5ème Journée et Prix de la Recherche Clinique

Jeudi 31 mai 2012
13h30 – 18h30

HUG – Site Cluse-Roseraie
Salle Opéra, niveau 0

Programme final
et
Recueil des résumés

UNIVERSITÉ DE GENÈVE
FACULTÉ DE MÉDECINE

CRC Centre de Recherche Clinique

HUG Hôpitaux Universitaires de Genève

PROGRAMME

13h30 Introduction
Pr. Henri Bounameaux, Doyen de la Faculté de médecine de l'Université de Genève

13h45 Présentations orales – Partie I (9 minutes de présentation, suivie de 3 minutes de discussion)
Modérateur: Pr. Henri Bounameaux

13h45	Dr T. Chevalley:	**Fractures During Childhood and Adolescence in Healthy Boys: Relation with Bone Mass, Microstructure and Strength**
13h57	Dr G. Ehret:	**Genetic variants in novel pathways influence blood pressure and cardiovascular disease risk**
14h09	Dr A. Finckh:	**Adalimumab in acute sciatica reduces the long-term need for surgery: A three-year follow-up of a randomized double blind placebo controlled trial**
14h21	Dr P. Merlani:	**Burnout in ICU caregivers: A multicenter study of factors associated to centers**
14h33	Dre B. Martinez de Tejada:	**Prevention of preterm delivery with vaginal progesterone in women with preterm labor. Results of the intermediary analyses**
14h45	Pr B. Hirschel:	**Commentaire: Deux problèmes fréquents: recrutement et « futilité »**

15h00 Visite des posters et vote du public du meilleur poster
Café et douceurs à disposition

16h15 Présentations orales – Partie II
Modérateur: Pr. Jérôme Pugin, Vice-doyen à la recherche de la Faculté de médecine de l'Université de Genève

16h15	Dre F. Gumy-Pause:	**GSTP1 Hypermethylation is Associated with Reduced Protein Expression, Aggressive Disease and Prognosis in Neuroblastoma**
16h27	Dr S. Vulliemoz:	**Electroencephalographic source imaging: a prospective study of 152 operated epileptic patients**
16h39	Dr H. Miozzari:	**Prospective randomised study comparing screw versus helical blade in the treatment of low-energy trochanteric fractures**
16h51	Dr J.-L. Reny:	**Antiplatelet drug response status does not predict recurrent ischemic events in stable cardiovascular patients: results of the ADRIE study**
17h03	Dr L. Spahr:	**A capillary blood ammonia bedside test following glutamine load to improve the diagnosis of hepatic encephalopathy in cirrhosis**
17h15	Dr P. Makrythanasis:	**Consanguinity as a means to identify pathogenic recessive mutations**

17h30 Conférence par **Le Professeur Michel Kazatchkine**, Directeur exécutif du Fonds mondial de lutte contre le sida, la tuberculose et le paludisme :
2002 -2012 : dix ans de progrès sans précédent dans la lutte contre le sida, le paludisme et la tuberculose dans le monde en développement.

18h10 Remise des Prix de la Recherche 2012 et du prix du meilleur poster et clôture de la journée par le Pr Pierre Dayer, Directeur médical

18h20 Apéritif

MOT DE BIENVENUE

Cher(e) Collègue,

La Journée de la recherche clinique est dorénavant bien établie dans le programme des manifestations de notre institution : elle a lieu un jeudi du mois de mai et reflète l'activité de recherche par l'intermédiaire des contributions soumises.
Un jury dirigé par le Pr Th. Berney a choisi les résumés qui seront présentés oralement et parmi ces résumés, celui qui recevra le Prix de la recherche clinique 2012. Mais ce n'est pas seulement le Jury du Prix qui peut voter mais également vous, le public, qui choisirez le meilleur poster. Pour que votre choix soit informé, les auteurs des posters seront tous présents pendant la visite entre 15h00 et 16h15 et répondront à vos questions.

Les présentations orales seront suivies par la Conférence du Professeur Michel Kazatchkine Directeur exécutif du Fonds mondial de lutte contre le sida, la tuberculose et le paludisme :

2002-2012 : dix ans de progrès sans précédent dans la lutte contre le sida, le paludisme et la tuberculose dans le monde en développement

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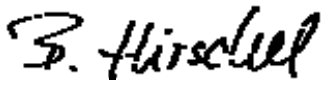
Comme d'habitude, la distribution des prix par le Directeur médical, le Pr Pierre Dayer, clôturera la journée.

Je me réjouis de vous voir nombreux le 31 mai 2012 !



Centre de recherche clinique

INFORMATION GENERALE

Qui participe?

Tous les chercheurs des HUG et de la Faculté de médecine ayant terminé récemment un projet de recherche clinique dont les résultats sont directement applicables aux soins ou aux patients.
65 recherches provenant de services très variés ont été soumises pour cette cinquième édition.

Le jury :

Pr Thierry Berney, chirurgie (Président)
Pr François Pralong, pour le CHUV
Pr Claudine Burton-Jeangros, pour l'Université de Genève, section de sociologie
Pr Antoine Hadengue, gastro-entérologie
Pr Gilles Bertschy, psychiatrie
Pr Jean-Paul Vallée, radiologie
Pr Michel Boulvain, gynécologie-obstétrique
Dr Patrice Lalive d'Epinay, neurosciences

Le jury a sélectionné les recherches présentées par oral et a désigné l'équipe de recherche lauréate du Prix.

Le Prix de la recherche clinique :

Un diplôme ainsi qu'une somme de CHF 1'000.- sont décernés aux auteurs.

Le Prix du meilleur poster :

Un prix sