hepatology, UMC Utrecht, [2]Gastroenterology and Hepatology, St Antonius Hospital, Nieuwegein, [3]Pathology, UMC Utrecht, [4]Pathology, St Antonius Hospital, Nieuwegein, [5]Surgery, [6]Pathology, Diakonessenhuis Hospital, Utrecht, The Netherlands

09.20 Colorectal cancer screening in a Dutch population - assumed asymptomatic: symp-tommatic patients will participate despite advice against it
L. van de Schans[1], L.G.M. van Rossum[1], A.F. van Rijn[2], R.J.F. Laheij[3], P. Fockens[2], J.B.M.J. Jansen[4,5], J.P.H. Drenth[4], E. Dekker[2], [1]Dept of Epidemiology, Biostatistics and HTA, Radboud University Nijmegen Medical Centre, Nijmegen, [2]Dept of Gastroenterology and Hepatology, Academic Medical Centre, Amsterdam, [3]Dept of Gastroenterology and Hepatology,

University Medical Centre Utrecht, [4]Dept of Gastroenterology and Hepatology, Radboud University Nijmegen Medical Centre, Nijmegen, [5]Dept of Gastroenterology and Hepatology, Elkerliek Hospital, Helmond, The Netherlands

09.30 Quality indicators for colonoscopy; great variation of adenoma detection rates between endoscopists in a large community hospital
N. van Lelyveld, M.P. Schwartz, Meander Medical Centre, Amersfoort, Dept. of Internal Medicine & Gastroenterology, The Netherlands

09.40 Advantages of full diagnostic colonoscopy over flexible sigmoidoscopy in patients over 50 years of age presenting with rectal blood loss
K. Soufidi[1], H.J.M. Pullens[1], M. A. Brink[1], [1]Gastroenterology and Hepatology, Meander Medical Centre, Amersfoort, The Netherlands

09.50 Patients presenting with rectal blood loss or a change in bowel habits are at increased risk of finding colorectal cancer during colonoscopy
H.J.M. Pullens, R.J.F. Laheij, F.P. Vleggaar, P.D. Siersema, Dept. of Gastroenterology and Hepatology, University Medical Centre, Utrecht, The Netherlands

10.00 Cardiopulmonary events during colonoscopy screening under conscious sedation
C. Khalid- de Bakker, D. Jonkers, W. Hameeteman, R. de Ridder, A. Masclee, R. Stockbrügger, Divisie Maag-, Darm-, Leverziekten, Dept. of Internal Medicine, Maastricht University Medical Center (MUMC), The Netherlands

10.10 Formation of tertiary lymphoid tissue in dextran sulfate sodium induced colitis is partially dependant on $LTa_1 b_2$-LTbR axis (MLDS voordracht)
B.J. Olivier[1], M. Knippenberg[1], M.J. Greuter[1], G. Goverse[1], E.D. Keuning[1], A.A. te Velde[2], G. Bouma[3], R.E. Mebius[1], [1]Dept. of Molecular Cell Biology and Immunology, VU Medical Centre, Amsterdam, [2]Tytgat Institute for Liver and Intestinal Research, Academic Medical Centre, Amsterdam, [3]Dept. of Gastroenterology, VU Medical Centre, Amsterdam, The Netherlands

10.20 The zebrafish; a novel model to study bacterial-host interactions in health and disease (MLDS-voordracht)
S. Brugman, E.E.S. Nieuwenhuis, Laboratory of Translational Immunology, Pediatric Gastroenterology, Wilhelmina Children's Hospital UMC Utrecht, The Netherlands

10.30 Koffiepauze

NVGE / NESPEN — Parkzaal

Voorzitters: G. Wanten en C.F. Jonkers

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

11.00 Faecal calprotectin for screening children with suspected inflammatory bowel disease: a phase III diagnostic accuracy study.
W.R. Cnossen[1], A.B. Schreuder[1], E. van de Vijver[1], A.C. Müller-Kobold[2], P.F. van Rheenen[1] (on behalf of the North Netherland Paediatric IBD Consortium), [1]Dept. of Paediatric Gastro-enterology, [2]Dept. of Laboratory Medicine, University Medical Centre Groningen, The Netherlands

11.10 Fish-oil-based lipid infusion results in significant n-3 fatty acid incorporation in plasma phospholipids and leukocyte cell membranes in healthy volunteers.
M.W. Versleijen[1], H.M. Roelofs[1], C. Rombouts[2], P. Noakes[2], P.C. Calder[2], E.R. Simonetti[3], P.W. Hermans[3], G.J. Wanten[1], [1]Dept. of Gastroenterology and Hepatology, Radboud Uni-versity Nijmegen Medical Centre, the Netherlands, [2]Institute of Human Nutrition, School of Medicine, University of Southampton, UK, [3]Laboratory of Pediatric Infectious Diseases, Radboud University Nijmegen Medical Centre, The Netherlands

11.20 'Gut feeling' of physicians and nurses concerning patient compliance to antiseptic procedures in home parenteral nutrition: some are right, some are wrong.
L. Knaapen, L. van Rossum, R. Vissers, G. Wanten, Dept. of Epidemiology, Biostatistics and HTA and Dept. of Gastroenterology and Hepatology, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands

11.30 Effects of a preoperative oral nutritional supplement on postoperative glucose meta-bolism in rectal cancer patients.
M.F.M. van Stijn[1], P.A.M. van Leeuwen[4], M.R. Soeters[2], M. Ankersmit[1], H.Y. Haas[3], M.T. Ackermans[3], M.J. Serlie[2] , A.P.J. Houdijk[1], [1]Dept. of Surgery, Medical Centre, Alkmaar, Depts. of [2]Endocrinology and Metabolism, [3]Clinical Chemistry, Laboratory of Endocrinology, Academic Medical Centre, Amsterdam, [4]Dept. of Surgery, VU University Medical Centre, Amsterdam, The Netherlands

11.40 Perioperative nutritional treatment is associated with improved postoperative outcome in patients with oesophageal, gastric or pancreatic cancer
N.D. te Boveldt[1], G.C. Ligthart-Melis[1], H.M.W. Verheul[2], D.L. van der Peet, [3]VU University Medical Centre, [1]Nutrition & Dietetics, [2]Medical Oncology, [3]Surgical Oncology, The Netherlands

11.50 DRIFT: The Dutch online Registry of Intestinal Failure and Intestinal Transplantation
A.M. Roskott[1], F.Imhann[2], M.J. Serlie[3], E. Rings[4], C. Jonkers[5], R. Ploeg[1] , G. Dijkstra[6], G. Wanten[7], V. Nieuwenhuijs[1] and Dutch Working group for Intestinal Failure and Intestinal Transplantation, [1]Transplantation&Organ Donation, UMCG, [4]Pediatrics, [6]Gastroenterology and Hepatology, UMCG, [2]Healthcare IT Developer, Aceso BV, Groningen, [3]Endocrinology and Metabolism, [5]Home Parenteral Nutrition and Dietetics, Amsterdam Medical Centre [7]Gastroenterology and Hepatology, University Medical Centre Nijmegen, The Netherlands

12.00 Lunchpauze in expositiehal

Symposium STOET **Brabantzaal**

Voorzitter: H.F.A. Vasen

25 jaar Stichting Opsporing Erfelijke Tumoren

13.30 Inleiding
Prof. dr. H.F.A. Vasen, internist & medisch directeur Stoet

13.32 DNA-sequencing op steeds grotere schaal: kunnen we de uitkomsten wel klinisch interpreteren?
R. Sijmons, klinisch geneticus, afd. Klinisch Genetica, Universitair Medisch Centrum

13.43 Nieuwe resultaten van surveillance van het colon bij families met het Lynch syndroom, non-Lynch syndroom en familiair darmkanker.
Mw. dr. A.E. van der Meulen-de Jong, mdl-arts i.o., afd. Maag-, Darm- en Leverziekten, Leids Universitair Medisch Centrum

13.54 Het relatief hoge risico op maagkanker in Lynch syndroom families rechtvaardigt screening van de maag.
Mw. L.G. Capelle, mdl-arts i.o., afd. Maag-, Darm- en Leverziekten, Erasmus MC, Rotterdam

14.05 Subtotale colectomie is een goede behandelingsoptie voor (jonge) Lynch syndroom patiënten.
Dr. P. van Duijvendijk, chirurg, afd. Heelkunde, Gelre Ziekenhuis, Apeldoorn

14.16 Leefstijl verlaagt het risico op darmkanker in Lynch syndroom families.
Ir. A. Botma, epidemioloog, Wageningen Universiteit, Wageningen

14.27 Belangrijke verschillen tussen MUTYH- en APC-polyposis met implicaties voor de behandeling.
Mw. M Nielsen, klinisch geneticus i.o., afd. Klinisch Genetica, Leids Universitair Medisch Centrum

14.38 De mogelijkheid van prenatale diagnostiek dient door de MDL-arts met patiënten met FAP besproken te worden.
Mw. dr. K.F.L. Douma, psycholoog, Academisch Medisch Centrum, Amsterdam

14.49 Surveillance op pancreascarcinoom verbetert de prognose.
Dr. W.H. de Vos tot Nederveen Cappel, mdl-arts, afd. Maag-, Darm- en Leverziekten, Isala klinieken, Zwolle

15.00 Afsluiting met hapje en drankje

Vrijdag 8 oktober 2010

Symposium Richtlijn Bloedingen **Brabantzaal**

Voorzitter: R.W.M. van der Hulst

Mini symposium
Richtlijn acute bloedingen uit de tractus digestivus

13.30	Inleiding *Dr. R.W.M. van der Hulst, mdl-arts, Kennemer Gasthuis Haarlem*
13.35	Ulcus bloedingen *Mw. Dr. M.E. van Leerdam, mdl-arts, Erasmus MC Rotterdam*
13.55	Varices bloedingen *Dr. J.J. Nicolai, mdl-arts, Haga Ziekenhuis, Den Haag*
14.15	Onderste tractus digestivus bloeding *Dr. RJ.L.F. Loffeld, internist, Zaans Medisch Centrum, Zaandam*
14.30	Radiologische interventie bij bloedingen *Dr. O.M. van Delden, radioloog, AMC, Amsterdam*
14.45	Chirurgische interventie bij tractus digestivus bloedingen
15.00	Afsluiting met hapje en drankje

Na ieder onderwerp panel discussie. Per onderwerp 5-7 min

Verpleegkundigen & Verzorgenden Nederland (SEVA / VMDLV) Diezezaal

Ochtendprogramma

10.15 Opening
Mw. P. Bol, verpleegkundige, Meander Medisch Centrum, Amersfoort

10.20 Anale Intraepitheliale Neoplasie
O. Richel, arts-onderzoeker, Academisch Medisch Centrum, Amsterdam

10.40 6 –TG
Mw. B. Jharap, maag-darm-leverarts i.o., Kennemer Gasthuis, Haarlem

11.00 Film

11.05 De behandeling van het grote rectumadenoom, chirurgie of endoscopie?
Mw. Dr. E. Dekker, mdl-arts, Academisch Medisch Centrum, Amsterdam

11.25 Ontwikkelingen en de endoscoop
Mevr. N. Kuperij, onderzoeker chirurgie, Meander MC, Amersfoort

11.45 Ledenvergadering

12.30 Lunchbuffet in de Kempenhal

Middagprogramma

14.00 Hoe de kwaliteitsborging in Engeland is geregeld.
Mw. D. Johnson, Engeland

14-30 Burried bumper syndrom
Dr. B.J.M. Witteman, mdl-arts, Ziekenhuis Gelderse Vallei, Ede

14.50 Hybride procedure van de maag
H. Witjes, arts-assistent chirurgie, Meander MC, Amersfoort

15.10 Endoscopische behandeling door middel van Botoxinjecties, van achalasie.
Mw. L. Franssen, verpleegkundige, Maastricht Universitair Medisch Centrum

15.30 Sluiting
Mw. P. Bol, verpleegkundige, Meander Medisch Centrum, Amersfoort

The value of liver biopsy as a diagnostic tool in the evaluation of abnormal liver enzyme tests

P. de Boer, F. Ter Borg, M.E. Bartelink, Deventer Ziekenhuis, The Netherlands

Liver biopsy contribute to the diagnostic evaluation of abnormal liver enzyme tests of unclear etiology, after a thorough history, biochemical, serological, and imaging investigation have failed to elucidate a diagnosis. However, liver biopsy is an invasive procedure carrying risk of complications and does not always lead to a diagnosis or a change in management. The aim of this study is to compare the outcome and diagnostic contribution of liver biopsy in order to gain a better understanding of its use as a diagnostic tool. All histological findings of liver biopsies performed between 1999 and 2009 were retrospectively examined and reinforced with electronic medical files of patients. Diagnostic contribution was evaluated in those which were performed for diagnostic reasons. Complications of all liver biopsies were inventoried and investigated whether or not they were performed on diagnostic grounds. Relations between different variables and complications, diagnostic contributions and change of management were analysed.198 liver biopsie records were studied of which 105 (53,0%) were performed for diagnostic purposes. Complications occurred with 6.6% (n=13) of all liver biopsies. These complications occurred with liver biopsies which were performed for diagnostic reasons (5.6%) and investigation of liver lesions (1.0%). In 10,5% of all diagnostic liver biopsies there were complications. An increased risk of all complications was significant for all patients who underwent a diagnostic liver biopsie to investigate abnormal liver enzyme values (p=0.017). A diagnostic contribution was found in 60,0% of al liver biopsies. Only 18.1% of the cases led to a change in management of medication. 31.4% of the liver biopsies led to lifestyle recommendations or change of liver test monitoring, and 29.5% of the liver biopsies led to unchanged management. There was no significant connection found between diagnostic value of liver biopsy and a change in management (p=0,256).There was no significant connection between change in management and a liver biopsie which contributes to the diagnosis. There is a significant increase in risk of complications for these patients and restraint of liver biopsy for this group of patients is emphasized by this study. Pragmatic management of patients with elevated liver enzyme values of unclear etiology after biochemical, serological and imaging investigation may be as effective as performing liver biopsy.

IL28B polymorphisms are associated with histologicalrecurrence and treatment response following livertransplantation in patients with HCV Infection

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Background: Polymorphism in the IL28B gene region, encoding interferon-lambda(λ)-3, is strongly predictive of response to antiviral treatment in the non-transplant setting. We sought to determine the prevalence and impact on clinical outcomes of donor andrecipient IL28B genotypes among liver transplant recipients. Methods: Cohort study including 189 consecutive hepatitis C virus (HCV) patients who underwent liver transplantation between 1-1-1995 and 1-1-2005 in our center. Genotyping of the polymorphism rs12979860 was performed on DNA collected from all donors and recipients in the cohort. 65 patients received IFN-based antiviral therapy. Results: The CC IL28B variant was less common in the CHC recipients than in non-HCV donor livers (33% vs 47%, P=0.03). Recipient IL28B polymorphism was associated with delayed time to histologic recurrence of HCV (C allele, HR = 0.62, 95% CI 0.43 -0.88, P=0.0081). Donor and recipient IL28B genotype were independently associated with SVR (P<0.005). The presence of IL28B CC variant in either the recipient (R) or donor (D) liver was associated with increased rate of SVR (D-non-CC / R-non-CC = 3/19(16%) vs D-CC / R-non-CC=11/22 (50%) vs D-non-CC / R-CC=5/12 (42%) vs R-CC / D-CC=6/7 (86%), P=0.0095). IL28B genotype was not significantly associated with survival (overall / liver related).
Conclusion: Recipient IL28B genotype is associated with more rapid histological recurrence of HCV. Recipient and donor liver IL28B genotype are strongly and independently associated with IFN-based treatment response in patients post-OLT. The data suggest that CC donor livers might be preferentially allocated to patients with HCV infection.

The potent bile acid sequestrant Colesevelam is not effective in cholestatic pruritus: Results of a double-blind, randomized, placebo-controlled trial

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Background and Aims: Colesevelam is an anion exchange resin with a 7-fold higher bile acid binding capacity and fewer side effects than cholestyramine, the current first treatment option in cholestatic pruritus. The aim of this trial was to compare the effect of colesevelam with placebo in patients with cholestatic pruritus. Patients and Methods: In a randomized, double-blind, investigator-initiated multicentre trial, patients with cholestatic pruritus received 1875 mg of colesevelam or identical placebo twice daily during three weeks. The effect on pruritus was assessed by daily visual analogue scales (VAS), quality of life scores (QOL) and evaluation of cutaneous scratch lesions. The predefined primary endpoint was the proportion of patients with at least a 40% reduction in VAS pruritus scores. Results 35 evaluable patients were included: 17 colesevelam, 18 placebo, 22 females, 13 males, primary biliary cirrhosis n=14, primary sclerosing cholangitis n=14). Mean serum bile acid level was comparable between groups before treatment (p=0.74), and significantly different after treatment (p=0.01) in favor of patients treated with colesevelam. 36% of patients in the colesevelam group reached the primary endpoint compared to 35% in the placebo group (p=1.0). There were no significant differences between the groups with respect to pruritus scores, QOL scores and severity of cutaneous scratch lesions. Mild side effects occurred in one colesevelam and four placebo treated patients.
Conclusion: Although colesevelam significantly decreased serum bile acid levels, this trial was unable to demonstrate that it was more effective than placebo in alleviating the severity of pruritus of cholestasis.

Donor Mannose-binding lectin and Ficolin-2 gene polymorphisms compromise orthotopic liver transplant recipients with an increased risk for HCMV infection

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The lectin pathway of complement activation is a crucial effector cascade of the innate immune response to pathogens. Human cytomegalovirus (HCMV) infection occurs frequently in immunocompromised patients after orthotopic liver transplantation (OLT). Mannose-binding lectin (MBL-2), Ficolin-2 (FCN-2) and MBL-associated serine protease (MASP-2) of the lectin pathway are liver-derived and polymorphisms in their genes determine their level and functional activity, and potentially contribute to the risk for HCMV infection. The relationship between HCMV infection within one year after OLT and polymorphisms in the lectin complement pathway genes was investigated in 295 liver transplant recipients and their donor liver. HCMV infection occurred significantly more often in patients receiving a donor liver with a variant single-nucleotide MBL2 polymorphism (XA/O or O/O) [HR 1.65, P<0.02 compared to the wild-type A/A and YA/O genotypes], while the minor C-allele of the FCN2 of the donor liver conferred protection [HR 0.54; P<0.02 as opposed to the wild-type A-allele]. Combined analysis of variant MBL2 and wild-type FCN2 SNPs revealed that one or two risk genotypes had an increasing risk of HCMV infection [HR 2.02 and HR 3.26, respectively, P=0.004], especially in HMCV Donor-/Recipient+ patients [HR 4.7 and HR 10.0, respectively, P=0.01]. Multivariate Cox analysis showed a higher risk of HCMV infection in recipients of variant MBL2 and wild-type FCN2 donor livers [up to HR 3.00; P=0.003] independent from donor-recipient HCMV serostatus, antiviral prophylaxis and immunosuppressive therapy.
Conclusions: MBL2 and FCN2 lectin complement pathway risk alleles of a donor liver constitute an independent risk factor for HCMV infection after OLT. Patients receiving such a donor liver probably need intensified viral load or antigenemia monitoring with pre-emptive therapy or prophylaxis.

Etiologic Factors Underlying Budd-Chiari Syndrome and Portal Vein Thrombosis: the Role of Site-specific Thrombosis

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Various risk factors for thrombosis have been associated with both Budd-Chiari syndrome (BCS) and non-cirrhotic, non-malignant portal vein thrombosis (PVT). To date, it has not been fully established whether there are also differences in hypercoagulable states underlying these two forms of abdominal thrombosis. Also, the influence of the type or specific combinations of prothrombotic factors on disease presentation remains unclear. The aim of our study was to identify factors associated with site specificity of both rare forms of venous thrombosis. Underlying risk factors and multifactorial etiology of thrombosis were studied in 160 patients with BCS and 102 patients with acute PVT from the EN-Vie study, a prospective European collaboration. The frequency of the Factor V Leiden (FVL), Factor II (FII), methylenetetrahydrofolate reductase (MTHFR) and Janus kinase 2 (JAK2) mutations was compared to a cohort of 116 healthy controls. The presence of the FVL mutation was associated with an increased risk of BCS (OR 3.9, CI 1.3-11.9) but not of PVT (OR 1.0, CI 0.2-4.7) compared to healthy controls. In contrast, the FII mutation was significantly related to PVT (OR 10.1, CI 2.2-47.8) but not to BCS (OR 2.1, CI 0.4-11.1), as compared to the controls. Homozygous MTHFR mutation was not associated with either BCS or PVT. Comparing both patient groups, a myeloproliferative disorder (MPD) was more common in patients with BCS than in PVT-patients (39% vs. 22%, respectively, p=0.009). The JAK2 mutation was identified in 35 of 121 (29%) tested BCS-patients as compared to 14 of 82 (17%) patients with PVT (p=0.053). Polycythemia vera appeared to be the predominant subtype of MPD in BCS (56% of MPD-cases) whereas in patients with PVT essential thrombocythemia was most frequently diagnosed (52% of MPD-cases, p=0.002). The type, number and specific combinations of etiologic factors did not affect clinical presentation in both BCS-patients and PVT-patients.
Conclusions: There are significant differences in the risk profile leading to thrombosis in BCS or PVT. Inherited thrombophilia and MPD subtypes seem to be related to thrombosis at a specific site. Clinical presentation and extent of thrombosis are not influenced by a multifactorial etiology of thrombosis.

Week 24 HCV RNA determination during treatment with peginterferon alfa and ribavirin for chronic hepatitis C using the most sensitive HCV RNA assay prevents unnecessary treatment

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Background and aims: The development of more sensitive HCV RNA assays may necessitate re-evaluation of stopping rules, e.g. HCV RNA negativity at week 24 during treatment with peginterferon alfa and ribavirin (SOC) for chronic hepatitis C. The aim of this study was to assess discordance between week 24 HCV RNA test results of two PCR based assays (COBAS® AmpliPrep/ COBAS® AMPLICOR HCV TEST V2.0, LLOD 20 IU/mL (Amplicor) and COBAS® AmpliPrep / COBAS® TaqMan® HCV test v1.0, LLOD 15 IU/ml (TaqMan)) and the qualitative VERSANT® TMA HCV assay, LOD 5.3 IU/mL (TMA). The second aim was to determine the positive predictive value (PPV) and negative predictive value (NPV) of week 24 HCV RNA using different HCV RNA assays. Methods: Week 24 samples HCV RNA negative by PCR were retested with the TMA based assay to investigate discordance between tests results. Sixty three samples, negative by Amplicor, were obtained from patients treated with SOC. The remaining samples were obtained from patients treated within a trial investigating continuous interferon administration combined with ribavirin (IFN/RBV). These samples were HCV RNA negative by TaqMan. Results: A total of 75 samples of 72 patients (genotype distribution 1/2/3/4: 49/2/13/8) were analysed (3 pts were treated twice). SVR was achieved in 30 of 63 patients treated with SOC (PPV of HCV RNA negativity at week 24: 44%). Breakthrough occurred in 4 patients and 29 patients relapsed. All 63 HCV RNA negative week 24 samples were retested with the VERSANT TMA qualitative assay. Retesting failed in 7 samples. Of the remaining 56 samples, 9 had detectable HCV RNA. All patients with detectable HCV RNA had a viral relapse after treatment discontinuation (NPV 100%). SVR was achieved in 26 of 47 patients with undetectable HCV RNA using the TMA based assay achieved SVR (PPV 55%). Twelve samples were obtained from patients treated with IFN/RBV: 5 patients achieved SVR and 7 relapsed (PPV 42%). Eleven week 24 samples were retested successfully with the TMA based assay. Two samples had detectable HCV RNA, both patients had a viral relapse. Four of 9 patients with undetectable HCV RNA using the TMA based assay achieved SVR (PPV 55%).
Conclusion: Discordance was found between VERSANT® TMA HCV RNA qualitative assay and the less sensitive PCR based assays in 11 out of 67 retested week 24 samples (16%). All patients with detectable HCV RNA at week 24 using the TMA based eventually relapsed. Based on these results, the NPV of the TMA based assay was 100% and the use of this more sensitive HCV RNA assay could thus lead to the prevention of unnecessary treatment.

Quantitative HBV-DNA and AST are strong predictors for survival after detection of hepatocellular carcinoma

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Hepatitis B virus infection (HBV) is an important co-factor in the development of hepatocellular carcinoma (HCC). We studied whether quantitative HBV DNA at time of HCC detection influences survival of HCC patients. All diagnosed HCC cases between 2000–2008 at our University based reference centre were analysed to determine the influence of hepatitis B viral load on overall survival. The clinical and virological findings were evaluated in univariate and multivariate analyses, survival rates were assessed for HCC patients with high viral load (HBV DNA $\geq 10^5$ copies/mL) and low viral load (HBV DNA < 10^5 copies/mL).HCC was diagnosed in 597 patients, including 98 patients with HBV infection. The group of 37 patients (38%) who had high viral load contained more HBeAg-positive patients, had a lower serum albumin level and a higher serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT) level compared with the group of patients with low viral load. The 1- and 5-year survival rates of HCC patients with high viral load were 58% and 11%, respectively. For HCC patients with low viral load the 1-and 5-year survival rates 70% and 35%, respectively. A higher AST level and higher viral load were in multivariate analysis significantly associated with a shorter overall survival (HR = 2.30; p=0,018, HR = 1.22; p=0,015, respectively).
Conclusion: HBeAg positivity, a low albumin level or a high AST or ALT level in HCC patients is associated with a higher mortality. The level of HBV DNA at detection is associated with overall survival of HCC patients. These findings support the concept that after HCC detection adequate suppression of HBVDNA by nucleoside analogue therapy may improve survival.

Viral kinetics and immunological response with continuous subcutaneous administration of high-dose interferon alfa-2b in treatment-experienced chronic hepatitis C patients

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Background: The clinical benefit of retreatment with (Peg) IFN/RBV in treatment- experienced chronic HCV infected patients is generally poor. Early virological and im-munological parameters may identify patients who can benefit from retreatment. Methods: We analyzed 28 PegIFN/RBV-experienced HCV infected patients (n=22 genotype 1, n=6 genotype 4) treated with high dose IFN alfa-2b (daily 12, 9 or 6 MU) by continuous subcutaneous administration combined with RBV. HCV RNA levels, serum IFN-alfa levels, serum markers of immune activation (neopterin, 2,5-OAS, beta 2-microglobulin), in vitro T cell proliferation and IFN-gamma production were analyzed. Samples were collected at T=0,4,8,12,24,48,72,96 hrs, wk1,2,3,4 and 24 wks post-treatment. Results: Based on HCV RNA load at wk 4, we identified 13 responders (> 2log drop), 10 intermediate responders (1-2 log drop) and 5 nonresponders (<1log drop). A typical biphasic viral dec was seen in responders. All patients achieving SVR after 48 weeks of therapy (n=5) had >2 log drop of HCV RNA at wk 4. IFN levels increased dose-dependently, reaching peak-levels between 48hrs and wk1 followed by steady-state. Responders achieved higher IFN levels than nonresponders (mean 304.0 vs 160.2 pg/ml at wk 4). Neopterin increased equally among all patients between 48 and 96 hrs, with higher steady-state levels in patients receiving 12MU/d. Beta 2-microglobulin increased moderately in all patients; higher base levels were seen in responders (mean 16.9 vs 13.4 ug/ml). 2,5-OAS levels peaked between 24 and 96 hrs followed by slow decline, without differences in responders and nonresponders. Base T cell proliferation was strongly reduced when cultured in vitro with IFN-alfa in most patients, suggesting responsiveness to IFN, irrespective of treatment outcome. However, desensitization of the cells for IFN-alfa with regard to T cell proliferation was seen especially in nonresponders at T=24 hrs. Base IFN-gamma production was variable between patients when cultured in vitro with IFN-alfa. Unres-ponsiveness of IFN-gamma production when cultered in vitro with IFN-alfa at T=0 and T=24 hrs was seen in the limited group of nonresponders.
Conclusion: A strong HCV RNA dec at wk 4 can be induced by high dose continuous IFN therapy in patients who failed previous PegIFN/RBV therapy. A more than 2log viral dec at wk 4 is essential for achieving SVR. Responders showed higher IFN levels during the first weeks of treatment, but no relation with markers of immune activation was seen. Interestingly, in vitro T cell and IFN-gamma proliferation before and shortly after start of therapy may identify patients unlikely to respond.

Viral kinetics and immunological response with continuous subcutaneous administration of high-dose interferon alfa-2b in treatment-experienced chronic hepatitis C patients

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Introduction: Narlaprevir, belonging to the second wave of first generation hepatitis C virus (HCV) NS3 serine protease inhibitor has demonstrated robust reductions of HCV RNA after 1 week of monotherapy and after 2 weeks of combination therapy with peginterferon alfa-2b (Peg-IFN) with or without ritonavir. Treatment outcome and analysis of emerging resistance in patients treated with narlaprevir during a placebo controlled phase I clinical trial and during subsequently offered standard of care (SOC) is reported here. Methods: HCV genotype 1-infected patients (16 treatment-naïve and 16 treatment-experienced) received 1 week of narlaprevir monotherapy (period 1) followed by a 1 month washout period. Subsequently, all patients received 14 days of combination therapy with narlaprevir and Peg-IFN with or without ritonavir (period 2). At the end of this proof-of-concept study, all patients started SOC with Peg-IFN and ribavirin for 24 or 48 weeks. Samples with a viral load exceeding 1000 IU/mL were selected for longitudinal viral resistance analysis by population sequencing. Subsequently, in patients with proven resistance samples were subjected to longitudinal clonal (n=20) analysis. Results: At the end of the experimental treatment period, HCV RNA exceeded 1000 IU/mL in 7/32 patients and all 7 patients did not develop a sustained viral response. In 5/7 of these patients mutations associated with resistance (V36M, R155K, A156S/T and T54S) were found in different combinations by population sequencing. The A156S mutation, which results in high level resistance, disappeared quickly (1 week after initiation of SOC) from the population. In contrast, R155K, V36M or the combination of these two (also conferring high level resistance) could still be found in 3 patients up to 4 weeks after initiation of SOC. In contrast to the population sequence analysis, clonal analysis of these samples gave a better overview of the population variation. During the SOC period the resistance mutations V36M, R155K and T54S could be found for a prolonged period of time (up to 24 weeks after treatment) in different combinations as minor populations. Clonal analysis during narlaprevir dosing is pending.
Conclusion: Despite robust declines in HCV RNA, several HCV variants were detected after narlaprevir dosing and may be conserved for months after SOC is initiated. Longer follow up and 'ultra deep' clonal analysis is needed to fully understand the kinetics of these resistance mutations.

Surgical randomised trials in PubMed journals in 1999 and 2009: systematic review of volume and methodology

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Randomised controlled trials are essential for evidence-based decision making in surgery. It has repeatedly been suggested that surgical trials are both scarce and of mediocre methodological quality. Our aim was to assess the volume and methodological quality of surgical trials in 1999 and 2009. We used the Cochrane Highly Sensitive Search Strategy to identify randomised surgical trials published in the last 6 months of both 1999 and 2009 in PubMed. We screened 10,711 abstracts and appraised general and geographical characteristics from the included full-text papers. Methodological quality of all included trials was evaluated according to a seven-item list adapted from the Cochrane tool for assessing risk of bias. Trials were designated as 'high quality' only when all of these items were reported: adequate generation of allocation, concealment of allocation, intention-to-treat analysis, and adequate handling of dropouts. A total of 265 surgical trials were included, 100 in 1999 and 165 in 2009 (65% increase). The gastro-intestinal surgery was the leading speciality area for surgical trials with a doubling of the numbers of RCTs since 1999 (from 44 in 1999 to 88 in 2009). Geographically, the number of trials from the UK (14 vs 13) and USA (29 vs 24) remained unchanged, whereas the number of European (57 vs 72) and Australasian (12 vs 59) trials increased. In 2009, trial reports more frequently reported on the primary outcome of the study (51% in 1999 vs 64% in 2009), sample size calculation (37% vs 52%) and adequate generation of allocation (30% vs 44%). The number of high-quality trials increased from 4% to 7% (prevalence ratio 1.8, 95%CI 0.6-5.5).
Conclusion: Although the volume and the methodological quality of surgical trials have improved in the previous decade, only a minority of trials fulfilled the criteria for 'high quality'. There is a clear need for structured education, improved research infrastructure and enforced adherence to existing guidelines on randomised trials.

Cyclooxygenase isoenzyme-2 and vascular endothelial growth factor expression are significantly associated with prognosis in esophageal adenocarcinoma

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Cyclooxygenase isoenzyme-2 (COX-2) and vascular endothelial growth factor (VEGF) show increased expression in esophageal adenocarcinoma (EAC). Moreover, VEGF and COX-2 expression may be interlinked in the cancer cell as elevated COX-2 levels induce VEGF production thereby promoting tumour angiogenesis. This study assessed the prognostic value of COX-2 and VEGF expression and the relationship between ex-pressions of the two markers in EAC. A tissue micro array (TMA) was constructed comprising tumour cores of 156 consecutive patients undergoing esophagectomy with curative intent. Only patients with complete follow up (143 of 156; 92%) were included for analysis of median survival and disease-free survival (DFS). COX-2 and VEGF ex-pressions were analysed using immunohistochemistry and TMA sections were scored based on staining intensity. Fifty-two (33%) patients had T1 or T2 and 104 (67%) experienced T3 disease. High COX-2 expression was seen in 51 of 154 (33%) assessable EACs and low levels were shown in 103 (67%) patients. Median survival was 23 months for patients with high COX-2 levels and 35 months for low COX-2 expression (p= 0.026). DFS was 16 (elevated COX-2 levels) and 27 months (low COX-2 levels) respectively (p= 0,048). COX-2 expression proved to be an independent prognostic marker of poor survival using Cox regression analysis (HR 0,456; 95% CI, 0.293-0.709). Thirty-seven of 150 (25%) assessa-ble tumours revealed high VEGF levels, whereas low expression was seen in 113 (75%) cases. In patients with T1 and T2 disease median survival and DFS were 54 and 49 months in the VEGF high expression group and 65 months in patients expressing low COX-2 levels (p= 0,002 and p= 0,013 respectively). VEGF and COX-2 expression were not related with other clinicopathologic parameters such as lymph node metastasis and grade of tumour differentiation and no correlation could be detected between COX-2 and VEGF expression (p= 0,573, Spearman's rank test).
In conclusion, increased COX-2 expression is significantly associated with decreased survival in all T stages while elevated VEGF expression is significantly related with poor survival only in early EAC. However, a correlation between elevated COX-2 and VEGF expression was not seen in this study population.

Second PET-CT in the detection of metastatic disease after neoadjuvant therapy in esophageal carcinoma

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Several studies have evaluated integrated PET-CT as a predictor of response to neoadjuvant chemo-radiotherpy (NT) in esophageal carcinoma; however PET-CT in the detection of metastatic disease after NT has not been reported previously. Therefore we present our prospectively collected data of patients with esophageal carcinoma who underwent a second PET-CT in the detection of metastatic disease after NT. All patients planned for curative esophagectomy who underwent a second PET-CT after NT were included in this study. The first PET-CT was performed as part of the diagnostic work- up, the second PET-CT was performed after completion of NT. In case of suspected metastatic disease on the second PET-CT a biopsy was performed, if metastases were confirmed patients were excluded from surgical resection. Between November 2008 and May 2010 a total of 46 patients with esophageal carcinoma underwent neoadjuvant chemoradiotherapy prior to esophagectomy. All patients underwent a second PET-CT after NT. 80% of patients were diagnosed with esophageal adenocarcinoma, 20% with squamous cell carcinoma. Stage IB, II and III were present in 2, 35 and 63% of patients respectively. Metastatic disease on the second PET-CT was confirmed by a biopsy in 8.7% of cases (4/46 patients). There was one false-positive result (2%). This study shows that of all patients with esophageal carcinoma planned for esophagectomy after neoadjuvant therapy, 8.7% presented with metastatic disease on PET-CT after NT. A false-positive result was present in only one patient. Although this is a small group of patients, it shows that an additional PET-CT after NT can prevent palliative resection in patients with metastatic disease.

Surveillance and Follow-up Characteristics of Patients with High Grade Dysplasia in Barrett's Esophagus: a Dutch Population-Based Study

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Once high grade dysplasia (HGD) in Barrett's Esophagus (BE) is diagnosed, the risk of developing esophageal adenocarcinoma (EAC) is increased. In this study, we aimed to characterize surveillance participation and follow-up strategies in HGD patients in The Netherlands and to identify risk factors for progression to EAC. Patients with HGD in BE between 1999 and 2008 in The Netherlands were identified in a nationwide histo-pathological registry (PALGA). All pathology reports related to the esophagus prior to and at least 1 year after HGD diagnosis were evaluated. We assumed that patients who had undergone at least 2 upper endoscopies prior to HGD were participating in a surveillance program. Cox proportional hazards regression analysis was performed to identify inde-pendent predictors for progression to EAC. Eight-hundred-five patients with HGD in BE were included. Of these, 316 (39%) participated in a surveillance program according to our definition. Of all patients with HGD (n=805), 104 (13%) underwent surgical resection, 192 (24%) endoscopic mucosal resection (EMR), 63 (8%) ablative therapy, 322 (40%) endos-copic follow-up and 124 (15%) had no (endoscopic) follow-up. The latter group was signify-cantly older compared to the other patient groups (mean 74±13 vs. 65±11 yrs., p=0.01). Progression towards EAC was demonstrated in 232 (34%) of 681 HGD patients in whom follow-up was available. In 138 (20%) patients, this was detected within 3 months after HGD diagnosis. EAC was more often demonstrated during follow-up in patients in whom no upper endoscopy was performed prior to HGD diagnosis (123/259; 48%), compared to patients having undergone one (35/127; 28%) or two (74/295; 25%) prior endoscopies (p<0.001). Multivariate Cox proportional hazards regression analysis showed that age above 75 years increased EAC risk (HR 1.6, 95% CI 1.1- 2.2), whereas surveillance participation (HR 0.6, 95% CI 0.4-0.8), presence of focal HGD (HR 0.5, 95% CI 0.3-0.7), or undergoing EMR (HR 0.2, 95% CI 0.1-0.4) and ablative therapy (HR 0.1, 95% CI 0.0-0.3) independently reduced progression to EAC.
Conclusion: It is likely that adherence to surveillance endoscopy prior to a diagnosis of HGD has been low (less than 40%) in the last 10 years in The Netherlands. Older age was associated with an increased EAC risk in this nationwide HGD cohort. Participation in an endoscopic surveillance program prior to HGD diagnosis, presence of focal HGD and endoscopic treatment reduced the risk of progression towards EAC.

Validation and reproducibility of tumour-stroma ratio scoring on oesophageal adeno-carcinoma biopsies

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Recently, we investigated the tumour stroma ratio (TSR) on histological sections of oesophagectomy specimens. TSR proved to be a prognostic characteristic for survival in patients with oesophageal adenocarcinoma. Since neoadjuvant therapies are increasingly used, it would be of interest to analyse TSR on biopsy specimens. The objectives of this study were to assess inter- and intraobserver agreement for TSR scoring on oesophageal adenocarcinoma biopsies and to validate these biopsy results with the results derived from the surgical specimens. Biopsies of 91 patients who underwent resection for oesophageal adenocarcinoma were available. TSR was determined on the original haematoxylin-eosin (H&E) tissue sections from the primary tumour biopsies. To assess interobserver variation, TSR was scored by three experienced pathologists. TSR was defined as very low (0-25%), low (25-50%), high (50-75%) or very high (75-100%). A second scoring was done to examine intraobserver variation. Then, there were 2x3 scores for each biopsy. The definitive TSR biopsy score (four or more similar scores) was compared with that of the resection specimen. Kappa statistics were applied to evaluate agreement. Biopsies of 10 patients were rejected because of poor quality of the tissue specimen. Biopsies of 81 patients were analysed. Interobserver correlations for TSR biopsy scores ranged from 0.239 to 0.486 ($p<0.001$ for all correlations). When classifying scores into two groups (<50% and ≥50%), interobserver correlations improved (maximum $\kappa=0.886$; $p<0.001$ for all correlations). Intraobserver agreement was moderate to substantial ($\kappa=0.509$, 0.603, and 0.683; $p<0.001$ for each). Using the cut-off value of 50%, intraobserver agreement was substantial to near-perfect (maximum $\kappa=0.848$; $p<0.001$ for each). Definitive TSR biopsy scores (12 patients with TSR <50% and 69 patients with TSR ≥50%) showed moderate correlation with TSR scores on surgical specimens ($\kappa=0.506$; $p<0.001$). The definitive TSR biopsy score was an independent prognostic factor for survival in multivariate analysis ($p=0.03$).

Conclusion: Reproducibility of tumour stroma ratio scoring on oesophageal adenocarcinoma biopsies was good. The ease of TSR scoring on H&E sections together with its correlation with patients' survival may have clinical relevance in this era of neoadjuvant therapy.

How to define a positive circumferential resection margin in patients with T3 adenocarcinoma of the esophagus

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Negative circumferential resection margin (CRM) is associated with improved survival. However, definition of tumor positive margin remains unclear. The Royal College of Pathologists (RCP) considers the CRM positive if tumor is found within 1 mm of the lateral margin while the College of American Pathologists (CAP) suggest that only tumor which is microscopically identified at the lateral margin results in a positive CRM. This study evaluates the clinical prognostic significance of CRM involvement on survival and recurrent disease in patients with T3 adenocarcinoma of the esophagus. Patients were selected from a prospectively collected database and analyzed retrospectively. All 167 patients underwent esophagectomy between 1988 and 2008 for a T3 esophageal adenocarcinoma. None of the patients received neoadjuvant therapy. Original pathologic slides were reassessed by a single experienced pathologist and CRM was measured in tenths of millimetres with inked lateral margins. One hundred thirty-two patients (79,0%) were analyzed. Mean follow-up was 28,4 months. Positive margins were found in 26 cases (19,7%) corresponding to CAP criteria versus 89 cases (67,4%) corresponding to RCP criteria. Median survival in CRM+ and CRM- negative patients was 9,4 months (95% CI, 7,6-11,2) versus 21,6 months (95% CI, 18,9-24,3) respectively in the CAP group ($p<0,001$). Median survival using RCP criteria was 16,4 (95% CI, 8,5-24,2) for CRM+ patients versus 21,0 (95% CI, 16,3-25,6) in CRM- patients ($p=0,14$). Overall median disease free survival was 13,0 months (95% CI 9,4-16,7) showing significant difference when analyzed according to CAP criteria ($p<0,001$). RCP criteria did not show significance between groups ($p=0,26$). Involvement of the circumferential resection margin is an independent prognostic factor for survival and recurrence in patients with T3 adenocarcinoma of the esophagus. The circumferential margin should be considered positive (R1) if tumor is found at the inked lateral margin of resection.

Removable and repositionable covered metal self-expandable stents for post-surgical leaks in the upper gastro-intestinal tract. Experiences in a tertiary referral hospital.

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Anastomotic leaks are severe complications of upper gastro-intestinal surgery, occurring in 4-30% with extensive morbidity and mortality (35%). Until recently, drainage of abscesses caused by leakage was the only possible treatment. Since 2007 removable and repositionable covered metal self-expandable stents (RReCoMSeS) are used in our hospital to cover leaks in the upper gastro-intestinal tract.All patients with postsurgical upper gastro-intestinal tract leaks treated with RReCoMSeS between January 2007 and March 2010 were retrospectively described.Twenty-seven patients (15 females, mean age 52.9 years) were treated with overall 34 RReCoMSeS in 44 procedures. Three different stents were used: totally covered CHOO® and Hanaro® (M.I. Tech, Korea) and partially covered Endoflex® (Germany) stents, with 18 or 24 mm diameter and 80 or 140 mm length. Fifteen patients had leaks after oesophageal resection with gastric tube reconstruction, 11 after bariatric surgery, and 1 after gastric resection. Overall success in clinical sealing of the leak was 88.9%. Ten patients (37%) needed more than one procedure for a successful sealing, of whom five (18.5%) needed more than one stent due to migration, stent disintegration or persistent leak. In total 34 RReCoMSeS were placed in 27 patients, with a mean of 1.3 stent and 1.6 procedures per patient. Twenty-one of 34 RReCoMSeS sealed the leak successfully (61.8%). Complications were: migration in seven (20.5%), disintegration of three (8.8%) and perforation of one of the 34 used RReCoMSeS (2.9%). Fixating RReCoMSeS by clipping the margins did not decrease migration rates. Five patients (18.5%) died during the observed period, but not related to RReCoMSeS.
Conclusions: RReCoMSeS seem safe in treating post-surgical leaks in the upper GI-tract. In 88.9% of patients the leak was sealed successfully, with few complications. Stent migration is the major problem which should be attacked in future.

The effect of patient characteristics, with special reference to socioeconomic status, on treatment choice in esophageal cancer

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Primary esophageal cancer (EC) is increasing in incidence; however, there is only limited data available on which factors determine the treatment choice in these patients in Western Europe. It has been suggested that apart from tumor characteristics, patient characteristics, i.e. socioeconomic status, also determine whether a curative or non-curative treatment modality is chosen. We used the Eindhoven Cancer Registry maintained by the Comprehensive Cancer Centre South to select all patients diagnosed with EC in the period 1990-2008. Treatment was divided in curative and non-curative modalities. Curative treatment was defined as surgery with or without (neo-) adjuvant chemo- or radiotherapy, or chemo- or radiotherapy alone in patients with M0 and T1-3 disease. In total, 1914 patients with EC (55% adenocarcinoma, 45% squamous cell carcinoma) were included. Of these, 37% were treated with a curative modality, whereas the remainder received either no treatment or treatment directed to metastases. Multi-variable logistic regression analysis showed that patients with a higher socio-economic status (SES) were more likely to receive a curative treatment (OR 1.58; 95% CI: 1.06–2.36). In contrast, older age at diagnosis correlated with lower odds of receiving curative treatment (age: 60-69, OR 0.53; 95% CI: 0.39–0.77; age: 70-79, OR 0.22; 95% CI: 0.14–0.33; age: ≥ 80, OR 0.04; 95% CI: 0.02–0.09), compared to patients younger than 60 years. Patients with 2 or more comorbidities were also less likely to receive curative treatment (OR 0.54; 95% CI: 0.36–0.79). Patients with EC localized in the distal esophagus were more likely to undergo curative treatment, while the opposite was true for a cervical localisation of the tumor (distal: OR 1.60; 95% CI: 1.02–2.49; cervical: OR 0.09; 95% CI: 0.02–0.45), compared to the mid-esophagus. Not surprisingly, pre-treatment tumor stage played a role in treatment choice as well (T4 vs. T1: OR 0.01; 95% CI: 0.001–0.02; N1 vs. N0: OR 0,435; 95% CI: 0.29–0.66; M1 vs. M0: OR 0.02; 95% CI: 0.01–0.03). Gender, period of diagnosis (1990–2000 vs. 2001–2008) and tumor histology did not affect treatment choice.

Conclusion: Our results show that treatment choice is not only determined by tumor characteristics, i.e., pre-treatment stage and tumor localization, but also by patient characteristics, i.e. SES, age and comorbidity. It remains to be determined whether the effect of SES is caused by patient- or physician-related factors.

Effect of centralization on morbidity and mortality after surgical treatment of esopha-geal cancer

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To evaluate the effect of centralization of esophagectomy on morbidity and mortality in the Eastern part of the Netherlands. A retrospective comparison of 174 patients operated on for esophageal cancer in five hospitals between January 2000 and June 2005 (group 1, pre-centralization) and 61 patients operated on between March 2008 and May 2009 in two dedicated esophageal cancer hospitals, after implementation of centralization in the Eastern part of The Netherlands (group 2, post-centralization). The mean duration of follow-up was 24.9 months (0.1-83.7) for group 1 and 12.8 months (0.9-22.5) for group 2. The mean number of operated patients per hospital increased from 7 to 25 patients per year. Neoadjuvant therapy introduced as part of the CROSS trial increased from 8.5% to 52.5% of the patients (P<0.001). Median blood loss decreased from 1250 to 575 mL (p<0.001). The number of harvested lymph nodes increased from 8 to 11 per patient (p<0.001), and R0-resection rate increased from 75% to 84% of patients (p=0.155). The incidence of postoperative pneumonia decreased from 35% to 23% (p=0.031). Median ICU- and hospital stay decreased from 3 to 2 days (p=0.018) and from 16 to 10 days (p<0.001) respectively. In-hospital mortality rate decreased from 5.7% to 1.6% (p=0.30), and one year mortality rate decreased from 30% to 16% (p=0.035).
Conclusion: Centralization of esophagectomy was successfully implemented in the Eastern part of the Netherlands. Centralization reduces postoperative morbidity and one year mortality rate.

Efficacy of an integrated multidisciplinary approach of patients with severe functional gastrointestinal disorders

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Background: Treatment of patients with functional gastrointestinal disorders (FGIDs), such as irritable bowel syndrome (IBS), remains challenging especially in patients with severe and invalidating symptoms. At our centre FGID patients with psychiatric comorbidity (mostly panic or mood disorder) are referred to the Medical Psychiatric Unit (MPU). In an ambulatory setting, we provide a standardized, integrated approach. After medical and psychiatric diagnostic procedures, the following options are available: psychotherapy, treatment with SSRIs (selective serotonin reuptake inhibitors), or a combination of both. Previously, we have shown that treatment at the MPU in a clinical setting is cost-effective, but data about efficacy in the ambulatory setting are not available. The aim of this observational study was therefore to evaluate our integrated multidisciplinary approach of patients with FGIDs at the MPU with regard to control of gastrointestinal symptoms, psychiatric symptoms and quality of life. Methods: All patients who visited the MPU starting from August 2009 were asked to complete validated questionnaires at their first visit and 6 months later: the Gastrointestinal Symptoms Rating Scale (GSRS), the Cognitive Scale for Functional Bowel Disorders (CS-FBD), the State-Trait Anxiety Inventory (STAI), the Hospital Anxiety and Depression Scale (HADS), and the SF-36 Health survey (SF-36). Scores were compared using Wilcoxon-signed rank test. Results: 56 patients visited the MPU during the study period. Of them, 80% completed questionnaires. Mean age was 43 years and 76% was female; 64% was diagnosed with IBS, and 76% with a psychiatric disorder, of which 53% panic disorder. Treatment: 46% SSRIs, 27% psychotherapy, and 27% both SSRIs and psychotherapy. There was a significant improvement in score after 6 months for the GSRS ($p=0.002$), the STAI state version ($p=0.032$), the Physical Role Functioning subscale of the SF-36 ($p=0.017$), the Bodily Pain subscale of the SF-36 ($p=0.018$), and the Emotional Role Functioning subscale of the SF-36 ($p=0.006$).
Conclusion: This is the first study to report about the effects of a standardized integrated multidisciplinary approach of complex FGID patients in an ambulatory MPU-setting. These data indicate that an integrated approach may be effective in improving gastrointestinal and psychological symptoms and quality of life. Based on these encouraging findings a controlled trial focussing on efficacy and costs is justified.

Clinical trial on the short and long term effect of two psychological interventions for irritable bowel syndrome

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Treatment of patients with functional gastrointestinal disorders such as irritable bowel syndrome (IBS) is challenging. Recent studies indicate that psychotherapy may be effective in reducing symptoms in IBS patients. We have previously shown in a University Hospital setting that relaxation training, as brief psychological group intervention, is effective. Aim of the present study was to compare whether two distinct psychological interventions, known to improve IBS symptoms, are effective in a regular hospital setting. A randomised controlled trial was performed comparing gut centered standardised hypno-therapy (8 sessions of one hour, individual basis) with a group intervention of relaxa-tion training (4 group sessions of 2 hours focussing on relaxation and implementation into daily life) with standard medical care (access to gastroenterologist upon request). At baseline, 3, 6 and 12 months symptoms, quality of life (SF36), anxiety and depression (HADS) and dysfunctional cognitions were scored at regular intervals. A total of 113 patients (age range 18-75 years; 80 females) were included based on Rome II criteria. Patients were randomised to 3 groups: hypnotherapy (HYPNO, n=41), relaxation training (RT, n=39) or care as usual (CAU, n=33).Results: at 3 months (short term) symptom severity (range 0-5) decreased significantly vs. base in the HYPNO group (2.8 to 2.3; $p<0.05$) and in the RT group (2.9 to 2.6; $p<0.05$) but not in the CAU group (2.8 to 2.8). However, after 12 months (long term) no significant effect on symptoms was found versus base nor between the three groups. The number of symptom free days (per 14 days) at 3 months increased sign.($p<0.05$) in the HYPNO group (from 1.0 to 2.7) but not in the RT group (0.9 to 1.4) or CAU group (1.2 to 1.4). Neither anxiety nor depression scores were affected by any of the interventions. Analyses were based on the intention to treat. Drop-out rate varied between 30 and 40% in the 3 groups.
Conclusions: Hypnotherapy as intensive individual therapy and relaxation training as brief group intervention both reduce IBS symptoms on the short term, but neither of these therapies affects symptoms on the longer term. Although psychological interventions are effective on the short term, the focus should be long term (at least 12 months). Future studies should also pay attention to the setting (academic or specialised versus regular care) and to patient compliance (low in IBS patients).

Anorectal function evaluation and predictive factors for fecal incontinence in 600 patients

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Aim: To comprehensively investigate the anorectal function in fecal incontinent patients compared to continent patients, to determine predicting factors in a model for fecal incontinence and to test the model in patients after stoma closure. Methods: Between 2003 and 2009, all consecutive patients referred to our function laboratory were prospectively assessed by a questionnaire, anorectal manometry and anal endo-sonography. Predictors were identified by logistic regression analysis. Results: Of the 600 patients (519 women), 285 (48%) were fecal incontinent. Incontinent women (mean Vaizey-score 15.4), were older (57 vs 44 years; P<0.001), had more liquid stool (21 vs 10%; P< 0.001), more deliveries (2.1 vs 1.6; P<0.001), more urine incontinence (36 vs 20%; P=0.001), lower basal (39 vs 53 mmHg; P<0.001), and squeeze pressures (29 vs 40 mmHg; P<0.001), shorter sphincter length (3.0 vs 3.2; P=0.01), smaller rectal capacity (184 vs 215 ml; P<0.001), and more sphincter defects (53 vs 49%; P=0.01) than continent women. Incontinent men (mean Vaizey-score 15.3) were older (63 vs 54 years; P=0.02) and had lower basal (45 vs 55 mmHg; P=0.03) and squeeze pressures (43 vs 63 mmHg; P=0.01) than continent men. Incontinent and continent patients showed an overlap in tests results. Predictors for women were age, stool consistency, basal and squeeze pressures, rectal capacity and combined internal and external sphincter defects (Figure). The area under the ROC-curve was 0.84 (P<0.001, 95%CI: 0.80-0.87). Using a cut-off point of 0.4 to predict fecal incontinence, a sensitivity of 86% and a specificity of 68% were obtained. The positive and negative predictive values were 74% and 82% respectively. Five patients with a temporary stoma were available to test the model. The model was accurate in predicting the incontinence.

Conclusions: Incontinent patients have lower pressures, smaller rectal capacity and more sphincter defects then controls, but show a large overlap. Incontinent women were older, had more deliveries, liquid stool and urine incontinence. Our feasible predictor model shows a relatively high sensitivity and negative predictive value for predicting fecal incontinence in women. The model seems promising in the tested patients with a temporary stoma.

The association between proton pump inhibitors and bone fractures revisited: results of a systematic review

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Recently, concerns have been raised on the long-term use of proton pump inhibitors (PPIs). In addition, patients using long-term PPIs have been found to be at a higher risk for community-acquired pneumonia, Clostridium difficile gastroenteritis, and osteoporosis. In May 2010, the FDA published a warning and revised the labelling of PPIs concerning the risk of bone fractures, although the evidence seems scarce. The aim of our study was to systematically review all published literature on the association between long-term PPI use and fractures. We performed a structured search of PubMed to identify published reports about cohort and case-control studies regarding the association between long-term PPI use (defined as ≥1 year) and bone fractures (hip, vertebra, or wrist).A total of 9 studies matched our criteria, of which 4 cohort and 5 matched case-control studies. Although major heterogeneity was present in definitions on study population, exposure, outcomes and analyses, all but one included studies showed a moderately increased risk for osteoporosis related fractures. The risk was highest in populations with PPI use for over 10 years (adjusted odds ratio 1.85, 95%CI 1.41–2.43), and for vertebral fractures (adjusted risk ratio 3.50, 95%CI 1.14–8.44). In one study, two prospective cohorts were studied. In the solely male cohort of this study, the association was not found for non-spine fractures (adjusted hazard ratio (HR) 1.21, 95%CI 0.91–1.62), which was in contrast to the female cohort (adjusted HR 1.34, 95%CI 1.10–1.64). Interestingly, bone mineral density was studied as a secondary outcome in 2 studies, but no association was found with PPI use.
Conclusion: Despite much heterogeneity, almost all published studies showed an increased risk for fractures after long-term PPI use, which was most pronounced after long-time use, in females, and for vertebral fractures. No association was found with bone mineral density, indicating that the association between PPI use and bone fractures is unrelated to osteoporosis.

Use of proton ump inhibitors (PPI) may cause false positive tumour marker elevation of chromogranin A: a potential pitfall in the evaluation of neuroendocrine tumours.

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Neuroendocrine tumours are slowly growing tumours (NET) mainly derived from the intestinal tract. In the presence of liver metastases diarrhoea and flushing are often the presenting symptoms and related to the secretion of peptides among which serotonin is the most well-known. The degradation product 5-HIAA in the 24-hour urine was generally used to evaluate treatment result. Recently, the serum marker chromogranin A (CgA) proved to be a more reliable and convenient tumour marker. Initially, the long term use of proton pump inhibitors (PPI) was thought to induce gastric carcinoids. This is not a clinical problem, but a rise in gastrin and ECL-cell hyperplasia do occur. ECL-cells may produce chromogranin A and hence cause a rise in the serum value.The aim of the present study was to evaluate the effect of PPI's on CgA in the evaluation of NET patients.All patients with a NET (n=198; 88m and 110f, mean age 65 yr) with two or more blood samples drawn in 2007-2009 were included in the study. 48 patients were on a PPI, while 150 were not. Tumour status was based on symptoms, CT-scan and radionuclide Octreoscan (based on somatostatin receptor binding).In 144 the CgA-level was elevated: in 23 patients, all on PPI, this could not be explained by tumour deposits or progression at repeated CT-scan or Octreoscan. In 8 of these 23 no tumour was found after resection of the primary: median CgA was 366 (range 123-1610). After discontinuation of PPI during 2 weeks CgA dropped in all >50% to 44 (range 15-245), in 5 it was normal. Rechallenge in two of them led to increased CgA-levels again.In 15 with metastatic disease and a rise in CgA no tumour progression was found for at least 6 months, median CgA 589 (range 206-35710). After stopping PPI CgA dropped >50% in 7 among 5 within normal range; the median dropped to 240 (range 38- 40500).
Conclusion: In 23 of the 48 NET patients (48%) on PPI a rise in the tumour marker CgA was unexplained. In all 8 patients (100%) without tumour CgA dropped significantly after discontinuation; in 7 (47%) of the 15 (with stable metastatic disease) the rise in CgA was misleading and dropped significantly. It is always important to be aware of pitfalls when using a tumour marker in the evaluation of treatment.

Glasgow Blatchford bleeding scale identifies patients who do not need in hospital treatment in a Dutch Emergency Department

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Acute upper gastrointestinal bleeding (UGIB) is a frequently presented problem at the Emergency Department (ED). Instruments for optimal triage of patients for early endoscopy and clinical admission are needed. The Glasgow Blatchford bleeding scale (GBS) stratifies patients according to their probability of need for in hospital intervention. Unlike most other scoring systems this scale does not require endoscopic findings. The aim of this study was 1) to evaluate the GBS scale for use in the emergency department of a combined regional and university hospital in the Netherlands and 2) to determine the most adequate cut off value for safely treating UGIB patients as outpatients. The GBS scale was compared with the Rockall and HUPS scores for their ability to distinguish patients with and without need for in hospital treatment. We reviewed the patient charts for a 7 months period and we included all patients (n =103) who presented at the ED with signs of acute UGIB. We retrieved clinical, laboratory and endoscopic data and calculated the GBS score for each patient. We constructed receiver-operating curves for the different scoring systems to compare their discriminatory ability for the need for in hospital intervention. Receiver operating characteristic analysis showed very good discriminative ability for the GBS with an area under the curve of 0.94 (95% CI 0.90-0.98). Using a cut off value of 2 (score range 0-23), we found a positive predictive value of 78.7% (95%CI 68.1-86.4) and a negative predictive value of 100% (95%CI 81.6-100), which means that, when the decision were based on the GBS, no patients needing in hospital treatment would have been treated as an outpatient. Using a cut-off level of 2 instead of the traditional 0, 18.5% instead of 4.3%, of the patients could have safely been sent home. The GBS was superior to the Rockall score 0.85 (95%CI 0.75 - 0.95) and the HUPS score 0.88 (95%CI 0.79 - 0.96).
Conclusions: The Glasgow Blatchford bleeding scale is a useful risk stratification tool for patients with acute upper gastrointestinal bleeding in the Emergency Department to identify patients who do not need in hospital intervention. A cut off value of 2 seems safe to use and identifies more patients who can be treated as outpatients than the originally proposed cut off value of 0. Prospective studies are needed to determine the best cut-off value and evaluate cost effectiveness.

In-hospital costs of laparoscopy and/or fast track multimodal management versus open and/or standard care in colonic surgery (LAFA-trial)

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Aim of this study is to compare in-hospital costs of patients randomized to a laparoscopic or opencolectomy, and to fast track or standard care. For this purpose the data from the LAFA trial were used. In this trial, fast track was compared with standard perioperative care regimen in 400 patients undergoing laparoscopic or open surgery for colorectal cancer. The marginal direct medical costs were calculated per patient for the 4 treatment strategies. These costs included outpatient care, operating time, patient-days, the additional costs of laparoscopy and of fast track care, as well as the costs of complications, reoperations and readmissions within 30 days after the index operation. Both tertiary hospitals and teaching hospitals included patients in this study. Costs are calculated differently in these types of hospitals and therefore we separately analysed the overall costs for tertiary and teaching hospitals. In-hospital costs were calculated for 112 (64%) out of 176 patients operated in a tertiary hospital and for 133 (59%) out of 224 patients operated in a teaching hospital. There were no statistically significant differences, adjusted for the type of hospital, between in-hospital costs per treatment strategy (P=0.560 and P=0.411, respectively). As in-hospital costs were comparable, a cost-effectiveness analysis was not performed.
Concluding, in-hospital costs for patients operated with a laparoscopic or open resection combined with fast track care or standard care are similar.

High diagnostic yield of direct endoscopic mucosal oxygen saturation measurements in patients suspected for chronic upper gastrointestinal ischemia

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Chronic mesenteric ischemia (CMI) is recognized as a fairly common condition with a wide clinical spectrum. Evaluation of mucosal ischemia is one of the main stays of correctly diagnosing CMI. We showed that measuring mucosal oxygen saturation with visible light spectroscopy (VLS) during endoscopy was equal to 24-hour tonometry for detecting mucosal ischemia. We investigated whether VLS, could be used as a pre-test in patients suspect of having CMI. Evaluation of CMI comprised a standard work-up, consisting of evaluation of symptoms, imaging of gastrointestinal arteries, and VLS. VLS measurements were performed during upper endoscopy in the duodenum, duodenal bulb, gastric antrum, and corpus using saturation cut-off values as previously validated by direct comparison with tonometry. After multidisciplinary assessment a consensus diagnosis was made: 1) normal arteries, no ischemia, 2) stenotic arterial vessel(s) without ischemia, 3) normal arteries with ischemia (non-occlusive), and 4) stenotic arterial vessel(s) with ischemia (occlusive). The latter 2 groups were advised to undergo treatment: either vasodilating medication, endovascular or surgical. The definite diagnosis CMI was made after persistent clinical response at ≥ 6 months after adequate therapy. In a 2-year period, 152 patients were included: 102 female, age 59 (20 – 85) yrs. A definite diagnosis of CMI was made in 84 pts: 66 with occlusive CMI and 18 pts with non-occlusive CMI. The clinical success rate of therapy was 96% for occlusive disease (endovascular or surgical) and 64% for non-occlusive disease (medical therapy). 77/89 (87%) pts with mucosal ischemia (VLS+) had CMI, against 7/63 (11%) of pts without mucosal ischemia (VLS-)(sensitivity of VLS 92%, and specificity 82%; $p<0.001$). 65 (73%) of the VLS+ pts had a significant stenosis on CT-angiography against 10/63 (16%) of the VLS- pts ($p<0.001$). VLS was false-negative in 7 pts: 4 pts with occlusive CMI (reevaluation due to worsening symptoms) and 3 with non-occlusive CMI (identified by 24-hour tonometry). VLS appeared false-positive in 12 pts: 3 with occlusive and 9 with non-occlusive disease.
Conclusion: Direct endoscopic measurement of mucosal oxygen saturation (VLS) allows adequate discrimination between CMI and no ischemia. This makes VLS an important new tool in this area with a previous lack of functional tests. VLS may be used as an alternative screening test for CMI in pts with a high clinical suspicion.

Symptomatic Wilson disease during long-term zinc maintenance monotherapy after initial penicillamine decoppering: Experience in 30 patients.

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Outcome of exclusive zinc monotherapy for symptomatic Wilson disease may be unfavourable, particularly in case of advanced hepatic disease. Initial decoppering with penicillamine might improve outcome, but available data are scarce and long-term follow up is not available. We here report our experience with such approach in 30 symptomatic pts during (median) 29 (range 0.5-48) yrs follow up (FU). Presentation was exclusive hepatic, exclusive neurologic or combined in 14, 3 and 13 cases resp. Mean age at diagnosis was 14 (range 7-37) yrs. Duration and dose of initial penicillamine were 2 (0.5-21) yrs and 873 (162-2000) mg resp. and of subsequent zinc 23 (0.5-42) yrs and 175 (68-279) mg resp. Of the 27 pts with hepatic or combined presentation, 3 exhibited initial decompensated cirrhosis, 11 compensated cirrhosis and 13 less severe disease. Of 3 pts with initial decompensated cirrhosis, one improved to compensated cirrhosis and remains so during 23 yrs FU, 1 was transplanted after after 0.5 yr, and one initially improved but died 12 yrs later from complications of cirrhosis. Of 11 pts with initial compensated cirrhosis (median FU 31 yrs), 1died after 2 yrs from penicillamine-induced myelinolysis, 3 died from complications of liver disease after 17, 20 and 30 yrs therapy and 7 remain stable after median 29 yrs FU. Of 13 pts with less severe hepatic disease, 9 deteriorated, including 5 to compensated and 1 to decompensated cirrhosis (the latter recompensating after trientine addition). Progressive hepatic disease was associated with longer follow up (median 31 vs 26 yrs, P=0.03) but could not be clearly explained by dose or duration of therapy or efficiency of decoppering (based on 24-hr urine copper excretion and serum non-ceruloplasmin bound copper conc. at end of FU). Of the 16 pts with initial neurologic or combined presentation, neurologic symptoms improved in 7, remain stable in 4, and deteriorated in 5 (including 1 with subsequent death from pneumonia). 3 pts with exclusive hepatic presentation developed neurologic symptoms and one pt with exclusive neurologic presentation developed hepatic disease during follow up. Major side effects occurred exclusively during penicillamine: glomerulonefritis (n=2) and death from myelinolysis (n=1). In conclusion, athough short term clinical outcome is often satisfactory, hepatic Wilson disease tends to progress during long term zinc monotherapy, even after initial penicillamine decoppering.

Post-ERCP Cholecystitis - incidence and risk factors

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Although post-ERCP complications like pancreatitis and cholangitis have been studied extensively, little is published on the incidence of post-ERCP cholecystitis (PEC). We retrospectively investigated the incidence of PEC, interval of time between ERCP and cholecystitis and risk factors for PEC. In this study 651 consecutive patients (1107 procedures) in the period July 2006 until January 2009 were analysed retrospectively. Primary outcome was development of cholecystitis during 3-months follow-up. Medical history, patient characteristics and endoscopic findings and procedures were recorded and analysed as potential risk factors.A total of 229 patients were excluded (history of cholecystectomy, n=168; clinical or radiological signs of cholecystitis before ERCP, n=47; other, n=14). The data of 422 patients (684 procedures) were used in the analysis. Cholecystitis was found after 20 ERCPs (2.9 %). Onset of symptoms was between 2 and 44 days after ERCP with a median of 10 days. Univariate analysis of the first ERCP showed a significant risk of PEC in young age (p=0.001), gallbladder stones (p=0.008) and common bile duct stone (CBD) extraction during ERCP (p=0.020). Furthermore the incidence of PEC was higher among females (odds ratio M/F =1:2.7). We found no significant benefit in the use of prophylactic antibiotics.
Conclusions: After ERCP patients have an increased risk of developing cholecystitis, occurring mostly within two weeks. The risk is highest in young and female patients and in patients after ERCP with CBD stone extraction. Therefore, to prevent acute cholecystitis especially these patients will benefit from early cholecystectomy.

High prevalence of common bile duct dilatation among hepatitis C infected methadone users

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Introduction: Methadone is widely used as maintenance therapy for former and current drug users (DU). Because chronic hepatitis C (HCV) infection is highly prevalent among DU, many undergo liver imaging as part of decision making towards antiviral therapy. Narcotics have shown to increase sphincter of Oddi pressure and thereby induce bile duct dilatation. Some small studies demonstrated a higher frequency of common bile duct dilatation (CBDD) among patients on methadone prescription. CBDD is generally considered a clinically significant finding that warrants exclusion of malignancy. However, the prevalence and clinical importance of CBDD in methadone users is unclear. Our aim was to study the prevalence of asymptomatic CBDD in HCV-infected patients with and without methadone prescription. Methods: We conducted a retrospective observational study among 815 HCV-infected patients. Patients were included when HCV-mono-infected and visited our outpatient clinic unit between January 1990 until May 2010. Liver imaging was done with ultrasonography, computed tomography and / or magnetic resonance. CBDD was defined as a diameter of the common bile duct of more than 6 mm. Association between prevalence of CBDD and methadone use, gender and age were tested with Pearson chi-square and Mann-Whitney tests. Results: Of the 815 subjects enrolled, 139 (17%) were on methadone prescription at time of imaging, and 539 (66%) were male. Median age at time of imaging was 48 years (range 14-83 years). 2 of 676 subjects (0.3%) not on methadone prescription showed CBDD with a mean diameter of 7.5 mm (7.0 – 8.0 mm) versus 20 of 139 subjects (14.4%) on methadone prescription with a mean diameter of 9.2 mm (6.5 – 15.0 mm). Imaging of the subjects with CBDD did not reveal an explanation for the dilatation. CBDD showed to be significantly associated with methadone use ($p<0.001$). Gender was not associated with CBDD ($p=0.79$). Mean age showed not statistically associated with CBDD; 43 years without CBDD and 48 years with CBDD ($p=0.90$).
Conclusion: Asymptomatic CBDD is highly prevalent among HCV-infected methadone users when compared to HCV-infected patients who do not use methadone. Because asymptomatic CBDD is regarded a first sign of possible severe pathology, correct interpretation of abdominal imaging requires knowledge of the methadone status, as this may limit excessive and unnecessary medical examination.

Maintenance treatment is necessary even when auto immune hepatitis is in remission

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Background: Autoimmune hepatitis (AIH) is a chronic inflammatory autoimmune disorder of the liver of unknown etiology. Treatment is aimed at suppressing the exaggerated inflammatory response and includes steroids and azathioprine. It is generally believed that discontinuation of therapy leads to rapid relapse of the disease, however literature to support this thesis is scarce. Aim: To determine the number of relapses in a cohort of AIH patients. Methods: We reviewed the charts of 140 patients (40.M; 100 F) that fulfilled the diagnostic criteria of AIH. In a group of 32 patients, treatment was reduced with the aim to eventually discontinue the treatment. Mean time after diagnosis was 5,3 years (2- 18,7). At the start of reduction therapy 5 patients (15,6%) used mono therapy azathioprine average dose 95 mg (50-150) , 11 patients (34,4%) mono therapy prednisone average 6.4 mg (2.5-10) and 16 patients (50%) prednisone in combination with azathioprine. Relapse was defined as increasing aminotransferase levels above the upper limit of normal, with or without concomitant clinical symptoms. Results: In a group of 32 patients, treatment was discontinued due to longstanding (≥ 2 years) normal aminotransferases and no other clinical or biochemical abnormalities. In 7 of these patients (21,9%) liver biopsy confirmed the absence of active inflammation. In 18 patients, all medication was discontinued. In 14 patients, medication was tapered, however not fully discontinued, because of a relapse. After a mean follow up of 165 days (range: 74-1259), 29 out of 32 had a relapse requiring restarting of increasing immunosuppression. The three patients who did not have a relapse had a follow-up of 8.1, 1.2 and 1.5 years without medication. A total of 15 (51,8%) of the relapse patients had no therapy when they got a relapse, while 14 patients (48,2%) got a relapse during tapering of the therapy.
Conclusion: Relapse of AIH patients in remission occurs in virtually all patients when therapy is tapered or discontinued after a period of at least two years of maintenance therapy. These data indicate that AIH patients should therefore be kept on maintenance therapy.

Sperm DNA integrity is not affected by treatment with peginterferon alfa and ribavirin for chronic hepatitis C

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Background: Treatment with peginterferon alfa and ribavirin (PEGIFN/RBV) is the standard of care for chronic hepatitis C. Animal studies have repeatedly proven the teratogenicity of ribavirin. Limited data is available on the effect of PEGIFN/RBV treatment on human sperm quality. Furthermore there is some evidence that sperm quality may be impaired in HCV patients. For this reason we conducted a study to investigate the effect of chronic hepatitis C and PEGIFN/RBV treatment on spermatogenesis and sperm DNA integrity. Methods: Sperm samples of chronic HCV patients treated with PEGIFN/RBV were collected before, during (week 12, 24, end of treatment) and 6 months after treatment (FU). Samples were analysed on motility, morphology, volume and concentration. Furthermore we analyzed sperm DNA integrity which plays an important role in sperm function and fertilizing capacity. The sperm chromatin structure assay (SCSA) was used to determine sperm DNA integrity which is expressed as the DNA fragmentation index (DFI). A DFI larger than 30% is considered abnormal. Results: Base sperm samples were available in 22 patients. Median age was 43.5 years (interquartile range (IQR) 13 years). One patient had cirrhosis. Nineteen of 22 patients (86%) had base asthenospermia (<50% moving spermatozoa). Median percentage (%) of progressively motile spermatozoa at base was 37.5% (IQR 22%). The % of progressively motile spermatozoa did not change during treatment: 38% (IQR 33%) and during FU: 34.5% (IQR 39.5%). Data on morphology were available in 8 patients. Median % of normal morphology at base was 6.5% (IQR 3%) which decreased to 4% during treatment (not significant). Median base volume was 1.55 ml (IQR 2.25 ml) which decreased to 1.1 ml (IQR 1.05 ml) during treatment (p=0.025) and increased to 1.95 ml (IQR 2.23 ml) at FU. Median sperm concentration at base was $30x10^6$/ml (IQR 169 $x10^6$/ml). Nine of 22 patients (41%) had oligospermia at base (<20 $x10^6$ spermatozoa/ml). Concentration did not change significantly during therapy and FU. Data on sperm DNA integrity were available in 15 patients. At base 4 of 15 patients (27%) had a DFI >30%. Median DFI at base was 20.3% (IQR 20.5%), during treatment: 17.2% IQR (42.9%) and at FU: 28.5% (IQR 35.1%). Methadone users had a higher DFI compared to non users, 32% vs. 19% (p=0.061).
Conclusion: Sperm abnormalities were common in HCV patients, however PEGIFN/RBV treatment did not lead to further impairment of sperm quality except for a decrease in sperm volume. Sperm DNA damage, which is associated with poor reproductive outcome and possibly with birth defects, was not increased by PEGIFN/RBV treatment.

Assessment of hepatic involvement in sarcoidosis

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Sarcoidosis is a multisystemic inflammatory granulomatous disease, with rare symptomatic hepatic involvement. Diagnosis of hepatic sarcoidosis is a clinical challenge, because of the wide spectrum of disease presentation and course. The aim of this study is to evaluate the association between severity of liver test abnormalities and histopathological characteristics. In this retrospective analyses patients with confirmed extrahepatic sarcoidosis presenting with liver test abnormalities (alka phosphatase, γ-glutaryl transaminase, alanine aminotransferase and/or aspartate aminotransaminase >1.5 times the upper limit of normal (ULN)) classified according to severity into mild (0 liver tests ≥3x ULN), moderate (1 or 2 liver tests ≥3x ULN) and severe (3 or 4 liver tests ≥3x ULN) were studied. The association between severity of liver tests and histology was examined using non-parametric statistics and multiple regression analysis (p-value<0.05 statistically significant). Liver test abnormalities were found in 208/841 (24.7%) chronic sarcoidosis patients, 123 (14.6%) of which were suspected of having hepatic sarcoidosis (76/123 male, 106 Caucasian, 17 other races). In 24/123 (20%) a liver biopsy was obtained, of which 21 were compatible with hepatic sarcoidosis. Severity of liver test abnormalities was significantly associated with extensiveness of granulomatous inflammation (ρ=0.582, p=0.006) and degree of fibrosis (ρ=0.643, p=0.002). This was not changed after multiple regression analysis for treatment status, gender, genetics, ethnicity and age.
Conclusions: In hepatic sarcoidosis severe and moderate liver test abnormalities are associated with more advanced histopathological disease. Therefore, in the management of sarcoidosis patients with moderate and severe liver test abnormalities a liver biopsy is recommended. Future studies are needed to assess the effect of treatment on disease progression and complications.

Prevalence and risk factors of hepatic steatosis in elderly: results of a population-based study

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Background and aims: The prevalence of NAFLD appears to increase with age through the fourth to sixth decade of life. There is a lack of population-based studies that have assessed the prevalence of NAFLD in elderly. We aimed to 1) determine the prevalence of hepatic steatosis among elderly in a population-based cohort and to 2) generate insight into the correlation of hepatic steatosis with several cardiovascular risk factors, including components of the metabolic syndrome and smoking. Methods: Abdominal ultrasound (US) was performed in 1030 participants (aged 65-95 years) of the population-based Rotterdam Study. Liver brightness was determined using standardized criteria. Participants with any known secondary fatty liver disease (e.g. due to excessive alcohol consumption) were excluded. During detailed interview, data on cigarette, pipe and cigar smoking were collected (current smoking, amount of pack years, daily amount of cigarettes, cigars and pipes (DA)). Laboratory tests and anthropometric measurements were performed to assess components of the metabolic syndrome, defined according to ATP III criteria. Results: Hepatic steatosis was present in 320 of 999 included subjects (32.0%). Metabolic syndrome was present in 33.6% of the population, 12.8%). Mean amount of pack years in the current smokers was 57.13 (range: 17-73). Mean DA in current smoking was 11.8 (range: 2-35). The prevalence of hepatic steatosis in current smokers was 34.4%, compared to 31.7% in non-smokers (overall prevalence of hepatic steatosis: 32%). In logistic regression analysis waist circumference >88cm for women and >102 cm for men (OR 3.6; p<0,001), fasting glucose ≥5.6 mmol/L (OR 2.9; p<0.001), triglycerides ≥1.7 mmol/L (OR 2.0; p=0.001), blood pressure ≥130/85mmHg (OR 1.7; p=0.03) and higher age (OR 0.93 per year; p<0.001) were independent risk factors of steatosis. Subjects meeting more metabolic syndrome criteria were more likely to have steatosis (OR_1 3.8; OR_2 11.0; OR_3 22.9 OR_4 36.6 OR_5 44.7). This correlation weakened with increasing age (p<0.001). There was no significant association between current smoking (p=0.51), amount of pack years (p=0.21), DA (p=0.23) and steatosis.
Conclusion: We observed a significantly lower prevalence of steatosis with increasing age in elderly. Further studies are needed to explore potential factors contributing to this apparent positive selection effect in the elderly. Additionally, current smoking, amount of pack years and DA are no independent risk factors for the prevalence of hepatic steatosis in this study.

Prediction of sustained response to peginterferon alfa-2b for HBeAg-positive chronic hepatitis B using on-treatment HBsAg decline

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One year of peginterferon (PEG-IFN) therapy for HBeAg positive chronic hepatitis B results in an off-treatment sustained response (SR) in a limited number of patients. Reliable prediction of non-response during the first weeks of therapy is therefore essential to optimal utilization of this agent. Serum hepatitis B surface antigen (HBsAg) levels may reflect the sustained immunological effect of PEG-IFN, and consequently be associated with SR. Serum HBsAg (Abbott ARCHITECT) was measured in samples taken at baseline, week 4, 8, 12, 24, 52 and 78 of 221 patients treated with PEG-IFN alfa-2b±lamivudine (LAM) for 52 weeks. HBsAg dec was compared between treatment arms and sustained responders and non-responders. SR was defined as HBeAg loss with HBV DNA<10,000 copies/mL at 26 weeks post-treatment (week 78). The optimal cut-off in HBsAg dec for prediction of non-response was identified using a grid-search of possible cut-off points.43 of 221 (19%) patients achieved a response. One year of PEG-IFN±LAM resulted in a significant dec in serum HBsAg, which was sustained post-treatment (dec 0.9 log IU/mL at week 78, P<0.001). Patients treated with combination therapy experienced a more pronounced on-treatment decline, but relapsed subsequently (declines were 0.98 and 0.86 log IU/mL for combination and monotherapy, P = 0.63). Considering the equal response rates and HBsAg levels at week 78 in the two treatment groups, we analysed the relationship between HBsAg dec and SR in all 221 patients. Responders experienced a more pronounced dec in serum HBsAg compared to non-responders (dec at week 52: 3.3 versus 0.7 log IU/mL, P<0.001). At week 12, a cut-off of any dec in serum HBsAg level from base ($(HBsAg_{on\text{-}treatment})$-$(HBsAg_{baseline})$<0) proved superior for prediction of non-response at week 78. Of the 31% who did not achieve a dec in HBsAg levels through 12 weeks of therapy, only 3% achieved a response at week 78, and none lost HBsAg. Consequently, the negative predictive value of the presence of any dec in HBsAg at week 12 is 97% for prediction of SR at week 78, and 100% for prediction of HBsAg loss. In a representative subset of 149 patients similar results were found for prediction through long-term (mean 3.0 years) follow-up.
Conclusion: PEG-IFN induces a significant dec in serum HBsAg levels in HBeAg-positive patients, predominantly in patients who achieve a sustained response. Patients who experience no dec from base through 12 weeks of therapy have little chance of achieving a SR and no chance of HBsAg loss and should be advised to discontinue therapy with PEG-IFN.

Biliary atresia in The Netherlands: outcome of 232 patients diagnosed between 1987-2008

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Biliary atresia (BA) is a cholestatic disease of infancy in which the bile ducts are obliterated. Treatment consists primarily of surgical correction. When bile flow is not adequately restored, liver transplantation is the second treatment option. BA is the most important indication for liver transplantation in childhood. This study aims to determine the short- and mid-term outcome, and to identify prognostic factors for outcome of BA using a national database. For this purpose, all children born between January 1987 and December 2008 who underwent surgical correction for BA were retrieved from Netherlands Study group on Biliary Atresia Registry (NeSBAR) database. We compared the outcome in terms of clearance of jaundice (bilirubin<20 µmol/l within 6 months post-surgery), transplant-free survival and overall survival of cohort A (1987-1997, 110 patients) and cohort B (1998-2008, 104 patients). Prognostic factors were determined. Clearance of jaundice was 38% (42/110) in cohort A and 33% (34/104) in cohort B (p=0.58). Four-year transplant-free survival was 49% (54/110) in cohort A and 46% (48/104) in cohort B (p=0.21). The 4-year overall survival was 69% (76/110) in cohort A and 79% (82/104) in cohort B (p=0.26). In cohort A, 26% (28/110) underwent OLT before the age of 4, this was 40% (41/104) in cohort B (p<0.01). Transplant-free survival rate of patients with type I/II was 61% (25/41) and of type III 44% (76/171, p<0.05). Transplant-free survival rate was 57% (67/118) in patients operated on ≤ 60 days of age and 36% (34/95) in patients operated on > 60 days (p<0.01). The case-load per center ranged from 0.5-2.23 patients/centre/year. Center size was not correlated to transplant-free survival.
Conclusion: Over the last two decades, liver transplantation has increasingly been used as a treatment for BA. The 4-year survival rates remained similar. Surgical correction before 60 days of age results in a higher transplant-free survival rate. We argue that more efforts should be taken to encourage timely referral, in order to increase transplant-free survival and thereby postpone OLT. The establishment of a national database allows for the evaluation of treatment and prognosis of rare diseases, such as BA.

Suboptimal endogenous erythropoietin response in chronic hepatitis C patients during ribavirin and PEG-interferon treatment

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During treatment of chronic hepatitis C (CHC), anemia may necessitate PEG-interferon and ribavirin dose reductions, with reduced sustained viral response rates. Although erythropoietic growth factors are frequently used to improve anemia, it is controversial whether endogenous erythropoietic response is insufficient under these circumstances. We aimed to evaluate endogenous erythropoietic response during antiviral therapy and to identify risk factors for more pronounced anemia. 145 naive CHC patients on antiviral therapy including PEG-interferon alfa-2b and ribavirin were evaluated for Hb, Ht, serum ribavirin and erythropoietin (EPO) levels. The relation between $\log_{10}$ EPO and Ht was compared to the normal human response to anemia, based on previously described data of normal blood donors and patients with iron deficiency anemias. The regression lines obtained for either study population were compared by their 95% confidence intervals, and a likelihood ratio test was used to test for the significance of the perceived differences. 99% of patients developed anemia (Hb <8.6 mmol/L in males and <7.4 mmol/L in females), with maximal decrease in Hb of 2.5±1.0 mmol/L (range 0.3-5.5). Older age, lower base creatinine clearance, higher base Hb, more pronounced week-2 Hb decrease and higher week-24 serum ribavirin concentrations were independent risk factors for more pronounced anemia. Serum EPO levels increased from a median of 12 IU/L (range 4-63) at base to 41 IU/L (range 12-683) after 12 weeks of therapy and to 43 IU/L (range 7-3238) at week 24 ($p<0.001$). EPO levels at baseline, week 12 and week 24 negatively correlated with Ht ($r=-0.195$, $p=0.02$, $r=-0.531$, $p<0.001$ and $r=-0.312$, $p<0.001$). The regression equations for $\log_{10}$ EPO levels versus Ht in normal subjects and CHC patients clearly excluded each other ($p=1x10^{-11}$). Erythropoietic response to anemia in our study population was significantly different from the normal human response to anemia, i.e. CHC patients had lower erythropoietin levels in case of the same corresponding hematocrit.
Conclusions: Older age, lower base creatinine clearance, higher base Hb, more pronounced week-2 Hb decrease and higher week-24 serum ribavirin concentrations were independent risk factors for more pronounced anemia during antiviral therapy. Our data clearly establish that endogenous erythropoietin production is diminished during antiviral therapy, supporting use of erythropoietic growth factors.

Lower serum ribavirin concentrations are associated with non-response to PEG-interferon and ribavirin therapy in naive chronic hepatitis C patients

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Non-response to current antiviral therapy for chronic hepatitis C (CHC) remains a considerable problem. This might be related to ribavirin pharmacodynamics. We aimed to evaluate relevance of serum ribavirin concentrations for non-response. We analyzed 242 treatment-naive CHC patients who received in a previous trial at least 24 weeks antiviral therapy, including PEG-interferon alfa-2b and ribavirin. 53% were infected with hepatitis C virus (HCV) genotype 1-4, 71% exhibited high viral load and 32% had severe fibrosis/ cirrhosis. Median week-24 serum ribavirin level (HPLC) was 2.7 mg/L (range 0.2-7.4 mg/L). By multivariate analysis, only higher average ribavirin dose during the first 24 weeks of therapy (in mg/kg/day) was identified as an independent predictive factor for higher week-24 serum ribavirin concentrations (coefficient 0.07, 95% CI 0.02-0.13, p=0.01). However, only 3% of variability in serum ribavirin concentrations could be ascribed to differences in ribavirin doses. After 24 weeks treatment, 39 patients (16%) were non-responders (defined as detectable HCV RNA), whereas the remaining 203 patients were responders (HCV RNA undetectable). Week 24 ribavirin concentrations (2.2 vs. 2.8 mg/L, p<0.001), average ribavirin doses (14.5 vs. 15.2 mg/kg/day, p=0.03) and week-24 hemoglobin decreases (1.7 vs. 2.0 mmol/L, p=0.02) were lower in non-responders. In multivariate analysis, lower serum ribavirin concentrations, HCV genotype 1-4 and higher base γ-GT predicted non-response. Non-response rates increased progressively at decreasing ribavirin concentrations: 4%, 11%, 13% and 36% in case of serum ribavirin concentrations ≥4, 3–4, 2–3 and ≤2 mg/L respectively (p=0.001). Non-response was exceptional in HCV genotype 2-3 patients and always associated with ribavirin concentrations <2 mg/L. Analysis for final treatment outcome revealed essentially the same results, with increasing ribavirin concentrations in the order non-response, relapse and SVR patients.
Conclusions: Chance of non-response in treatment-naive chronic hepatitis C patients is in part determined by serum ribavirin concentration. This is especially the case in patients with HCV genotype 1-4, although HCV genotype 2-3 patients with serum ribavirin concentrations levels below a threshold of 2.0 mg/L may experience non-response.

Bedside reagent strip analysis of ascites can reliably rule out spontaneous bacterial peritonitis and is a cost-effective strategy

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Background/aims: Spontaneous bacterial peritonitis (SBP) is a serious complication in patients with decompensated cirrhosis of the liver. Timely diagnosis of SBP is essential to prevent complications like sepsis and hepatorenal syndrome. The golden standard for diagnosis of SBP is an ascitic polymorphonuclear (PMN) count ≥ 250/mm^3, but this test is time-consuming and is not uniformly available, especially during after-office hours. Reagent strip testing of ascites for diagnosing SBP may be a promising bedside diagnostic tool. The aim of this study was to assess the reliability of reagent strip testing for diagnosing or excluding SBP and to assess its clinical implication. Methods: Consecutive samples of ascites obtained from patients with cirrhosis and ascites were included. All samples were tested simultaneously for ascitic PMN-count using standard laboratory methodology as well as reagent strips (Combur-10®, Roche Diagnostics). The reagent strip had 4 outcomes: 0, 25, 100, 500 leukocytes/µl. The strips were independently analyzed visually by a dedicated observer and at the same time by an electronic analyzer (Urisys 1100®, Roche Diagnostics). Results: 157 ascites samples were analyzed. According to the laboratory PMN-count SBP was diagnosed in 12 (7.6%) samples. Automated analysis of these samples indicated the presence of ≥100 leukocytes/µl in all cases. Using this cut-off value resulted in the following diagnostic test characteristics of the reagent strip as obtained from the independent observer: Sensitivity of 75% (95% CI 42.8-93.3), specificity of 98.6% (95% CI 94.6-99.7), positive predictive value of 81.8% (95% CI 47.8-96.8) and a negative predictive value of 97.9% (95% CI 93.6-99.5). Results obtained by the Urisys analyzer show a sensitivity of 100% (95% CI 69.9-100), specificity of 93.1% (95% CI 87.3-96.5), positive predictive value of 54.5% (95% CI 32.6-74.9) and a negative predictive value of 100% (95% CI 96.6-100).
Conclusion: In this population with a relatively low prevalence of SPB a negative reagent strip result reliably ruled out SBP. A positive test should be followed by conventional work-up (PMN-count and culture). Using an automated analyzer was not superior to standard visual reading of the strips. Using reagent strips would have obviated the need for more laborious and expensive laboratory studies in more than 90 cases. This suggests that using this simple and quick bedside test may result in a significant lowering of costs.

Serum HBsAg levels decrease through long-term follow-up in HBeAg-negative patients achieving a sustained response to peginterferon alfa-2a

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In a recently reported international multicenter trial 48 weeks of peginterferon alfa-2a (PEG-IFN) induced a combined response (HBV DNA <10,000 copies/mL + normal ALT) at 24 weeks after treatment discontinuation in 20% of patients with HBeAg-negative chronic hepatitis B. Addition of ribavirin (RBV) did not improve response rates. We aimed to evaluate the long-term response to PEG-IFN in HBeAg-negative patients. All patients enrolled in the original trial who completed the treatment phase were eligible for this long-term follow-up (LTFU) study. Patients received PEG-IFN alfa-2a (180 µg weekly) ± RBV (1000-1200 mg daily) for 48 weeks and had at least one additional LTFU visit after completing the initial follow-up phase of 24 weeks (mean follow-up duration 2.1 ± 0.2 years). Given the similar response rate for PEG-IFN ± RBV, results are presented for both treatment arms combined. Re-treated patients were considered non-responders. Of 117 patients who completed the treatment phase of the initial study, 79 (68%) were included in the LTFU study. Sixty-one (77%) patients were infected with HBV genotype D. Among 19 patients with a combined response (HBV DNA <10,000 copies/mL + normal ALT) at the end of the initial follow-up (week 72), 12 (63%) sustained this response through LTFU. Three additional patients developed a combined response at LTFU, resulting in a combined response in a total of 15 (19%) patients. Among these combined responders, HBV DNA was suppressed below 400 copies/mL in nine (11%) patients and five (6%) were HBsAg negative at LTFU. Levels of HBsAg at LTFU were available in 35 of 38 patients who had not been re-treated. The mean HBsAg dec compared to base in patients who had a combined response progressed from 1.9 to 2.6 log IU/mL between W72 and LTFU (p=0.046). In contrast, the corresponding values in non-responders were 0.3 log IU/mL at both time points (p<0.01 for both comparisons).

Conclusion: About one third of HBeAg-negative patients with a response to PEG-IFN at 24 weeks post treatment relapse during 2 years of follow-up, resulting in an sustained response rate of 19%. Despite the limited overall efficacy of PEG-IFN, a high degree of serum HBsAg dec was observed in sustained responders resulting in HBsAg loss in 6% of patients. These results further emphasize the need for predictors of response to PEG-IFN in HBeAg-negative disease.

Performance of the Bordeaux criteria for liver adenoma classification in a large single centre study in the Netherlands

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Over a number of years the Bordeaux group established a molecular and pathological classification system for hepatocellular adenomas (HCA). They divided HCA in four subgroups by using immunohistochemical markers: HNF-1α inactivated HCA with a lack of expression of liver fatty acid binding protein (LFABP), inflammatory HCA with expression of serum amyloid A (SAA) and C-reactive protein (CRP), β-catenin activated HCA and unclassified HCA without a specific marker. We evaluated the usefulness and clinical relevance of the immunohistochemical markers and evaluated the subtypes in our surgical series. Paraffin fixed liver tissue slides and resection specimens of patients with a firm or possible radiological diagnose of HCA or focal nodular hyperplasia (FNH) were retrieved from the archives of the department of pathology. Immunostainings included LFABP, SAA, CRP, glutamine synthetase (GS) and β-catenin. Macroscopic and microscopic features were noted and clinical data were analysed.From 2000 to 2010, 58 cases (71 lesions) with a firm or possible radiological diagnosis of HCA or FNH were surgically resected. 56 patients (97%) were female with oral contraceptive use documented in 50 women. Mean age at diagnosis was 37 years. 12 lesions showed FNH with a characteristic map-like pattern of GS. Inflammatory HCA with expression of both CRP and SAA was documented in 36 of 59 adenomas (61%) of which 3 were β-catenin and GS positive, 1 was β-catenin positive and 3 were GS positive. We identified 3 β-catenin activated HCA (5%) and 10 LFABP-negative HCA (17%). 10 HCA were unclassifiable (17%). In five patients multiple resected adenomas (range 2-3) were of the same subtype. Two patients showed one unclassified and one inflammatory HCA, and another patient showed two β-catenin positive HCA and one unclassified HCA. Pathological signs of bleeding were seen in 31 of 59 HCA lesions (53%). The frequency of multiple adenomas was almost equivalent in the LFABP- group and the inflammatory group (50% vs 42%) based on radiological imaging.
Conclusion: Immunohistochemical markers can discriminate between different types of HCA. An accurate pathological adenoma classification identifying β-catenin positive adenomas has important implications in the decision for surveillance or any treatment on the basis of preoperative risk for malignant transformation. However due to the low number of positive cells, the identification of nuclear staining for β-catenin can be very difficult.

Transoral incisionless fundoplicationfor treatment of gastroesophageal reflux disease in clinical practice Three year follow-up in 38 chronic GERD patients

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Transoral incisionless fundoplication is a recently introduced endoluminal technique for treatment of gastroesophageal reflux disease. The objective of this study was to determine outcomes of this new technique in chronic GERD patients who were referred for surgical GERD management. Endoluminal fundoplication was offered to patients who met the inclusion criteria for the procedure. Pre and post procedure assessment included GERD-related quality oflife questionnaires, PPI usage, 24-hour pH-metry, upper gastro-intestinalendoscopy and registration of adverse events. The study population consisted of 38 patients (71% male, median 46years and BMI 26.3 kg m^{-2}). Median GERD duration was 6 years (1-25) and patients were treated with daily PPIs for a median of 3 years (1-24). Small (1-2 cm) or medium (3-5 cm) hiatal hernia was present in 95% and esophagitis was diagnosed in 39% of patients at screening endoscopy. The procedure was feasible in all patients and gastroesophageal valves were constructed of 4 cm (4-6) in length and 220° (180-240) in circumference. At a 6 (3-15) months, quality of life scores showed statistically significant improvement ($p<0.0001$) and daily use of antisecretory medication was discontinued by 82%. However, post procedure esophageal acid exposure did not significantly improve ($p>0.05$). Hiatal hernia was reduced in 56% and esophagitis was cured in 47% of patients. There was one serious adverse event consisting of intraluminal bleeding at one fastener site. At 36 (29-41) months follow-up 14 patients (36%) needed revisional laparoscopic fundoplication. Quality of life scores of the remaining cohort showed significant improvement ($p<0.0001$) and daily use of antisecretory medication was discontinued by 74%.

We conclude that endoluminal fundoplication appeared to be relatively safe and was shown effective in improvement of quality of life and reducing the need for PPIs in a subgroup of patients at three years follow-up. The amount of patients requiring revisional surgery was high. Additional studies are necessary to indentify predictors for success, to study technical modifications and to compare the endoluminal procedure to conventional treatment modalities for GERD.

Laparoscopic Nissen Fundoplication after Failed Endoluminal EsophyX Fundoplication

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Reflux control has shown to be ineffective in a substantial number of patients after endoluminal EsophyX fundoplication for gastro-oesophageal reflux disease. Subsequent laparoscopic Nissen fundoplication (LNF) might be required to reach treatment goals. The aim of this study was to evaluate the outcome of LNF after previous EsophyX fundoplication.Consecutive patients who underwent LNF after failed EsophyX were indentified. Herein, EsophyX failure was defined as recurrence or persistence of typical symptoms with anatomical failure of the wrap or persisting pathological oesophageal acid exposure. Preoperative and intraoperative data were prospectively collected. Symptomatic outcome was obtained by standardised questionnaires, and objective outcome by endoscopy, oesophageal manometry and pH monitoring. Eleven patients were included. During LNF, intraoperative gastric perforation occurred in two patients (18.2%) and one patient (9.1%) developed a subphrenic abscess after surgery. Daily heartburn was present in one patient (9.1%) after LNF, and three patients (27.3%) had daily troublesome dysphagia. General quality of life did not increase significantly after surgery. Oesophageal acid exposure was normalised in all patients after surgery. Oesophagitis was absent after LNF in all except one patient (9.1%) who had persisting grade A oesophagitis.
Conclusions: this study has shown that symptomatic and objective reflux control are satisfactory after LNF for failed EsophyX fundoplication. Previous EsophyX, however, is associated with a risk of gastric injury during LNF and a relatively high rate of refractory postfundoplication dysphagia.

Staging laparoscopy for hilar cholangiocarcinoma: is it still worthwhile?

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Radical surgery for hilar cholangiocarcinoma (HCCA) is still the only curative treatment. However, only half of patients who are explored with curative intent are ultimately amenable to a potentially curative resection. In an attempt to avoid unnecessary laparotomies in patients with HCCA, diagnostic laparoscopy (DL) was applied in our department as of 1993. In a previous study we showed that DL should be performed routinely. The accuracy of imaging techniques however, has significantly improved in the past decade, which is likely to impact the yield and accuracy of diagnostic laparoscopy in the work-up of patients with HCCA. The aim of this study was to evaluate the benefit of laparoscopy for staging in patients with suspected HCCA in the last ten years. Between May 2000 and May 2010, 195 patients with suspected HCCA were retrieved from a prospectively collected database. The yield of DL was calculated by dividing total number of avoided laparotomies by the total number of laparoscopies. The accuracy of DL was determined by dividing the number of avoided laparotomies by all patients with unresectable disease. Patients' demographics, preoperative imaging, preoperative Bismuth classification, surgical findings, resectability, complications and length of hospital stay were analyzed. Factors associated with better yield and accuracy were assessed using chi-square-test. Of 195 HCCA patients, 175 patients underwent DL. The yield of DL was 14% and the accuracy 31%. Operative morbidity of DL was 3%, and included only minor complications. Operative morbidity of laparotomy for unresectable disease was 33%, and included major complications (death, and reoperation) in 2 patients (3%). No significant factors associated with better yield of DL were found. Nonetheless, presence of an attending surgeon during DL, DL performed in the first years after 2000 (until 2003), and preoperative imaging using PET-CT seemed to have a beneficial effect on the yield.
Conclusions: Overall yield and accuracy of DL for HCCA were 14% and 31%, respectively. In contrast to the previous period, the results of the present study hardly justify routine use of DL in patients with HCCA. This finding is likely to be the result of improved imagingin the past decade. DL should therefore be reserved for selected HCCA patients with increased risk of unresectability.

Randomized controlled trial analyzing the effect of 15 or 30 minutes intermittent Pringle manoeuvre on hepatocellular damage during liver surgery

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Aminotransferases are commonly used to assess the optimal duration of ischemic intervals during intermittent Pringle manoeuvre (IPM). However, they might not be responsive enough to detect small differences in hepatocellular damage. Liver fatty acid-binding protein (L-FABP) is a more sensitive marker. This randomized controlled trial aimed to compare hepatocellular injury reflected by L-FABP in patients undergoing liver resection with IPM using either 15 or 30 minutes ischemic intervals.Twenty patients requiring IPM during liver surgery were randomly assigned to 15 (15IPM) or 30 (30IPM) minutes ischemic intervals. Ten patients without the need for IPM (noIPM) served as controls. Blood samples from the radial artery, portal and hepatic vein were collected according to a fixed protocol. Net fluxes over the gut, liver and splanchnic area were calculated to determine the source of systemic L-FABP levels. Primary endpoint was hepatocellular injury during and after liver surgery reflected by L-FABP. Between and within group comparisons were performed using area under the curve (AUC) and repeated measures two-way ANOVA. L-FABP fluxes were tested using a one-sample t-test with a theoretical mean of zero.The 15IPM and 30IPM group had similar characteristics. Aminotransferases did not significantly differ between the 15IPM and 30IPM group at any time point. L-FABP levels rose up to 1853 ± 708 ng/mL in the 15IPM and 3662 ± 1355 ng/mL in the 30IPM group after finishing liver transection and decreased rapidly thereafter. There were no significant differences between the 15IPM and 30IPM group in cumulative L-FABP level (p=0.378) or L-FABP level at any time point (p=0.149). L-FABP fluxes over the gut were 7441 ± 4119 ng/kg bw/min after 15IPM and -128.1 ± 790 ng/kg bw/min after 30IPM, which was not significantly different from zero (p=0.104 and p=0.875, respectively). NoIPM resulted in significantly lower cumulative L-FABP and ALAT levels (p=0.019 and p=0.049). Blood loss, remnant liver function and morbidity were comparable.
To conclude, this study provides novel data showing that 30IPM induced similar hepatocellular injury reflected by the sensitive damage marker L-FABP compared with 15IPM, without induction of intestinal damage or difference in remnant liver function. The present study confirms the results of earlier trials, suggesting that IPM with 30 minutes ischemic intervals may be used if pedicle clamping during liver surgery is required.

Preoperative infliximab therapy and postoperative complications after proctocolectomy with ileum pouch anal anastomosis

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Aim was to compare complication rates after proctocolectomy with ileum pouch anal anastomosis (IPAA) in refractory ulcerative colitis patients with vs. without preoperative infliximab therapy. Retrospectively, all pouch procedures from 2006 until 2009 were assessed. Included were ulcerative colitis patients and therapy refractoriness; excluded were patients with other diagnoses or other surgical indications. Postoperative complications and infliximab use were assessed.Seventy-two patients were included; 33 underwent a 1-stage procedure (proctocolectomy with IPAA) and 39 had a 2-stage procedure (emergency colectomy and later completion proctectomy with IPAA). In the 1-stage procedure, patient characteristics were comparable. Of those, 21 patients had preoperative infliximab therapy. Total and infectious complications were not different. However more infliximab-treated patients had anastomotic leakage (4/21 vs. 0/12; risk difference (RD) 19%; 95% CI: 2 to 36) and non-infectious complications (8/21 vs. 1/12; RD 30%; 95% CI: 4 to 56). Although several patient characteristics in the 2-stage groups were not comparable, complication rates were similar in these 17 infliximab and 22 non-infliximab patients (total number of patients with complications: 8/17 vs. 8/22; RD 11%; 95% CI: -20 to 42; infectious complications: 6/17 vs. 5/22; RD 12%; 95% CI: -16 to 41; non-infectious complications 6/17 vs. 3/22; RD 21%; 95% CI -5 to 49).
Conclusion: The data in this small study support a 2-stage procedure in patients who have been on infliximab therapy

Viable tumor tissue adherent to needle applicators after local ablation: a risk factor for local tumor progression

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Background: Local tumor progression (LTP) is a serious complication after local ablation of malignant liver tumors, negatively influencing patient survival. LTP may be the result of incomplete ablation of the treated tumor. In this study we determined whether viable tumor cells attached to the needle applicator after ablation was associated with LTP and disease-free survival. Methods: In this prospective study, tissue was collected of 96 consecutive patients undergoing local liver ablations for 130 liver malignancies. Cells and tissue attached to the needle applicators were analyzed after ablation for viability using glucose-6- phosphate-dehydrogenase (G6PD) staining and autofluorescence intensity levels of H&E stained sections. Patients were followed-up until disease progression. Results: Viable tumor cells were found on the needle applicators after local ablation in 26,7% of patients. The type of needle applicator used, an open approach and the omission of track ablation were significantly correlated with viable tumor tissue found adherent to the needle applicator. The presence of viable cells was an independent predictor of LTP as determined with uni- and multivariable analysis. Mean time to local disease progression was 9 months. The attachment of viable cells to the needle applicators was associated with a shorter time to LTP, but not with disease-free or overall survival.
Conclusion: Viable tumor cells adherent to the needle applicators were found in as many as 26.7% of patients after local ablation. Adherence of viable tumor cells to the needle applicator after local ablation was an independent risk factor for LTP.

The C-seal; a biofragmentable drain protecting the stapled colorectal anastomosis from leakage

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Colorectal anastomotic leakage (AL) is a serious complication in colorectal surgery associated with high morbidity and mortality rates. The incidence of AL varies between 2.5 and 20%. Over the years, many strategies aimed at lowering the incidence of anastomotic leakage have been examined. Currently a new device is developed in our institute aimed at protecting the colorectal anastomosis and lowering the incidence of AL. This so called C-seal is a biofragmentable drain, which is stapled to the anastomosis with the circular stapler. It covers the luminal side of the colorectal anastomosis thereby preventing leakage. It is a tubular device composed of biodegradable polyurethane. Two flaps with adhesive tape at the open end of the tube are used to attach the C-seal to the anvil of the circular stapler. In this way the C-seal can be pulled through the anus after the anastomosis is made. The C-seal remains in situ for at least 10 days. Thereafter it will lose strength and will degrade to be secreted from the body together with the gastrointestinal natural contents. The C-seal can be used in both open procedures as well as laparoscopic procedures. Any type or anastomosis can be performed when using the C-seal (end-to-end, side-to-end etc). The C-seal is only applied in stapled anastomoses within 15cm from the anal verge. The C-seal does not prevent the formation of anastomotic dehiscences. However, it prevents extravasation of faeces into the peritoneal cavity. This means that a gap at or below the anastomotic site does not necessarily lead to leakage. In 2007, a pilot study is performed testing the feasibility of the C-seal in 15 patients undergoing colorectal surgery. The C-seal was well compatible with the stapler and none of the patients developed clinical or radiological anastomotic leakage. Currently, a phase II study testing the C-seal in 35 patients undergoing (colo-) rectal resection with stapled anastomosis is recruiting. At this moment, 17 patients are enrolled in this phase II study. Of these 32 patients treated with a C-seal, only 1 patient developed clinical anastomotic leakage leading to re-intervention. Our future goal is to test the C-seal in a randomised setting to precisely determine the incidence of anastomotic leakage when using the C-seal. At this moment, the C-seal seems a promising technique to lower the incidence of anastomotic leakage in colorectal anastomoses.

C-reactive protein concentration is associated with prognosis in patients suffering from peritoneal carcinomatosis of colorectal origin

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Background: Only a limited number of patients with peritoneal carcinomatosis (PC) of colorectal origin benefit from palliative chemotherapy. Identification of prognostic factors may aid in patient selection. The plasma concentration of C-reactive protein is increasingly recognized as prognostic factor in a variety of malignancies. However, its value in PC of colorectal origin is currently unknown. Aim of the present study was to investigate the association of plasma CRP concentrations with survival in patients suffering from PC of colorectal origin who receive palliative chemotherapy. Methods: Fifty patients with colorectal PC were identified from our regional Cancer Registration. Relevant data were retrieved from their clinical records. The most discriminatory CRP concentration was identified and patients were stratified accordingly, resulting in a group with low and a group with high CRP concentrations. Further comparisons were made between these groups. Results: A CRP concentration < 35 mg/L was associated with a better prognosis (median survival 22.4 months) than a CRP concentration ≥ 35 mg/L (7.9 months) (p=0.0002).CRP concentrations were inversely related to albumin concentrations which could predict survival at a cut-off value of 35 g/L (median survival 7.2 vs 12.9 months, p=0.01). High CRP concentrations were related to a decreased resectability rate of the primary tumor.
Conclusion: Elevated CRP plasma concentrations are associated with decreased survival in patients with colorectal PC. This reflects the importance of inflammation in cancer survival. Further research is warranted to assess the clinical applicability of the current findings.

Can we identify high risk stage II colonic cancer patients?

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Usually, patients with curatively resected colonic cancer without nodal tumour involvement do not receive adjuvant chemotherapy in the Netherlands. However, a subgroup of stage I-II colonic cancer patients are currently considered at high-risk for recurrent disease and/or metastases based on 1) tumor obstruction or perforation at presentation 2) less than 10 lymph nodes detected in the surgical specimen 3) T4 lesions and 4) lymphangio-invasion at pathological examination. These patients, especially those having stage II disease, are regarded as comparable to stage III colon cancer and should therefore receive adjuvant chemotherapy. The proposed the following questions 1) is it possible to identify these and/or additional high-risk factors in these stage II colonic cancer patients? 2) does the number of high risk factors relate to outcome? and 3) do we adhere to our national high risk N0 colon cancer patient guidelines? We retrospectively analysed 236 stage II colonic cancer patients for high-risk factors undergoing surgery between January 2002 and December 2008. Univariate and multivariate analyses for high-risk factors were performed using the Cox regression analysis. Significance was reached if $p < 0.05$. Mean follow up was 39 months (95% CI 36-42 months). Three-year disease free survival (DFS) of the entire group was 90%. The following 9 significant factors for recurrent/metastatic disease were identified in the univariate analysis: age, length of hospital stay, emergency surgery, obstruction, perforation of the tumour, lymphangio -invasion, number of known high risk factors, length of surgical specimen and chemo-therapy. Multivariate analysis identified 4 independent risk factors for recurrent/ metastatic disease: age (p=0.001, hazard ratio(HR) 1.069), obstruction (p=0.003, HR 3.226), perforation of the tumour (p=0.003, HR 4.524) and lymphangio-invasion (p=0.048, HR 3.232).
The often in national guidelines mentioned criterium of less than 10 lymph nodes detected in the surgical specimen, did not reach significance in our multivariate analysis. The three-year DFS-rates for the low risk group, the high risk group with 1 high-risk factor and the high risk group with ≥ 2 high-risk criteria are 90.0%, 91.7% and 47.3% respectively. Patients meeting >2 high risk criteria had a significantly worse disease free disease survival ($p < 0.001$). Of the entire stage II high risk group only 23/179 (12.8%) received adjuvant chemotherapy.
Conclusions: The number of high risk factors was related to outcome and four independent high risk factors were identified, however, not all the recurrences were explained by these known high risk factors. Possibly, other unknown high- risk factors, for example isolated tumour cells or micrometastasis, can influence outcome in stage II colon cancer patients. Further research, therefore, is warranted. Despite easy, tangible criteria for high-risk stage I and II colonic cancer patients in the Netherlands, just a minority of the selected high-risk patients did receive adjuvant chemotherapy. Therefore, adherence to national guidelines is less than expected and more attention should be given to the treatment schedule and definition of high-risk N0 patients.

Evaluation of the IRIS scoring system in predicting in hospital mortality and morbidity after colorectal surgery

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Purpose: Operative mortality is an objective measure of outcome that is often used to evaluate the outcome of colorectal surgery. In order to make a meaningful comparison between institutions, the influence of comorbidity and operative severity should be assessed. The Identification of Risk in Surgical patients (IRIS) score was designed to stratify surgical patients into outcome related groups. The system uses a six point scale addressing: age, acute admission, acute operation and severity of surgery. The objective of this study was to evaluate the predictive value of the IRIS score in patients undergoing colorectal surgery. Methods: All patients that underwent colorectal surgery in our hospital between 1990 to 2005 were included in the study. Identification of Risk In Surgical patients (IRIS) scores were calculated for all patients. The discriminating capacity of the scoring system was estimated based on the area under the receiver-operator characteristic curve (AUC ROC). Values above 0.8 were considered to represent good discriminating capacity.
Results: All of the individual IRIS parameters proved to be statistically significant predictors of mortality, morbidity and length of stay (LOS) in univariate analysis ($p<0.05$). The AUCs for IRIS predicted mortality and morbidity in patients undergoing colorectal surgery were respectively 0.88 and 0.79. The AUC for IRIS predicted mortality and morbidity were respectively 0.80 and 0.61 after colorectal resection.
Conclusions: This study has shown that the IRIS score is a good predictor of mortality and morbidity in patients undergoing colorectal surgery. In patients undergoing colorectal resection the predictive capacity of the IRIS score is good with regard to mortality and mediocre with regard to morbidity. The IRIS score consists of four readily available parameters that leave no room for open interpretation. These qualities make the IRIS score a practical and objective tool for surgical audit.

Acute toxicity and surgical complications of preoperative chemoradiotherapy with capecitabine for locally advanced rectal cancer - in need of uniform definitions

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Background: Preoperative chemoradiotherapy (CRT) has become standard of care in locally advanced rectal cancer to facilitate downsizing and subsequent complete resection of the tumour. Capecitabine, an oral 5-fluorouracil analogue, is an attractive radio-sensitizer. We evaluated acute toxicity and surgical complications in patients undergoing total mesorectal excision (TME) after preoperative (CRT) with capecitabine. Methods: Between 2004-2008, all consecutive patients with cT3-4 (T3 with a threatened circum-ferential resection margin or <5cm from the anal verge) or cN2 rectal cancer were treated with preoperative CRT (25x2 Gy, capecitabine 825 mg/m^2 bid, days 1-33) in our institute. TME followed 6 weeks later. Toxicity was scored according to the Common Terminology Criteria (v3.0) and Radiation Therapy Oncology Group scoring systems. Treatment-related surgical complications were scored according to strict definitions and evaluated up to 30 days after hospital discharge. Severity of complications was scored using the modified Clavien-Dindo classification. Results: 147 patients were analysed. The mean cumulative dose of capecitabine was 95% of prescribed, while 97% of patients received ≥ 45 Gy of radiotherapy. One patient died (grade 5) due to sepsis following haematological toxicity. Grade 3 toxicity developed in 32 patients (22%), especially diarrhoea (10%) and radiation dermatitis (12%). In 131 of the 138 patients who underwent a laparotomy, resection was possible. No 30-day postoperative deaths occurred. Anastomotic leakage developed in 13/47 (28%) low-anterior resections and perineal wound complications occurred in 23/62 (37%) abdominoperineal resections. Major (Clavien-Dindo grade ≥ 3) complications developed in 36 (26%) patients, including predominantly anastomotic leakage, perineal and abdominal wound complications and fistula. Surgical reintervention was required in 30 patients. Twenty-seven (20%) patients were re-admitted within 30 days after initial hospital discharge.
Conclusion: Preoperative CRT with capecitabine is associated with acceptable acute toxicity, significant surgical morbidity, but minimal postoperative mortality. The lack of uniform definitions for major surgical complications makes a comparison with other studies difficult.

Costs, short- and long-term results of open versus laparoscopic appendectomy

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Clinical advantages of laparoscopic appendectomy have been shown in numerous trials and reviews. Most of these advantages are small and of limited clinical relevance, while laparoscopic operation costs are reportedly higher. This study compares short- and long-term results and in-hospital costs of conventional appendectomy (OA), diagnostic laparoscopy followed by conventional appendectomy (DL+OA), laparoscopic appendectomy (LA) and mid laparotomy (MA).All adult patients who underwent appendectomy in our institution from 1995 to 2005 were included. Patient data were retrieved from medical records, general practitioners and questionnaires sent by mail. Primary outcome parameters were long-term readmissions and reinterventions. Secondary outcome parameters were short-term readmissions and reinterventions and the in-hospital costs. The LA group had a shorter initial hospital stay than the OA and DL+OA group, despite a higher incidence of abdominal abscesses and associated diagnostic investi-gations, interventions and readmissions. The DL+OA group showed a higher number of abdominal abscesses than the OA group as well. Concerning the long-term complications, the MA group had a higher mortality and readmission rate and developed more incisional hernias. The LA group had significantly higher in-hospital expenses than OA in the five most recent years. This retrospective study showed that the potential advantages of laparoscopic appendectomy are almost completely counterbalanced by a higher incidence of intra-abdominal abscesses. Since laparoscopic appendectomy is about to become the standard of care, future research must be directed to solve this issue.
We found no evidence that the laparoscopic approach for appendectomy leads to lower costs for the patient with an acute appendicitis.

A retrograde-viewing auxiliary imaging device improves detection rates for adenomas and other polyps during colonoscopy

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Colonoscopy is the best method for detecting and removing colorectal polyps. Tandem studies show adenoma miss rates of 21-24%. Little information is available on colonoscopic miss rates in older patients, who can be more difficult to examine. The Third Eye® Retroscope® (TER) provides an additional, retrograde view, which may detect polyps behind folds. This study evaluated the extent to which the TER improves polyp and adenoma detection rates during colonoscopy. This prospective, multi-center, randomized, controlled trial was undertaken in 4 European and 5 U.S. centers. In total, 448 eligible subjects were enrolled, of whom 372 completed same-day, tandem examinations using a standard colonoscope with and without the TER. Subjects were randomized to standard colonoscopy followed by TER (Group A) or TER followed by standard colonoscopy (Group B). Primary outcome measures were detection rates for all polyps and adenomas (adenoma detection rates (ADR)) during standard colonoscopy vs. colonoscopy with TER. Secondary outcome measures were withdrawal time, total procedure time and polyp size and histology. Additionally we performed sub-analysis in which we divided subjects into two age groups, age <65 and age ≥65. In the 173 subjects with standard colonoscopy first (Group A), 107 adenomas were detected, including 21 advanced adenomas. Second procedures with TER yielded 49 additional adenomas, an additional ADR of 45.8%, including 3 advanced adenomas, 2 of which were >10 mm and located in the ascending colon. In the 176 subjects with TER first (Group B), 115 adenomas were detected, with 27 advanced adenomas including 3 adenocarcinomas. Second procedures with standard colonoscopy yielded 26 adenomas, an additional ADR of 22.6%, including 1 advanced adenoma (a 3 mm tubular adenoma with high-grade dysplasia located in the rectum). Net additional detection rates with TER were 29.8% for all polyps and 23.2% for adenomas. Relative risk of missing lesions with standard colonoscopy vs. TER was 2.56 for all polyps.

Can surveillance intervals be increased after a negative faecal immunochemical test in asymptomatic high risk patients?

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Background: The goal of surveillance programs after polypectomy or after resection of colorectal cancer (CRC) is to detect advanced adenomas before malignant transformation. Given the increasing burden on colonoscopy capacity, the use of faecal immunochemical tests (FITs) to postpone elective colonoscopy in asymptomatic high risk patients, has been suggested. Aim: The aim of this study is to evaluate the miss rate of CRC and advanced adenomas by using a FIT to select for potential adjustment of surveillance colonoscopy in high risk individuals. Methods: Between June 2006 and October 2009, all subjects (≥ 18 years) scheduled for colonoscopy were asked to perform a FIT (OC sensor®) before colonoscopy and bowel preparation in five participating centres. Asymptomatic high risk patients referred for surveillance / screening colonoscopy because of a personal history of adenomas or CRC, or a family history of CRC, were selected. Colonoscopy and histology were considered as gold standard for the detection of colonic neoplasia. Sensitivity, specificity, positive and negative predictive values (PPV and NPV) of FIT for the detection of CRC and advanced adenomas, and the number of missed lesions were determined (cut-off value 50ng/ml). Results: In total, 943 patients (mean age 60.5 years; range 27-87; 50.1% females) were included, of which 469 (49.7%) with a personal history of adenomas, 153 (16.2%) with a personal history of CRC and 321 (34.0%) with a family history of CRC. In all patients, 3 (0.3%) CRCs and 91 (9.7%) advanced adenomas were detected by colonoscopy. The FIT resulted in a sensitivity, specificity, PPV and NPV for CRC of 100%, 89%, 3% and 100%, respectively (cut-off value 50ng/ml). Sensitivity, specificity, PPV and NPV of FIT for advanced adenomas were 28%, 91%, 24% and 92%, respectively. No cancers (0/3) were missed in patients with a negative FIT result. However, FIT was false negative in 66/91 (72%) of advanced adenomas. No significant differences in test characteristics were found between the three indication groups.
Conclusion: In the present study of patients at high risk for colorectal neoplasia, 72% of all advanced adenomas were not detected by one-time FIT sampling. Therefore, one-time FIT sampling before elective colonoscopy is unsafe as a tool for deciding to increase surveillance intervals in asymptomatic high risk patients.

Developing competence in ERCP

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Introduction: Measures for ERCP competence are ill defined. Currently, Dutch guidelines state that competence is reached when a minimum of 100 ERCP procedures are performed. This arbitrary number is lacking any scientific support and needs to be reconsidered. Furthermore, there is a general awareness that procedural competence certification should be based on objective performance criteria, rather than threshold numbers. To date few attempts have been made to describe a learning curve for achieving competence in ERCP. Continuous self-assessment using the Rotterdam Assessment Form for ERCP (RAF-E) can be useful to describe procedural skill development. The aim of this study is to express competence development as a learning curve. Methods: From January 2008 - May 2010 all trainees in our center entered the ERCP self-assessment program. All procedures were appraised using RAF-E. The indication for each ERCP was classified and complexity was graded on a 3-point scale. The primary parameter was CBD cannulation success rate, expressed as a 'simple moving average' per 30 procedures. Adherence to filling out the assessment forms was calculated by comparison to the ERCP reports database (Endobase®, Olympus, Hamburg). Results: A total of 703 ERCPs were assessed by 9 novice trainees. Base cannulation rate averaged 37.5%. After a 100 ERCPs CBD cannulation rate improved to 74%. Individual performance plotted against the group learning curve in our center reveals the performance percentile. Adherence to filling out the assessment forms varied from 48 to 100% initially but improved to a median of 87% after stimulating feedback.
Conclusion: ERCP competence should be based on objective performance criteria, rather than threshold numbers. Learning curves are a valuable means of assessing competence. The Rotterdam Assessment Form (RAF-E) is a rapid and easy tool to monitor individual as well as group performance.

Therapeutic delay and survival after surgery for cancer of the pancreatic head with or without preoperative biliary drainage

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Patients with obstructive jaundice due to cancer of the pancreatic head often undergo preoperative biliary drainage (PBD). Recently we have shown that a strategy with PBD leads to significantly more overall treatment complications than an 'early surgery' strategy. PBD may still be clinically relevant, for example in patients with severe jaundice or cholangitis, or because of logistic reasons. The associated delay in surgery could lead to more advanced cancer stages at exploration and thus might affect the resection rate, and eventually reduce survival. The aim of the present study was to evaluate the relation between delay in surgery due to PBD and survival in patients scheduled for surgery for pancreatic head cancer. We conducted a multicenter, randomized controlled clinical trial to compare PBD with early surgery (ES) for pancreatic head cancer for complications. We obtained Kaplan-Meier estimates of overall survival for patients with pathology-proven malignancy, and compared survival functions of ES and PBD groups using log-rank test statistics. Uni- and multivariable Cox regression analyses were performed to evaluate the prognostic role of time to surgery for overall survival. Mean times from randomization to surgery were 1.2 (0.9 to 1.5) and 5.1 (4.8 to 5.5) weeks in the ES and PBD groups, respectively ($P < 0.001$). In the ES group 60 of 89 operated patients (67%) underwent resection, versus 53 of 91 operated patients (58%) in the PBD group ($P = 0.20$). Median survival after randomization was 12.2 (9.1 to 15.4) months in the ES group versus 12.7 (8.9 to 16.6) months in the PBD group ($P = 0.91$). A longer time to surgery was significantly associated with slightly lower mortality rate after surgery (Hazard ratio 0.90, 95% CI: 0.83 to 0.97), when taking into account resection, bilirubin, complications, pancreatic adenocarcinoma, tumor positive lymph nodes and microscopically residual disease.
Conclusions: In patients with pancreatic head cancer the delay in surgery associated with PBD does not impair or benefit survival rate. If PBD is warranted, it can be performed without compromising survival. Considering the risk of procedural complications, early surgery remains the treatment of choice.

Does erytromycin increase the completion rate of small bowel capsule endoscopy?

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Capsule endoscopy has become a standard technique to investigate the small bowel. An important limitation of small bowel capsule endoscopy is that in around 20% of the procedures, visualization of the small bowel is incomplete because the capsule does not reach the cecum within recording time. A long gastric transit time has previously been recognized as a risk factor for incomplete capsule endoscopy (Westerhof, GI Endoscopy 2009), so there is a rationale to use prokinetic agents to increase the rate of complete small bowel examinations. Previous studies on this subject are inconclusive, mainly because of small sample size. The aim of this single-centre study was to examine if the prokinetic agent erytromycin increases capsule endoscopy completion rates within the 8-hour battery time as compared to domperidon. From July 2008 to May 2010, patients undergoing small bowel capsule endoscopy with the Given Imaging system received 250 mg of erythromycin 1 hour before the procedure. The control group consisted of patients undergoing capsule endoscopy with the Given Imaging system between March 2005 and July 2008 who recieved 10 mg of domperidone directly before the procedure. Outcome measurements were procedure completion rate, gastric transit time and small bowel transit time. Power calculation prior to the study required a minimum of 199 procedures in each group. In total, 695 procedures were studied. The erythromycin group consisted of 247 patients and results were compared with 448 patients receiving domperidone. The overall completion rate was 86 % in the erythromycin group versus 79 % in the domperidone group ($p = 0.04$). The difference remained significant ($p = 0.028$) after excluding hospitalized patients and patients with previous abdominal surgery (known risk factors for incomplete investigations). Gastric transit time was lower in the erytromycin group compared to domperidone (median 13 minutes versus 22 minutes, $p < 0.0001$). Small bowel transit times were similar in both groups (mean 259 minutes versus 272 minutes, $p = 0.31$).
In conclusion, erytromycin increases completion rates of small bowel capsule endoscopy by reducing gastric transit time without affecting small bowel transit time. Our study, the largest to date, supports the use of erythromycin 1 hour before small bowel capsule endoscopy.

Prevalence of benign disease and autoimmune pancreatico cholangitis in Whipple resections for presumed malignancy of the pancreatic head: are we doing better?

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Background: Five to 11% of patients undergoing resection for presumed malignancy of the pancreatic head is diagnosed with benign disease. One third of them is diagnosed with autoimmune pancreaticocholangitis (APC), a rare disease highly responsive to steroids. Increasing awareness of APC in the past decade is presumed to avoid unnecessary surgery in these patients. The aims were to determine the prevalence of benign disease and APC in patients who underwent pancreatico-duodenectomy for presumed malignancy, to investigate whether these prevalences declined over time, and investigate if and how surgery could have been avoided. Methods: All patients undergoing Whipple operation between 2000 and 2009 in a tertiary referral centre with multidisciplinary approach to pancreatic disease, were retrospectively analyzed. Demografic characteristics were evaluated in all patients. In negative Whipples clinical, radiological and laboratory findings were evaluated. Based on these data, the preoperative index of suspicion of malignancy was scored as non specific, suggestive or high. Current diagnostic criteria systems were applied in APC patients. Results: 274 Whipple operations were performed for presumed malignancy. Prevalence of benign disease was 8.4%. No mortality was reported in this group. Patients were significantly younger than patients with malignancy (mean 58.6 ±10 vs 63.7 ±13, p = 0.004). Prevalence of APC in benign Whipples was 30.4%. In APC patients the frequency of diabetes was significantly higher than in non APC (71% vs 19%, p=0.03).The prevalence of negative Whipples significantly declined over time (12.0% before 2005 vs 4.0% after 2005, p = 0.03), but proportion APC remained stable (27.8% vs 40%, p=0.62). In total, four patients (1.5%) had unnecessary surgery. Based on pre-operative index of suspicion of malignancy surgery could have been avoided in 3 nonAPC patients. All APC patients had sufficient index of suspicion to justify the surgery. In one patient however, surgery could have been avoided with steroid therapy. In four other APC patients, a positive pancreatogram and/or IgG4 would have justified steroid trial and might have influenced the decision to operate. In two others, surgery was inevitable.
Conclusions: Prevalence of benign disease in patients who underwent Whipple operation for presumed malignancy is 8.4%. One third of them are diagnosed with APC. In eight years, the prevalence of negative Whipples declined significantly. The proportion APC however remained stable, at least partially due to insufficient preoperative work up. Despite increasing awareness and knowledge of this rare disease, it remains difficult to make the diagnosis.

Serum intestinal fatty acid binding protein (I-FABP) levels accurately predict villous atrophy and mucosal healing in adult celiac disease

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Non-invasive tools for evaluating villous atrophy are needed to improve the diagnosis and follow-up of celiac disease (CD). Intestinal fatty acid binding protein (I-FABP), a small cytosolic enterocyte protein, is a sensitive marker for enterocyte damage in the small intestine. Recently we found that elevated I-FABP levels accurately predict villous atrophy in children with positive CD screening. In addition, I-FABP recovers rapidly in response to gluten free diet (GFD) in children. In adult CD patients, in whom villous atrophy at presen-tation is generally less pronounced, the accuracy of I-FABP needs to be esta-blished. This study aimed to evaluate the usefulness of I-FABP in diagnosing CD in adults with positive CD screening and for monitoring mucosal healing after GFD. I-FABP levels were analysed retrospectively in serum derived at the time of the initial biopsy of 35 adults (median age 42 years, range 21-76 years) with increased levels of tissue transglutaminase (IgA-tTG) and/or endomysium antibodies (IgA-EMA) and biopsy proven CD. In addition, I-FABP levels were measured in 15 patients on GFD (mean duration of GFD 27 months, range 3-59 months) at the time of follow-up biopsy. The control group consisted of 30 healthy adults. Initial serum I-FABP levels in adult CD patients (median 598 pg/ml, range 35-1913 pg/ml) were significantly elevated compared to healthy controls (median 212 pg/ml, range 68-543 pg/ml, $P < 0.001$). At the time of initial biopsy, in 26/35 patients (74%) I-FABP levels were above the calculated cut-off point. In the control group only one of 30 adults had an I-FABP level above the cut-off point. Initial I-FABP levels correlated with IgA-tTG levels ($R=0.406$, $n=24$, $P=0.049$). I-FABP levels were significantly lower during GFD (median 277 pg/ml, range 48-515 pg/ml) compared to the untreated CD patients ($P=0.004$). At this time, all patients showed normal antibody levels and Marsh stage 0 or 1. Conclusions: I-FABP levels accurately predict villous atrophy (positive predictive value 96.3%) in adults with a positive CD screening and therefore I-FABP might be a useful additional marker in diagnosing celiac disease in adults. Moreover, the results suggest that serum I-FABP levels are useful for monitoring mucosal healing after GFD. Further studies are required to evaluate whether increased I-FABP levels in patients with positive disease specific antibody tests justify a diagnosis of celiac disease without intestinal biopsy.

Acute pancreatitis and concomitant use of pancreatitis-associated drugs

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Background: Drug-induced pancreatitis (DIP) is considered as a relatively rare entity. We evaluated the prevalence of pancreatitis-associated drugs at admission according to a recent evidence-based DIP classification system in a Dutch cohort of acute pancreatitis (AP) patients (EARL study). Methods: Multi-center observational study. Etiology, disease course, usage of pancreatitis- associated drugs were evaluated. Results: First documented hospital admissions of 168 patients were analyzed. Seventy out of 168 (41.6%) patients used pancreatitis-associated drugs at admission. In 26.2% (95% CI: 20.1-33.3%) the pan-creatitis-associated drug was at least one class I drug and in 4.8% (95% CI: 2.4-9.1%) these were not stopped in the absence of other risk factors. In 7.1% (95% CI: 4.1-12.1%) there were no other risk factors besides the drugs. DIP was diagnosed in 5.4% (95% CI: 2.8-9.9%). In all patients with DIP the pancreatitis-associated drugs were stopped and no recurrence of AP developed until the end of the study period. The disease course was always mild.
Conclusion: A surprisingly high percentage of patients used drugs reported to be associated with DIP when admitted because of an attack of AP. One in 20 patients was still using a pancreatitis-associated class I drug that should have been stopped during admission. Physician should be more aware of the prevalence of DIP.

The Prevalence of Coeliac Disease in Infertile Couples in The Netherlands is at the Level of the General Population

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Objectives: Infertility is described as a long-term complication of untreated coeliac disease (CD) in both females and males, but the available evidence is inconsistent, mainly due to methodological issues. We studied the prevalence of (un)diagnosed CD in a large cohort of male-female couples visiting a fertility clinic in the Netherlands. Methods: Subjects were consecutive male-female couples that visited the fertility clinic of the Leiden University Medical Centre, the Netherlands, between 2003-2009. From all patients, serum was routinely collected and stored as part of the standard work-up. Serological screening for CD was performed by assessment of IgA anti-Tissue- Transglutaminase antibodies (tTGA; cut off for positivity ≥10 U/mL; ELIA™ Celikey® assay, Immunocap® 250 system, Phadia, Freiburg, Germany). Positive samples were re-tested for IgA Endomysium antibodies (EmA). CD was diagnosed if both tests were positive. We collected the following data: gender, age, height, weight, and diagnosis of infertility (ovulation disorder, tubal pathology, endometrial problems, male infertility, unexplained infertility, and other). All patients were anonymized. For adequate power (90% CI, sample proportion ±1.0% with estimated proportion 4%), a minimum of 632 infertile male-female couples should be studied. Results: We studied 1045 infertile male-female couples (2090 individuals; mean age 34 years, SD±5.5, range 20-63 years; mean BMI 25 kg/m^2, SD±4.6). Ten patients were diagnosed with unrecognized CD, 6 females and 4 males (mean age 32 years (SD±5.6, range 25-39 years; mean BMI 25 kg/m^2, SD±2.4). Eight of the CD patients were infertile (0.4%): anovulation disorder (3), unexplained (4) and male infertility (asthenospermia; 1). The 2 fertile CD patients had a partner with an infertility problem (anovulation disorder (1) and male infertility (1)). There were no couples where both partners had CD.
Conclusion: This is the first adequately powered study on the prevalence of CD in infertile male-female couples. In our cohort the prevalence of CD was comparable to the prevalence of unrecognized CD in the general Dutch population, which is 5/1432 (0.4%).(1) We were unable to confirm an association between CD and infertility in males and females. We suggest that the association between CD and infertility may be less strong than previously assumed. (1) Schweizer JJ et al. Scand J Gastroenterol 2004;39(4):359-64.

The pathological incidence of duodenopancreatic neuroendocrine tumors in the Netherlands, a PALGA study

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Duodenopancreatic neuroendocrine tumors comprise a very heterogeneous group of neoplasm, with regard to morphologic, functional and behavioral features. Although rare, current epidemiological studies worldwide suggest an increase in incidence of these tumors. We assessed the pathological incidence of duodenopancreatic neuroendocrine tumors over a period of 18 years in The Netherlands. Standardized excerpts from pathology reports of all patients diagnosed with duodenopancreatic neuroendocrine tumors from 1991 to 2009 were collected from PALGA and reviewed. This nationwide network and registry of histo- and cytopathology covers 100% of the pathology reports in The Netherlands. As a result, we identified 905 patients with pancreatic (n=692) or duodenal (n=213) neuroendocrine tumors. The majority of these patients (69.4%) had a non-functional tumor. Functional duodenopancreatic neuroendocrine tumors (gastrinoma, insulinoma, glucagonoma, somatostatinoma and VIPoma) were diagnosed at a significantly younger age compared to non-functional tumors (mean ± s.d. 52.3 ± 17.7 vs. 60.0 ± 14.6 years, respectively, $p<0.01$). Furthermore, functional pancreatic neuro-endocrine tumors were significantly smaller in size compared to non-functional tumors (mean ± s.d 2.3 ± 2.5 vs. 3.9 ± 3.2 cm, respectively, $p<0.01$). The average annual incidence per 1,000,000 persons over 1991 to 2009 was 2.54 for pancreatic and 0.81 for duodenal neuroendocrine tumors. The highest incidence of both tumors was found in patients 65 to 79 years of age. The incidence of non-functional duodenopancreatic neuro-endocrine tumors was found to have increased significantly over two decades with about 0.12 per year, $p<0.01$, while the incidence of functional tumors had remained stable. In-house analyses indicated, however, that an underestimation of these tumors of about 25% of clinical patients may occur due to the absence of histopathological evaluation, suggesting an even higher actual incidence.
Together, these findings imply that the increase in incidence is most likely to represent an increase in detection, rather than a raise in occurrence of non-functional tumors. We assume that the improvement of diagnostic techniques in combination with the introduction of the WHO classification for gastroenteropancreatic neuroendocrine tumors in 2000 have led to an increased awareness of pathologists and clinicians for these tumors. Eventually, earlier detection of these tumors may lead to less advanced disease.

Small intestinal alterations in severely obese hyperglycemic subjects - increased functional enterocyte mass and turnover is associated with chronic hyperglycemia

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Type 2 diabetes (DM2) is associated with small intestinal hyperplasia and hypertrophy in rodents. Furthermore, the small intestine is increasingly acknowledged to play a role in the pathophysiology of DM2. The aim of this study was to investigate the relation between plasma markers of small intestinal function and chronic hyperglycemia in man. A cross-sectional observational study was conducted of 40 severely obese subjects with chronic hyperglycemia and 30 severely obese subjects without chronic hyperglycemia. We assessed plasma levels of citrulline, representing small intestinal enterocyte mass, intestinal fatty acid binding protein (I-FABP), a marker of enterocyte loss, and glucagon-like peptide-2 (GLP-2), an intestinotrophic factor, and related them to glycated hemoglobin (HbA_{1c}) levels.Both plasma citrul and I-FABP levels were significantly elevated in severely obese subjects with chronic hyperglycemia (HbA_{1c}>6.0%) compared with severely obese subjects with a normal HbA_{1c} (≤6.0%) (citrul 35±2.1 µM vs. 26±1.4 µM, p=0.001; I-FABP 140±22 pg/ml vs. 69±14 pg/ml, p=0.001). Moreover, plasma citrul and I-FABP levels correlated with HbA_{1c} levels (citrulline: r_s=0.30, p=0.02; I-FABP r_s=0.33, p=0.03). To further explore the relation beween enterocyte mass, enterocyte loss, and enterocyte turnover, the I-FABP:citrul ratio was calculated, and found to be increased in subjects with an elevated HbA_{1c} (4.0 vs 3.1, p=0.03). This suggests that the increased enterocyte loss in chronically hyperglycemic subjects as indicated by I-FABP plasma levels cannot merely be explained by their relatively higher enterocyte mass. As a potential underlying mechanism, plasma GLP-2 levels were measured, but did not show a relation to citrul or I-FABP levels (r_s=0.06, p=0.67; r_s=0.08, p=0.54).
In conclusion, we presented evidence that an increased small intestinal functional enterocyte mass, increased enterocyte loss and turnover are associated with elevated HbA_{1c} levels in severely obese individuals. These findings argue for further exploration of the role of the small intestine in the pathophysiology of chronic hyperglycemia.

Comparison of a new flowcytometric method for diagnosing spontaneous bacterial peritonitis with other methods

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If a liver cirrhosis patient is suspected of spontaneous bacterial peritonitis (SBP), ascitic fluid should be analyzed promptly for polymorphonuclear neutrophil (PMN) cell count. PMN counts equal or higher than 250 cells/mm^3 indicate SBP and should initiate immediate antibiotic therapy. The current golden standard for PMN count in ascites is manual counting using a counting chamber. The goal of this study was to see if this manual golden standard could be improved analytically by a flowcytometric test. Additionally, we compared leukocyte esterase urine strips and an automatic cell counter as potential faster methods to gain time, and consequently survival of SBP-suspected patients.
EDTA-anticoagulated, ascitic samples (n=53) from 38 patients, admitted for various diseases including liver cirrhosis, were tested. PMN, lymphocytes, eosinophils, macrophages, monocytes, erythrocytes and non-hematological cells were defined in the flowcytometric assay by using fluorescent labelled antibodies (CD15-FITC, CD235-FITC, HLAdr-PE, CD16-ECD and CD45-PC5). Flowcount beads were added before measurement on an FC500 (Beckman Coulter) to determine absolute cell counts. The other methods were: automated leukocyte counting and differentiation by an LH750 automatic cell counter (Beckman Coulter), manual leukocyte differentiation on a cytospin and Combur2 (Roche) and UrifletS (Menarini) urine strips. The new flowcytometric assay was tested and found suitable for diagnosing SBP. Sensitivity and specificity of the other methods were calculated against this potential new golden standard. This demonstrated that manual counting of cytospins had the best sensitivity and specificity (both 100%). The LH750 gave some false positive results for PMN counting (sensitivity 100%, specificity 67%), whereas the leukocyte count correlated well with the flowcytometer (r^2 =0.98). Sensitivity of urine strips was too low for SBP diagnostics (56 and 67% for UrifletS and Combur2 resp).
We conclude that the flowcytometric test was easy to perform, was faster and required less handling than manual differentiation. Additionally, the flowcytometer discriminates leukocytes and non-hematological cells well. There was a perfect correlation between the leukocyte count of the flowcytometric test and the LH750. We recommend a leukocyte concentration determination with a suited automatic cell counter and PMN differentiation with this flowcytometric method as a new method for diagnosing SBP in ascitic fluid.

Peutz-Jeghers syndrome and family planning: the attitude towards prenatal genetic testing.

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Peutz-Jeghers syndrome (PJS) is a hereditary disorder caused by germ mutations in the LKB1 gene, characterized by mucocutaneous pigmentations, gastrointestinal hamartomas and an elevated cancer risk. Little is known about genetic test uptake, family planning and reproductive decision making among these patients. The aim of this study was to investigate predictors for genetic testing in PJS patients, their desire to have children and their attitudes towards the use of prenatal diagnosis (PND) and pre-implantation genetic diagnosis (PGD). In a cross-sectional study design, 61 adult Dutch PJS patients were invited to complete a questionnaire concerning genetic testing, the desire to have children, and the attitude towards the use of PND and PGD (outcome measures). We collected clinical and demographic variables and evaluated illness perceptions, in order to identify determinants for the outcome measures. The questionnaire was completed by 52/61 eligible patients (85% response rate, 56% females) with a median age of 45 (range 18-74) years. DNA mutation analysis was performed in 37 patients, revealing 33 (89%) LKB1-mutations. Female gender and parenthood were positive predictors for genetic test uptake. Twenty-four responders (46%) had children, of which significantly more were male ($p < 0.001$). Fifteen responders (29%) indicated that their diagnosis of PJS had influenced their desire to have children (i.e. less or no children), including 10 patients (9/10 females) reporting that they did not want to have children because of PJS. Termination of pregnancy after PND in case of a fetus with PJS in a personal situation was considered 'acceptable' for 15% of the respondents and 'unacceptable' for 73%. A higher age and stronger beliefs in treatment control were associated with a negative attitude. Fifty-two percent reported PGD to be 'acceptable' if the fetus could be a carrier of PJS in a personal situation, whereas for 17% this was 'unacceptable'. A stronger belief in personal control of PJS was shown to be associated with a positive attitude towards PGD.
Conclusion: The diagnosis of PJS influences the desire to have children in approximately one third of PJS patients, especially in women. Most PJS patients have a positive attitude towards PGD, but a negative attitude towards pregnancy termination after PND. These results emphasize the importance of informing PJS patients about the possibilities for prenatal genetic testing.

Increased prevalence of HLA DQ2 and DQ8 account for susceptibility to celiac disease in cystic fibrosis patients

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The prevalence of celiac disease (CD) was recently described to be increased in Scandinavian CF patients com-\pared to the general population. One of the explanations could be a genetic predisposition. 90-95% of patients with CD carry the human leukocyte antigen (HLA) DQ2 variant DQ2.5 (DQA1*05:01-DQB1*02:01) or HLA-DQ8 (DQA1*03: 01-DQB1*03:02). This is in contrast to 30-40% expression in the general population. HLA-DQ2.2 (DQA1*02:01-DQB1*02:02) has on its own a very low risk for CD, unless expressed together with DQA1*05:01 resulting in a DQ2.5 molecule by transcomplementation. HLA-DQ2.5 homozygous and HLA-DQ2.5/DQ2.2 heterozygous individuals have the highest risk for developing CD. We aimed to study the prevalence of CD in the Southern Netherlands CF population and to evaluate whether the susceptibility of CF patients to celiac disease is linked to HLA DQ2 and DQ8 genotype. CD screening (tissue-transglutaminase and endomysium antibodies) was performed in 59 CF patients (25 children, 34 adults). HLA-DR and HLA-DQ typing was performed by Luminex analysis and sequencing in 33 patients. 2/33 patients were diagnosed with CD. Results were compared to HLA frequencies in the European population. 5/59 CF patients had a positive CD screening before or at the time of the study. Four of them were diagnosed with CD by biopsy (n=1) or improvement of symptoms and normalization of antibody titers after gluten elimination (n=3). In three patients duodenal biopsies were not taken due to their physical condition. In one patient the biopsy did not confirm CD. These results demonstrate an increased prevalence of CD in the Southern Netherlands CF population (6.8%) compared to the general population (~1%). 66.7% of genotyped patients carried one or both HLA heterodimers DQ2 or DQ8; 48.5% were DQ2 positive, 15.2% were DQ8 positive and 3.0% carried both heterodimers. Genotype frequencies for DQ2.5, DQ2.2 and DQ8 were 19.7%, 12.1% and 9.1% respectively compared to 13.1%, 11.1% and 9.6% in the reference group. Three patients (9.1%) were homozygous for DQ2.5.
Conclusions: This is the first study in CF patients that shows an increased prevalence of HLA-DQ2.5 genotype, the most important risk factor for CD. These results suggest that HLA is a causal factor in the susceptibility to celiac disease of CF patients. Other disease related factors such as intestinal inflammation and disturbed intestinal integrity might be involved in CD development in this genetic predisposed population

Loss of intestinal barrier function in human intestinal ischemia-reperfusion: the role of goblet cells

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Human intestinal ischemia-reperfusion (I-IR) is a frequent phenomenon carrying high morbidity and mortality. Morbidity and mortality of I-IR is frequently related to loss of intestinal barrier function. This can result in translocation of harmful compounds from the lumen to the circulation, leading to massive inflammatory responses. The physical intestinal barrier, consisting of enterocytes connected by tight junctions, is covered by a protective mucus layer, secreted by goblet cells. The aim of this study was to investigate goblet cell viability during human intestinal IR, and to study IR-induced changes in mucin production. Goblet cell viability was studied using a unique human I-IR model. In 18 patients, 6 cm of healthy jejunum, to be removed for surgical reasons, was exposed to 45 or 60 minutes of ischemia followed by 30 and 120 minutes of reperfusion (n=9 for each ischemic period). Tissue was collected at all timepoints. Goblet cells were quantified on PAS stained sections by two independent observers by counting the number of goblet cells in 5 representative microscopic fields (100x) for each section. Double staining for PAS (goblet cells) and M30 (apoptosis) was performed to assess goblet cell apoptosis. Mucin (Muc2) expression was assessed using q-PCR. A significant loss of goblet cells was observed in human jejunum exposed to 45 and 60 minutes of ischemia with 30 minutes of reperfusion (P=0.003). Double stainings showed that a subgroup of goblet cells died apoptotically. Goblet cells were shed into the intestinal lumen leaving significantly decreased numbers of goblet cells after ischemia with 120 minutes of reperfusion (P=0.001). Interestingly, Muc2 mRNA expression did not show a consistent change in expression at all timepoints. In some patients Muc2 expression decreased as expected after ischemia and reperfusion, while in other subjects an increase in mucin expression was found. A possible explanation for the increase in mucin production is that the remaining, surviving goblet cells, account for appropriate mucin production.
In conclusion, this study shows that human intestinal IR results in a significant loss of goblet cells. Interestingly, mucin expression did not show a consistent change, indicating that the remaining goblet cells might have sufficient capacity to ensure adequate mucin production in some cases.

Malignant transformation of perianal- and enterocutaneous fistulas occurs rarely: Results of 17 years of follow-up from The Netherlands

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Malignant transformation of fistulas has been observed, in particular in perianal fistulas in Crohn's disease (CD)-patients. The prevalence of adenocarcinoma in enterocutaneous fistulas and non-CD related fistulas, however, is unknown. We investigated adeno-carcinoma originating from perianal and enterocutaneous fistulas in both CD-patients and non-CD patients from nine large, mostly tertiary referral, hospitals in The Nether-lands. Patients suffering from fistulizing disease and either dysplasia or adeno-carcinoma between January 1990 and January 2007, were identified using the nationwide automated pathology-database (PALGA). Clinical and histopathological data were collected and verified using hospital patient-charts and reported by descriptive statistics. The total CD-population comprised 6058 patients. In a study-period of 17 years, 2324 patients with any fistula were reported in PALGA. In 542 patients also dysplasia or adenocarcinoma was mentioned. After initial review and additional detailed chart review, 538 patients were excluded, mainly because the adenocarcinoma was not related to the fistula. In the remaining four patients, all suffering from CD, adenocarcinoma originating from the fistula-tract was confirmed. The malignancies developed 25 years (IQR 10-38) after CD-diagnosis, and 10 years (IQR 6-22) after fistula-diagnosis. Median age at time of adenocarcinoma-diagnosis was 48.3 years (IQR 43-58). Only one patient had clinical symptoms indicative for adenocarcinoma. In three other patients, the adenocarcinoma was found coincidently.
Conclusion: Adenocarcinoma complicating perianal or enterocutaneous fistula-tracts is a rare finding. Only 4 out of 6058 CD-patients developed a fistula-associated adenocarci-noma. We could not identify any malignant transformations in non-CD related fistulas in our 17 years study-period.

A short course of corticosteroids prior to surveillance colonoscopy to diminish mucosal inflammation in inflammatory bowel disease patients: results from a randomized controlled trial

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Active inflammation is a known pitfall of surveillance colonoscopy for inflammatory bowel disease (IBD) as it is difficult to differentiate between inflammation and true dysplasia. This randomized controlled trial aimed to assess the effectiveness of treating IBD-patients with a low dose of corticosteroids prior to surveillance colonoscopy. IBD-patients scheduled for surveillance colonoscopy between July 2008 and January 2010 were eligible to participate. Patients were randomized to either two weeks daily 20 mg Prednisone and Calcium vitamin D prior to surveillance colonoscopy or no treatment at all. The endoscopist and pathologist were blinded for medication-use. All histological biopsies were reviewed by an expert gastrointestinal pathologist. Statistics were performed using descriptive statistics, independent T-tests, non-parametric tests and binary logistic regression. In total, 60 patients participated: 31 (52%) in the treatment-arm and 29 (48%) in the control-group. In total, 31 patients (52%) had UC, 29 (48%) had CD, and 50% was female (n=30). In the treatment-arm, 247 biopsies were scored against 262 in the control-group: median inflammation score in the treatment arm was 1.1 (IQR 1.1-1.2) against 1.3 (IQR 1.1-1.2) in the control-group, p=0.045. In total, 58% of the treatment-arm compared with 66% of the control-group had endoscopic or histological mucosal inflammation (p=0.6). The maximum severity of histological inflammation per individual patient was on average 1.2 in the treatment-arm (IQR 1.1-2.4) against 2.1 in the control-group (1.2-3.3), p=0.15.
Conclusion: A short course of corticosteroids diminishes the overall histological disease activity in individual histological biopsies without major side effects. Moreover, there is a trend for corticosteroids to lead to a less maximum severity of both endoscopic and histological disease activity per patient and a lesser extent of disease. Further research is needed to assess the optimal dosage and duration of us to optimize the circumstances to detect dysplasia during surveillance colonoscopy.

HNF4α and CDH1 are associated with ulcerative colitis in a Dutch cohort

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Introduction: Inflammatory Bowel Disease (IBD) consisting of ulcerative colitis (UC) and Crohn's disease (CD) are complex disorders with multiple genes contributing to disease pathogenesis. A recent genome wide association scan identified three novel susceptibility loci for UC comprising HNF4α, CDH1 and LAMB1. We performed an analysis of these three loci in an independent cohort. Materials and methods: 821 UC patients and 1260 healthy controls of central European Caucasian descent were genotyped for SNPs: rs6017342 (HNF4α), rs1728785 (CDH1) and rs6949033 (LAMB1). Differences in allele and genotype distribution in cases and controls were tested for significance by the χ^2-test.
Results: Allelic association analysis showed that SNP rs6017342 in the HNF4α locus was strongly associated with UC (p-value = $1{,}04 \times 10^{-11}$, OR = 0.64, CI = 0.56-0.73) and SNP rs1728785 (CDH1) was associated with a P-value of 0.01 (OR = 0.82, CI = 0.70-0.95). SNP rs6949033 in LAMB1 was not associated in our cohort (p-value = 0.12, OR = 1.11, CI = 0.97-1.26). We found an association for SNP rs6949033 (LAMB1) for disease limited to the rectum limited disease (P-value = 0.02). However this association was lost after correcting for multiple testing. No further specific subphenotype associations were identified.
Conclusion: We confirm the associations between UC and two genetic loci comprising HNF4α and CDH1. The main candidate genes in these risk loci play important roles in the maintenance of the integrity of the epithelial barrier, highlighting the importance of the mucosal barrier function for UC pathogenesis

Two third of patients with inflammatory bowel disease in clinical remission has asymptomatic mucosal inflammation

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Endoscopic examination of asymptomatic inflammatory bowel disease (IBD) patients often reveals ulcers, erosions, or strictures. However, it is unknown whether the disease course is influenced by strategies to induce mucosal healing in these patients who are in clinical remission. Our aim was to assess the incidence of asymptomatic mucosal inflammation, the therapeutic decisions that are consequently made in clinical practice, and the impact on the disease course.All patients who underwent a surveillance colonoscopy in two Dutch academic medical centers between January 2001-December 2003 were included. Patients were followed-up until May 1st, 2009. Clinical data were collected from patients charts. Endoscopies and histology were reviewed. Statistical analysis were performed using descriptive statistics, independent T-tests, and nonparametric tests. In total, 159 patients were included, of whom 102 (64%) had ulcerative colitis, 48 CD (30%), and 9 patients (6%) unclassified colitis; 89 patients (56%) were male. Median follow-up time was 6.8 years (IQR 6-8). In 105 asymptomatic patients, mucosal inflammation was diagnosed: 55 (52%) had both endoscopic and histological inflammation (group A), 53 (50%) had only histological inflammation (group B) and 2 had only endoscopic inflammation (2%). In 92 of 105 cases (88%), treatment was not changed thereafter. In 42 patients of group A (76%) treatment was not changed compared with 51/53 patients in group B (96%), p=0.004. Two years later, 29% of all patients had endoscopic inflammation, and another 27% had only microscopic inflammation. Patients in group A+B had more often inflammation (n=63/100, 63%) two years later than those without asymptomatic inflammation (n=14/40, 38%), p=0.21. Additionally, they had a more severe inflammation, both endoscopic as histological (p=0.04/p=0.001). The proportion of patients with mucosal inflammation at 2 years follow-up was not different between group A and B, p=0.14.
Conclusions: A large proportion of IBD patients has asymptomatic mucosal inflammation, which is associated with more severe inflammation at two years follow-up. Moreover, one third of patients has microscopic disease activity, despite the lack of endoscopic ulcerations. Mucosal biopsies, in addition to symptoms and endoscopic analyses, are therefore indicated for disease monitoring.

Course of Life of Adolescents with an Inflammatory Bowel Disease

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Inflammatory bowel disease (IBD) is a chronic debilitating disorder occurring often in young patients, in the most productive period of their lives. It has become more and more acknowledged that IBD in adolescents and young adults has psychosocial consequences. However, little is known about the effect on the developmental trajectory or course of life of adolescents growing up with IBD. The purpose of this study was to asses and compare the course of life, quality of life and socio-demographic outcomes of adolescents with IBD compared to healthy peers. All patients aged 16-20 years who visited our department of paediatric gastroenterology were invited to participate in this study. They were asked to fill in two questionnaires: the Course of Life Questionnaire (which measures developmental milestones and socio-demographic outcomes) and the SF-36, a well-known Quality of Life (QoL) questionnaire. Normdata of healthy peers, representing the Dutch general population, were available for both questionnaires. A total of 62 adolescents (responsrate 74%, 51.6% male, mean age 18.6years) completed the questionnaires. Patients with IBD achieved significantly fewer milestones on the domains of autonomy, social and psycho-sexual development (all $p<0.05$). They were less frequently on holidays without adults before the age of 18 years ($p=0.002$), had fewer jobs during secondary school ($p=0.002$), were less frequently going out to a bar/disco during secondary school ($p=0.009$) and were falling in love for the first time later compared to their healthy peers ($p=0.003$). After school, IBD patients were significantly more often unemployment ($p<0.01$). The QoL of adolescents with IBD is impaired on domains of general health perception ($p=0.00$) and role limitations due to physical health ($p=0.013$).
Conclusions: Negative consequences in terms of QoL, and development, are prevalent in young adults with IBD since childhood. Health care physicians should be attentive to these consequences and provide additional support (emotional and educational guidance) if necessary. During transition to adults' clinics these topics are of major importance and should be an integral component of the comprehensive care of chronically ill children, adolescents and young adults.

Presentation of inflammatory bowel disease flare during pregnancy

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Background: Early diagnosis and treatment of active inflammatory bowel disease (IBD) during pregnancy is crucial to ensure favorable pregnancy outcomes. The presentation of an IBD flare is often difficult to be recognized since gastrointestinal (GI) symptoms and changes in laboratory results compatible with active disease can also be related to the pregnancy itself. Aim: To analyze the incidence and spectrum of clinical symptoms and laboratory changes related to flare of IBD during pregnancy. Patients and methods: Pregnant IBD patients recruited from one referral and several peripheral hospitals were included. Patients were followed during pregnancy at least three-monthly, GI symptoms and changes in C-reactive protein and blood count were assessed. Symptoms of nausea/vomiting beyond the first trimester, diarrhea, rectal blood loss, abdominal pain, weight loss and fever were noted. Patients with symptoms not resolving within one week underwent an endoscopy or MRI. The relationship of GI symptoms and changes in laboratory results with the disease flare was analyzed by Fisher`s exact test. Results: In total, 43 patients were included (average age 30 years, range 18-40; 29 Crohn`s disease/12 ulcerative colitis/2 unclassified). Twenty-one patients (49%) experienced GI symptoms during pregnancy, 13 patients (30%) fulfilled the criteria for further diagnostic procedure and in eight patients (19% of all patients) patients disease activity was confirmed at the endoscopy or MRI.From all GI symptoms, rectal blood loss, diarrhea and weight loss were related to the disease activity ($p<0.0001$, $p<0.0001$ and $p=0.004$; respectively). There was no relationship between any of the laboratory parameters assessed with disease activity.
Conclusion: Half of the pregnant IBD patients experience GI complains. Symptoms related to the flare of IBD during pregnancy are rectal blood loss, diarrhea and weight loss. Laboratory results do not help to differentiate between disease flare and non-specific pregnancy-related GI symptoms.

Educational level and risk of colorectal cancer in the European Prospective Investigation into Cancer and nutrition with specific reference to tumor location

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The existing evidence is inconclusive on whether educational inequalities influence colorectal cancer (CRC) risk, and whether a low or a high educational level decreases the risk of developing CRC. The aim of this study was to investigate the relationship between educational level and CRC. We studied data from 400,510 participants included in the EPIC (European Prospective Investigation into Cancer and Nutrition) study, of whom 2,447 developed CRC during a mean follow-up of 8.3 years. Cox proportional hazard regression models stratified by age, gender and center were used to estimate hazard ratios (HR) and 95% confidence intervals (95% CIs). Relative indices of inequality (RII) for education were estimated using Cox regression models. We conducted separate analyses by tumor location, gender and geographical region. Participants with a primary education or less and participants with a vocational secondary education had a lower risk of developing CRC compared to participants with a college or university education. When stratified for location, only risk estimates for the proximal colon were statistically significant (HR 0.63, 95%CI 0.45-0.89 for primary education or less, and HR 0.65, 95%CI 0.46-0.92 for vocational secondary education).Relative indices of inequality (RII) for education indicated that the decreased cancer risk for a lower educational level was found among women and participants from southern Europe. Despite correction for potential confounders, these estimates remained statistically significant for colorectal cancer, colon cancer and proximal colon cancer.

Conclusions: The risk of developing CRC, especially in the proximal colon, was lower in participants with a lower education, compared to participants with a higher education. This effect is most pronounced in women and in participants from southern Europe. We speculate that our findings could be explained by lead time bias among participants with a lower education and/or residual confounding by dietary factors.

Predictors of advanced colorectal neoplasia after polypectomy

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Patients with a previous colorectal adenoma are kept under surveillance because they are likely to develop metachronous neoplasia. It is important to identify predictive factors for adenoma recurrence in order to determine appropriate surveillance intervals. The objective of this study is to determine predictors of developing adenomas and advanced neoplasia after polypectomy. 488 outpatients were identified, who had a colorectal polypectomy of at least one adenoma in our hospital between 1988-2004, with follow-up until 2010. 54 patients were excluded for various reasons. Univariate and multivariate analysis of patient and adenoma characteristics during the base colonoscopy was performed to identify risk factors to develop adenomas and advanced neoplasia during follow up colonoscopies. An advanced neoplasm was defined as an adenoma with > 25 % villous features, size > 1 cm, high grade dysplasia or invasive carcinoma. The included patients (41 % female) had a mean age of 55 years (range 24-82 years). Mean follow-up time between base and last colonoscopy was 90 months (range 9-260 months). Base colonoscopy revealed > 3 adenomas in 67 of the cases (16%) and advanced adenoma in 251 of the cases (58%). 219 patients (51 %) had a recurrence of at least 1 adenoma and 86 patients (20 %) developed at least 1 advanced neoplasia, including 3 cases of a carcinoma. Univariate analysis revealed male gender (p=0.001), age > 55 year (p=0.004), >3 adenomas (p=0.001), proximal location (p=0.01) and high grade dysplasia (p=0.017) as risk factors for adenoma recurrence. Risk factors for advanced neoplasia recurrence were age >55 year (p=0.002), >3 adenomas (p=0.042), proximal location (p=0.046), high grade dysplasia (p=0.03), > 25% villous features (p=0.021) and size > 1 cm (p=0.015). Multivariate analysis showed male gender (p=0.001), >3 adenomas (p=0.001) and high grade dysplasia (p=0.038) as risk factors for adenoma recurrence and age >55 year (p=0002) and high grade dysplasia (p=0.014) as risk factors for advanced neoplasia.
Conclusion: Adenoma and advanced neoplasia development after polypectomy is common. Gender, age, number of prior adenomas and high grade dysplasia are the most strongly predictive factors for recurrence. Current guidelines and surveillance intervals should be reconsidered based on these results.

No change in colorectal cancer stage 4 years after revision of the surveillance guidelines after polypectomy in the Netherlands

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Guidelines for surveillance strategies after colonic polypectomy have changed over the years in the Netherlands. The first consensus guide from 1988 was last revised in 2002. The main change involved new follow-up intervals after polypectomy. The effect of this change on disease stage at the time of colorectal cancer (CRC) diagnosis is however uncertain. We compared tumor characteristics in patients diagnosed with CRC in 1996 and 2006 to investigate whether altered follow-up intervals resulted in the detection of more early stage CRCs. From the nationwide registry of histopathology results in the Netherlands (PALGA), we included all patients with histologically proven CRC in 1996 and 2006, and of whom previous colonic histopathology reports were available in the 10 years preceding this diagnosis. These data were analyzed for the presence and intervals of pre-cancerous colonic histopathology results, and tumor depth and nodal status (TN-stage) of CRC at diagnosis, and compared 1996 with 2006.The total number of individuals diagnosed with CRC was 7,993 in 1996 and 11,127 in 2006. In 12.6% (n=1,004) and 15.2% (n=1,696) of these patients, respectively, pre-cancerous colon histology was available ($p<0.05$). CRC stages T1-3 were not different between 1996 and 2006, however, more patients with a T4 tumor at diagnosis (19%) were found in 2006 compared to 1996 (6%) (OR 3.5 [95% CI 1.7-7.0]). In the 10 years preceding a diagnosis of CRC, a higher prevalence of villous adenomas (VAs) was found in 1996 (n=370, 36.9%) compared to 2006 (n=335, 19.8%) (OR 2.4 [95% CI 2.0-2.8]). No difference in other characteristics, such as grade of dysplasia, or tubular or tubulo-villous adenomas, was found.
Conclusions: Although a slightly larger proportion of patients with CRC in 2006 underwent colonoscopy in the 10 years prior to the diagnosis compared to 1996, patients with CRC in 2006 were more likely to have a T4 tumor compared to 1996. Four years after implementation of the new surveillance guidelines in the Netherlands, no beneficial effect on tumor stage of CRC is measured.

Haemorrhoids are an infrequent cause of false positive results on faecal immunochemical tests

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Background: Faecal immunochemical tests (FITs) are used for early detection of colorectal neoplasia. As FITs detect occult blood and not specifically colorectal cancer (CRC) or adenomas, they are hampered by false positive results. False positive tests consequently increase burden on colonoscopy capacity. As haemorrhoids are expected to result in positive FIT results, individuals with haemorrhoids may warrant a different screening strategy. Aims & Methods: The aim of this study is to determine the relation between haemorrhoids and false positive FIT. Results: Between June 2006 and October 2009, all subjects (≥18 years) scheduled for elective colonoscopy in five participating centres were invited to participate in this study. All individuals performed a FIT (OC sensor®) before bowel preparation and colonoscopy. FIT results were compared with colonoscopy as gold standard. Positivity rates were compared between subjects with haemorrhoids only and subjects without any abnormalities at colonoscopy. Specificity for advanced neoplasia (CRC or advanced adenomas) with and without having haemorrhoids was compared (cut-off 50ng/ml). Results In the present study, 3003 patients were included. Of these, 420 had haemorrhoids found at colonoscopy, whereas 2583 subjects had not. The positivity rates were 15% and 16% respectively (cut-off 50ng/ml). In 145 (34.5%) of the 420 subjects, haemorrhoids were the only abnormality found at colonoscopy, whereas 77 subjects (18.3%) also had diverticular disease and 160 individuals (38.1%) also had polyps or other potential causes of bleeding (but no advanced neoplasia). In the latter three groups, positivity rates were 7.6%, 9.1% and 18.1% respectively. In 846 individuals from the initial cohort, no abnormality was found at colonoscopy. The positivity rate in this group was 5.2%. This was not significantly different from subjects with haemorrhoids as a single finding at colonoscopy ($p = 0.25$, χ^2 test). Specificity in subjects with haemorrhoids (87.7%, CI 84-91) was not significantly different in subjects without haemorrhoids (90.6%, CI 89-92, $p = 0.08$, χ^2 test).
Conclusion: Even in a high risk population at a low cut-off value, haemorrhoids are an infrequent cause of false positive FIT results. Therefore, subjects known to have haemorrhoids might benefit equally from FIT based screening and a different approach is not necessary for these individuals.

Survival after colorectal cancer in young patients with a family history for this malignancy

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Introduction/objectives: Genetic predisposition is a known risk factor for the development of colorectal cancer (CRC). Approximately 10-15% of patients with CRC have an affected first-degree relative and epidemiological studies have shown that these individuals have a 1.6- to 8.0-fold higher risk of developing colorectal cancer during lifetime. In addition, survival and cancer recurrence is associated with a family history (FH) of CRC, although published studies are contradictory. We investigated whether a positive FH of CRC in a first-degree relative was associated with survival in young patients (<60 years) with CRC. Aims & methods: We retrospectively evaluated 710 patients diagnosed with CRC at an age of 60 years or younger between 1999 and 2008 in three hospitals (1 academic, 2 non-academic) in the central region of the Netherlands. The primary end point was overall survival. We used a univariate and multivariate hazard model and Kaplan-Meier curve to estimate survival over time. Results: FH was recorded in 416 of 710 cases. Of these patients, 89 (21%) had one or more first-degree relative(s) that have been diagnosed with CRC. The mean follow-up was 39.8 months; during follow up 123 (30%) patients died. Age at diagnosis, pathologic tumour status and pathologic node status were univariately associated with survival. Adjusted for these variables, the overall survival was increased in patients with a positive FH compared to those without (adjusted hazard ratio 0.80, 95%CI 0.50-1.27), although this was not statistically significant. Subgroup analyses for gender showed an adjusted HR of 0.38 (95%CI 0.17-0.87) for FH in women, and 1.38 (95%CI 0.74-2.58) in men.
Conclusions: A FH of CRC is in young (<60 years) female patients with CRC associated with increased survival. Our results confirm that a FH of CRC is clinically relevant for CRC prognosis, also in young patients.

Colorectal cancer screening in a Dutch population - assumed asymptomatic: symptommatic patients will participate despite advice against it

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In the Netherlands there has been a pilot screening program for colorectal cancer conducted on a large scale. In this pilot two kinds of fecal occult blood tests (FOBT's) were compared in a screening population. Invitees were advised not to perform the FOBT if they were experiencing symptoms of bowel cancer, but to contact their general practitioner (GP). There were signs that participants did not follow this advice. The aim of this research was to determine the participation of symptomatic participants. Possible risk factors were examined. Data were obtained by a questionnaire sent to the invitees of the pilot screening program; 20475 men and women aged 50-75. This questionnaire was not specifically designed for the purpose of this study. Single percentages were calculated. A multivariable logistic regression analysis was used to identify odds ratio's (OR) and 95%-confidence intervals (CI). 9474 (46%, CI=45%-47%) invitees responded of which 8976 (95%, CI=95%-95%) participated in the pilot screening program by performing their FOBT. 1795 (20%, CI=19%-21%) of the responding participants were symptomatic and 68 (4%, CI=3%-5%) of them contacted their GP. 104 (21%, CI=17%-25%) of the 498 responding non-participants were symptomatic and 11 (11%, CI 10%-12%) of them contacted their GP. 36 (6%, CI=3%-9%) of the participants with rectal blood loss contacted their GP and 55 (4%, CI=2%-6%) of the participants with bowel complaints contacted their GP. There is no significant difference between the type of symptoms. In both symptomatic and asymptomatic responding participants 1% (CI=1%-1%) thought the received brochure with information was not clear. 1325 (74%, CI=72%-76%) of the symptomatic participants felt healthy and 47 (4%, CI=4%-4%) of them contacted their GP. 391 (22%, CI=20%-24%) did not feel healthy and 21 of them (5%, CI=3%-7%) contacted their GP. Corrected OR for social economic status is 1.00 (0.94;1.05). Corrected OR's for male gender and age were respectively 0.81 (0.73-0.91) and 0.98 (0.97-0.98).
In conclusion many symptomatic patients will participate in colorectal cancer screening-despite the advice against it. This cannot be explained by insufficient information, general bowel symptoms or feeling of health. Women and younger participants are more inclined to participate when experiencing symptoms.

Quality indicators for colonoscopy; great variation of adenoma detection rates between endoscopists in a large community hospital

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Introduction: Adenoma detection rate (ADR) is currently recognized as one of the most important quality indicators for colonoscopy. An ADR of at least 20% has been stated as a minimum goal in screening colonoscopy. Recently it was shown that a low ADR significantly was associated with a higher incidence of interval carcinoma. In the current study, we investigated quality indicators for colonoscopy between several endoscopists in a large community hospital, in order to assess the need for structural future implementation. Methods: The data of all colonoscopies performed by five highly experienced endoscopists (4 gastroenterologists, 1 internist) in a 6-month period (November 2008 – April 2009) were retrospectively assessed. Patients with a sigmoido/colonoscopy in the last 3 years before current colonoscopy, and those with a history of colon surgery were excluded. The rate of cecal intubation and the ADR (percentage of colonoscopies in which at least one adenoma was found) was scored in all colonoscopies, and comparisons were done between endoscopists. Results: A total of 1006 colonoscopies were analyzed, of which 700 were included. Mean patient age was 61 years. Indications for colonoscopy were: change in bowel habits (12%), anemia (16%), rectal blood loss (19%), (suspicion of) IBD (10%), adenoma surveillance (15%) and other (28%). No difference in indications for colonoscopy was found between endoscopists. Mean cecal intubation rate was 93.3% with significant differences between endoscopists, ranging between 87.5% and 97% ($P = 0.045$). The adenoma detection rate differed significantly between endoscopists: 27% - 27% - 33% - 44% - 52% ($P < 0.001$). The same was found when only large adenomas (>15mm) were considered: 0.5% - 1% - 2% - 3% - 6%, ($P = 0.002$).
Conclusion: In a large community hospital great variation in quality indicators for colonoscopy was found between endoscopists. Although an adenoma detection rate of at least 20% was achieved by each endoscopist, differences were considerable and may have clinical implications. The results of this study stress the need for better definition, implementation and adherence to quality indicators for colonoscopy.

Advantages of full diagnostic colonoscopy over flexible sigmoidoscopy in patients over 50 years of age presenting with rectal blood loss

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Worldwide, colorectal cancer (CRC) is a frequent cause of morbidity and mortality. Rectal blood loss (RBL) is a common indication for colonoscopy and one of the presenting symptoms of CRC. Flexible sigmoidoscopy has been proposed as an alternative in cases in which distal pathology (distal to the splenic flexure) is most likely. In the Netherlands, an increasing shortage in endoscopists and demand for endoscopy support the need for more efficient patient management. The purpose of this study was to evaluate the presence of proximal and distal pathology in patients undergoing colonoscopy because of RBL and whether flexible sigmoidoscopy alone would have been sufficient. 120 Consecutive patients of 50 years and older were referred by their general practitioner to undergo colonoscopy because of RBL. All patients visited our out patient clinic to evaluate medical history and to obtain informed consent. The yield of colonoscopy was evaluated for distal and proximal findings. We investigated whether colonoscopy is indeed indicated for RBL in patients of 50 years and older. After excluding 12 patients (2 <50 years; 2 flexible sigmoidoscopy only; 5 no endoscopy; 3 other indication than RBL) 108 patients underwent colonoscopy. The mean age was 66 years (range 50-86) and 54% were men. In total 95 (88%) patients had one or more significant finding (total of 162). Premalignant polyps were the most frequent (52%) finding, followed by haemorrhoids (39%) and diverticulosis/-itis (34%). In 80% of the patients the cause of RBL was found. CRC was diagnosed in 15 (14%) patients of which 2 were located in the proximal colon. When present, haemorrhoids or CRC were the cause of RBL in all cases in contrary to polyps (16%). In total 101 (94%) of the patients would have met the criteria to undergo subsequent colonoscopy when only an initial sigmoidoscopy would have been performed. Proximal polyps were present in 40% of the patients with distal polyps. Twelve isolated proximal findings (11%; 2 CRC, 9 polyps and 1 angiodysplasia) would have been found with subsequent colonoscopy, all of which were documentated as the cause of RBL.
Conclusions: Although sigmoidoscopy alone would have revealed the cause of RBL in 86% of the patients, the high yield of pre-malignant, colonic polyps (84%) would have prompted a subsequent full colonoscopy with polypectomy. Furthermore, relevant isolated proximal pathology was present in 11% of the patients. Our findings support performing initial full diagnostic colonoscopy in patients of 50 years of age presenting with RBL.

Patients presenting with rectal blood loss or a change in bowel habits are at increased risk of finding colorectal cancer during colonoscopy

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There is an increasing demand on colonoscopy capacity due to the rising prevalence of colorectal cancer (CRC) and increasing implementation of CRC screening programs. In many centers, this has resulted in long waiting lists for colonoscopy procedures. It is important that patients with an increased risk of having CRC have priority to undergo colonoscopy to minimize doctor's delay until a diagnosis of malignancy is established. We investigated whether presenting symptoms of patients referred for colonoscopy could help in prioritizing this procedure in daily clinical practice. Between February 2007 and February 2010, consecutive outpatients referred for colonoscopy in a tertiary referral center were asked to fill out a questionnaire regarding the symptoms for which the colonoscopy was indicated. Informed consent was obtained to review the findings at colonoscopy. Multivariate analysis was performed to identify symptoms that may be predictive of the presence of CRC. In total, 1,106 of 4,817 (23%) patients returned the questionnaire, of which 52% were men. Mean age was 54 years [range 18-91 years]. Of these, 393 (36%) patients had undergone no prior flexible sigmoidoscopy or colonoscopy. CRC was detected in 31 patients (2.8%). After multivariate analysis with correction for age and gender, patients referred for rectal blood loss and change in bowel habits were found to be at a higher risk of finding CRC than patients without these symptoms (OR 6.6 [95% CI 2.8-15.6] and OR 4.9 [95% CI 1.7-13.8], respectively). Prior sigmoidoscopy or colonoscopy (OR 0.3 [95% CI 0.1-0.7]) and referral indication fatigue (OR 0.2 [95% CI 0.1-0.5]) decreased the risk of finding CRC. Weight loss, self reported anemia, abdominal pain and anal symptoms were not associated with finding CRC.
Conclusions Patients presenting with rectal blood loss or a change in bowel habits are at an increased risk of finding CRC during colonoscopy and should therefore have priority to undergo the procedure. Previous sigmoidoscopy or colonoscopy decreases the risk of finding CRC, which supports current or planned population screening programs.

Cardiopulmonary events during colonoscopy screening under conscious sedation

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Background: Colonoscopy (CS) is considered the current standard to detect colorectal neoplasia. Studies on diagnostic and therapeutic CS under conscious sedation have pointed to a frequent occurrence of cardiopulmonary events. Little is known about the occurrence of these events in primary CS screening in healthy subjects. Methods & aims: To evaluate the occurrence of bradycardia (pulse rate <60 min^{-1}), hypotension (systolic blood pressure (SBP) >90mmHg), hypoxia (blood oxygenation, SaO_2 <90) and ECG changes during CS screening in an average-risk workplace-based population (>50 yrs) and identify associated risk factors. Endoscopic, demographic and medical data were collected prospectively. During 214 consecutive colonoscopies the above mentioned parameters were monitored continuously. A standard dose and in case of discomfort during CS an additional dose of midazolam and pethidine was administered intravenously. Statistical analysis included Chi^2, Student T-test and a multivariate logistic regression analysis adjusted for age and gender. Results: The study population consisted of hospital personnel (mean age 54.0 ±3.8 yrs, 39.3% male) without major co-morbidity. Major complications or relevant ECG changes did not occur. Hypoxia occurred in 119 (55.6%), bradycardia in 12 (5.6%), and hypotension in 19 subjects (8.9%). Subjects with hypoxia had a longer mean total procedure time (31±12 vs. 28±12 min, p<0.05), higher dosages of midazolam (0.06±0.02 vs. 0.05±0.02 mg/kg, p<0.001) and pethidine (0.71±0.18 vs. 0.58±0.22 mg/kg, p<0.001), more frequently had a deeper sedation (level 3) (63.6 vs. 25.0%, p<0.001) and more frequently had severe abdominal pain (15.0 vs. 3.7%, p<0.05). In the multivariate analysis only sedation level 3 (i.e. conscious sedation) was associated with hypoxia (OR 4.8, CI 1.7-13.7). Subjects with bradycardia had a longer mean procedure time (38±12 vs. 29±12 min, p<0.05), which was also significant in the multivariate analysis (OR 1.000, 1.000-1.001). Subjects with hypotension had less often complete CS (68.4 vs. 94.3%, p<0.01), and less frequently biopsies/polypectomies performed (26.3 vs. 54.4%, p<0.05). In the multivariate analysis, incomplete CS (OR 6.1, CI 1.8-20.6) was associated with hypotension.
Conclusions: In this relatively young and healthy population, cardiopulmonary events (1) did not occur infrequently, (2) did not result in serious cardiopulmonary complications, and (3) were associated with procedure related but not patient related factors.

Formation of tertiary lymphoid tissue in dextran sulfate sodium induced colitis is partially dependant on $LTa_1 b_2$-LTbR axis (MLDS-voordracht)

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Patients with inflammatory bowel disease (IBD) suffer from chronic inflammation of the intestine, which may lead to the formation of lymphoid aggregates that closely resemble secondary lymphoid tissue. The formation of secondary lymphoid tissue is dependent on the lymphotoxin alpha1 beta2 - lymphotoxin beta receptor signaling axis. Hematopoietic lymphoid tissue inducer (LTi) cells express lymphotoxin alpha1 beta2 ($LT\alpha_1\beta_2$) which binds to the lymphotoxin beta receptor ($LT\beta R$) expressed on stromal organizers cells, and leads to the induction of chemokines (CXCL13 and CCL21) and adhesion molecules (VCAM-1, ICAM and MAdCAM-1). These molecules serve to attract and retain additional hematopoietic cells leading to the formation of secondary lymphoid tissue. Here we show, using dextran sulfate sodium (DSS) induced colitis, that stromal cells in the acute inflammatory setting have the ability to upregulate $LT\beta R$ expression along with CXCL13, CCL21, VCAM-1 and MAdCAM-1. In the more chronic setting tertiary lymphoid tissues were detected in inflamed colons and consisted of tightly clustered B cell follicles with distinct T cell areas. Surprisingly, these structures could also be found at the chronic phase of DSS colitis in $LT\alpha^{-/-}$ mice, although the B cell areas were devoid of follicular dendritic cells (FDCs) and germinal centers (GCs). These results show that lamina propria stromal cells become activated upon damage to the epithelial barrier and function as organizer cells to locally form lymphoid tissue. This process is only partially dependent on the $LT\alpha_1\beta_2$-$LT\beta R$ axis and must involve alternate pathways.

The zebrafish; a novel model to study bacterial-host interactions in health and disease (MLDS-voordracht)

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The pathogenesis of inflammatory bowel disease involves dysfunctional mucosal immune responses to commensal bacteria in genetically predisposed hosts. Interactions between host cells and bacteria are complicated, making it a challenge to assess their relative contribution to intestinal pathology. We developed a zebrafish model of enterocolitis to study these interactions. Enterocolitis was induced by intrarectal administration of the hapten oxazolone in adult wild-type and myeloperoxidase-reporter transgenic zebrafish in the presence or absence of antibiotics. Intestinal inflammation was evaluated by histological and flow cytometry analyses and cytokine profiling with quantitative real-time polymerase chain reaction. Changes in the composition of the intestinal microbiota following antibiotic administration were assessed by 16SrRNA sequencing and bacterial load was quantified by culture on nonselective media (colony-forming units). In zebrafish, the infiltrate and severity of oxazolone-induced enterocolitis are influenced by the composition of the microbiota. Inflammation is characterized by granulocyte influx; epithelial damage; goblet cell depletion; and increased expression of interleukin-1beta, tumor necrosis factor-alpha, and interleukin-10. Zebrafish given vancomycin had bacterial populations dominated by Fusobacteria and reduced enterocolitis scores, intestinal damage, and percentages of infiltrating neutrophils and eosinophils. In contrast, zebrafish given colistin sulphate had a predominance of proteobacteria and reduced eosinophil and lymphocyte infiltration, but enterocolitis scores were not reduced.
Conclusions: In zebrafish with oxazolone-induced enterocolitis, components of the intestinal microbiota affect the severity and composition of the intestinal infiltrate.

Faecal calprotectin for screening children with suspected inflammatory bowel disease: a phase III diagnostic accuracy study.

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In the diagnostic workup of children with suspected IBD endoscopy of the upper and lower gastrointestinal tract is considered indispensable. In a substantial proportion of suspected children no abnormalities are found during endoscopy. A screening test to increase the likelihood of IBD is desirable to justify invasive endoscopy. Under 'ideal experimental circumstances' (phase I and phase II diagnostic accuracy studies) faecal calprotectin proved to be a sensitive marker for inflammation in the gastrointestinal tract. The aim of this study was to evaluate the diagnostic value of calprotectin in children with suspected IBD under real clinical circumstances (phase III). A consecutive series of children suspected of IBD in the northern region of the Netherlands were prospectively included. In all children calprotectin was determined after the first consultation. Indications for endoscopy were defined independently of calprotectin test results and were based on strict criteria. IBD diagnosis was confirmed by endoscopic and histological evaluation. The diagnosis 'non IBD' was confirmed by negative endoscopy or by 6 months of clinical follow-up. A total of 109 children were included and 38 of them (35%) had IBD. Using the internationally accepted cut-off of faecal calprotectin (50 mg/kg stool), we found a sensitivity of 100% for IBD. Twenty children with the diagnosis 'non IBD' had a positive test result (specificity 72%). Eight of these children had functional abdominal pain with slightly elevated calprotectin values (median 143 mg/kg; range 57-760). Four children had infectious enterocolitis with high calprotectin levels (median 1450 mg/kg; range 1235-1730). A calprotectin result below the cut-off value excluded IBD with certainty (negative predictive value 100%).
Conclusion: When only children who test positive for calprotectin continue for endoscopy (instead of all children with a clinical suspicion of IBD), only 58 out of 109 children would be subjected to this invasive procedure. Screening patients with calprotectin will cause a 47% reduction in the number of urgent endoscopies (95% confidence interval 38 to 56%). Calprotectin is a good screening test to identify children with a high likelihood of IBD. This is good news for both patients and clinicians. Invasive endoscopy is prevented in patients with normal calprotectin values. Paediatricians now have a screening tool to justify clinical follow-up without endoscopy and to ease the pressure on overstretched endoscopic units with long waiting lists.

Fish-oil-based lipid infusion results in significant n-3 fatty acid incorporation in plasma phospholipids and leukocyte cell membranes in healthy volunteers.

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The high content of n-6 polyunsaturated fatty acids (PUFAs) in parenteral lipid emulsions derived from soybean oil (SO), which are world wide the most commonly used emulsions, might be unfavorable since n-6 PUFAs may promote the overproduction of pro- inflamematory cytokines and eicosanoids. Fish oil (FO) is rich in the less pro-inflammatory n-3 PUFAs such as eicosapentanoic acid (EPA), docosapentaneoic acid (DPA) and docosahexanoic acid (DHA). Higher plasma and cell membrane n-3 PUFA contents might, therefore, be beneficial especially in patients with an already imbalanced immune response. In the present study, plasma phospholipids and PBMC cell membrane fatty acid composition after intravenous infusion of a FO-based and a SO-based lipid emulsion in healthy volunteers was assessed. Lipid free control (saline), SO- and FO- based lipid emulsions were administered for 1 hour on three consecutive days (0.2 g/Kg BW/hr) with a wash-out interval of two weeks to 8 healthy volunteers in a randomized cross-over study design. Relative plasma phospholipid and PBMC cell membrane fatty acid contents were assessed prior to the first infusion (T=0, baseline), 1 day (T=4) and 8 days (T=11) after the third infusion. Data are expressed as ratio T=4/T=0 and T=11/T=0, which indicate early and late treatment effects respectively.The early effect of FO infusion consisted of significantly higher EPA (4.48), DPA (1.27) and DHA (1.70) plasma levels (ratio T=4/T=0) when compared to lipid free control (0,94, 1,04 and 1.12, respectively) and SO (0.77, 0.96 and 1.06, respectively). Levels of linoleic acid and dihomo-gamma-linolenic acid (DGLA) were significantly lower after FO infusion (0.80 and 0.79) than after lipid free control (0.98 and 1.04) and SO (1.01 and 0.95). At T=11, most levels had normalized. Also, relative EPA and DHA levels in PBMC cell membranes tended to be higher early after FO infusion (2.91 and 1.38, expressed as ratio T=4/T=0) when compared to lipid free control (1.13 and 0.98) and SO (0.94 and 0.93). No adverse effects were observed.
Conclusions: Short term infusion of a FO-based lipid emulsion to healthy volunteers is safe and increases the relative n-3 PUFA content of plasma phospholipids and PBMC cell membranes. The current FO infusion protocol can, therefore, be used to assess the beneficial effect of FO-based parenteral lipid emulsions in patients with an imbalanced (pro-) inflammatory state.

'Gut feeling' of physicians and nurses concerning patient compliance to antiseptic procedures in home parenteral nutrition: some are right, some are wrong

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Home parenteral (intravenous) nutrition (HPN) is the mainstay of nutritional support for severe longterm intestinal failure. The presence of a central venous access device (catheter) results in a high risk for catheter-related bloodstream infections (CRBSI), which in part are due to the inadequate performance of aseptic techniques by the patient or caregiver to administer the PN formulation. Surprisingly little is known about the patient characteristics that are associated with continued compliance to the aseptic techniques that were acquired during the HPN training. The aim of this study was to evaluate whether HPN physicians and HPN nurses are able to identify patient factors which correspond with lowered patient compliance to aseptic techniques when administering HPN. The study population comprised all HPN patients currently being treated at our centre, who use a tunneled central venous catheter (Hickman) or port that is locked by means of a taurolidine solution after each use. In this study the prospective 'Gut Feeling' tool was designed to compare the characteristics of patients, predicted by HPN physicians and nurses during interviews, with the characteristics associated with poor compliance reported by the patients in the questionnaires. The primary outcome measure was the consistency between predicted and reported patients characteristics associated with poor compliance to aseptic techniques of HPN patients measured on a continuous scale between 0 and 0,89. In data analyzes Mann-Whitney or Kruskal-wallis tests were used where appropriate. Sixty-four patients (out of a total population of 110 patients) matched the inclusion criteria and 89% returned the questionnaire. 63% of the responders reported complete compliance to the aseptic techniques when administering HPN. A poor compliance was reported by non-smoking female patients (p=0.119), young females in this population (age < 55; p=0.105), men who are not married 0.097) and men who lived alone (p=0.031). Only marital status and social situation were predicted risk factors by the physicians and nurses. Striking was the number of patients (42%) that forgot to remove their jewelry at least sometimes.

Overall, HPN patients reported good compliance to aseptic HPN administration techniques, although removing of jewelry was at least sometimes forgotten by almost half of the group. HPN physicians and nurses can rely in part, but certainly not entirely, on their gut feeling with regard to risk factors for non-compliance.

Effects of a preoperative oral nutritional supplement on postoperative glucose metabolism in rectal cancer patients.

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Insulin resistance after major surgery is associated with postoperative morbidity. Preoperative oral nutritional supplements (ONS) can reduce postoperative infectious complications, but their effect on postoperative glucose metabolism is unknown. Effects were studied of an ONS, containing carbohydrates, anti-oxidants and glutamine, on postoperative glucose metabolism. A double blind randomized controlled pilot study in rectal cancer patients was performed. ONS (A) or placebo (B) was given 15, 11 and 4 hrs before surgery. Patients were studied before and one day after surgery in the basal state and during a two-step hyperinsulinemic euglycemic clamp using a stable isotope. Basal endogenous glucose production (EGP), insulin-mediated suppression of EGP (hepatic insulin sensitivity), insulin-mediated suppression of plasma free fatty acids (adipose tissue insulin sensitivity) and peripheral insulin sensitivity (Rd) were measured. In this pilot study 19 patients were included; A: 7M/3F - B: 6M/3F, age A: 60 [53-69] - B: 63 [49-79] yrs, BMI A: 25 [21-28] - B: 26 [23-31] kg/m^2. Glucoregulatory hormones were not different. In the preoperative state basal EGP, hepatic insulin sensitivity and adipose tissue insulin sensitivity were not different between groups, while peripheral insulin sensitivity was significantly higher in group A. Surgery induced a significant reduction in hepatic, adipose tissue and peripheral insulin sensitivity in both groups. The ONS group had a less reduced postoperative peripheral insulin sensitivity compared to the placebo group (Rd A: 20.6 [14-28] vs. B: 15.3 [13-19] µmol/kg·min p=0.04).
Conclusions: Rectal cancer surgery induces hepatic and adipose tissue insulin resistance and profound peripheral insulin resistance. The preoperative ONS induces a higher postoperative peripheral insulin sensitivity compared to placebo, without effect on insulin sensitivity of the liver or adipose tissue. Further research is required to assess whether this positive effect of ONS results in lower postoperative morbidity rates.

Perioperative nutritional treatment is associated with improved postoperative outcome in patients with oesophageal, gastric or pancreatic cancer

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Oesophageal, gastric and pancreatic cancer patients are prone to malnutrition, because they are not only subject to cancer-induced cachexia but also to impaired digestive functioning. The present study was conducted to explore how perioperative nutritional treatment affects nutritional status and postoperative outcome in patients with oesophageal, gastric or pancreatic cancer. The study design was retrospective and observational. Forty-seven cases and fifty-six historical controls with mean age 64 ± 9.5 (41-82) were included. Cases received individual nutritional treatment preoperatively, during admission for surgery and after discharge by a dietician (February 2009 to March 2010). Historical controls were only visited by a dietician after surgery and received limited follow up by phone (January 2006 to December 2008). The Mann-Whitney test and Chi-square test or Fisher's exact test were used to compare nutritional status, postoperative complications, postoperative nutritional related problems and length of hospital stay. To assess predictor variables of postoperative complications univariate and stepwise forward multivariate linear regression analysis was conducted. Results are expressed as mean ± SD. A $p<0.05$ was considered significant. Cases sustained weight (0.27 kg ± 2.9; NS), whereas historical controls lost weight before surgery (-3.2 kg ± 3.7; p=0.001) (case vs. control: p= 0.002). Postoperative weight loss (2 weeks until 3 months after surgery) was more limited in cases (-2.1 kg ± 3.6; p=0.008), than in historical controls (-3.6 kg ± 4.1; p=0.001) (case vs. control: p=0.05). Cases experienced less postoperative complications (0.8 ± 0.8 vs. 1.6 ± 1.4; p=0.02), less postoperative nutritional related problems (1.3 ± 1.0 vs. 1.8 ± 1.0; p=0.03) and a shorter hospital stay (16 ± 19.7 days vs. 22.5 ± 19.6 days; p=0.05) than historical controls. Linear regression analysis confirmed the association between perioperative nutritional treatment and decreased number of postoperative complications (β: -0.72 ± 0.24 (95%CI:-1.19,-0.26); p=0.003).
In conclusion, the results of this exploratory study support the hypothesis that perioperative nutritional treatment by a dietician improves nutritional status and postoperative outcome in oesophageal, gastric and pancreatic cancer patients. A large prospective randomized, controlled trial would be warranted to confirm these results. However, such a study may be unethical to conduct.

DRIFT: The Dutch online Registry of Intestinal Failure and Intestinal Transplantation

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Rationale Chronic administration of total parenteral nutrition (TPN) enables patients with irreversible intestinal failure (IF) to survive. Complications, however, occur frequently and cause substantial morbidity and mortality. Intestinal transplantation (ITx) has evolved into a clinically feasible alternative treatment. Caregiver expertise and timely referral are key factors determining the outcome after ITx. DRIFT is developed by the Dutch Working group for IF (represented by the Dutch Home TPN Centers and the ITx Center) to monitor individual patients nationwide to improve the quality of care and warrant timely referral for ITx. (Inter)national on registration contributes to the establishment of a database for research and quality control with the aim to establish (inter)national guidelines for IF and ITx. Methods: DRIFT is a web-based, English-language database tracking IF-specific clinical patient data (pediatric and adult), including quality of life (QoL). DRIFT warrants directly available, complete, update patient information. The on forum for professionals aids the complex decision-making and correspondence through a PDF letter-creating function. Evidence-based care protocols are available for standardization of care. The website allows patients to access disease-related information, peer-group contact and completion of IF-specific QoL questionnaires to screen general well-being. Results: International experienced groups were consulted. After consensus on content and requirements, the software was developed. Patient-data safety was ensured according to ISO-27001 standards. DRIFT is available on (www.darmfalen.nl). Data of the Dutch IF and ITx population are entered. The IF-specific QoL questionnaire 'the burden measurer' is being validated internationally.
Conclusion: DRIFT is established to optimize IF management in the Netherlands and to promote universal care standards for TPN and ITx. The registration can be applied internationally to facilitate and improve the outcome of IF and ITx.

Plattegrond

Alfabetische lijst van standhouders B = Beneluxhal K = Kempenhal	*Standnummer*
Abbott BV	B 21
Acertys	K 5
Alvleesklliervereniging	B 34
AstraZeneca BV	B 20
Baxter	K 14
Boston Scientific Nederland B.V.	K 4
Bristol Myers Sqibb	B 9
Brunschwig Chemie BV / Lans medical	B 25
CameraPil BV	B 6
Cobra Medical B.V.	K 8
COOK Medical	K 16
Crohn&Colitis Ulcerosa ver.Nederland	B 30
Dr. Falk Pharma benelux B.V.	B 1
Dutoit Medical	B 13
Endomed B.V.	B 26
Endotechniek	B 3
Ferring B.V.	B 19
FMH Endoscopy B.V.	K 6
Fresenius Kabi Nederland B.V.	B 28
Getinge bv	B 14
Gilead Sciences Netherlands BV	B 10
Hitachi Medical Systems	B 16
Jansen Medicars BV	B 2
Janssen-Cilag B.V.	K 17
Medical Measurements Systems B.V.	B 24
Medicor	B 7
Mindray Medical	K 12
Minigrip Nederland BV	B 23
Minntech B.V.	B 8
Movetis	K 9
MTW-Endoskopie	K 7
Nederlandse Coeliakie Vereniging	B 29
Norgine	B 17
Novymed	K 1
NVFB	K 18
Olympus	K 11
Pentax Medical	B 15
Pfizer	B 4
PMT Partners Medische Techniek BV	B 11
Rescope BV	K 10
Roche Nederland BV	B 22
RVC B.V.	B 12
Schering Plough B.V.	K 19
Stichting Opsporing Erfelijke Tumoren	B 32
Stichting Vreemde Kronkels	B 33
Stöpler Instrumenten & Apparaten B.V.	K 13
TMI	K 15
TRAMEDICO B.V.	K 2
VCM Medical	B 18
Vereniging Ziekte van Hirschsprung	B 31
Vifor Pharma Nederland B.V.	K 20
Wassenburg Medical Devices B.V.	K 3

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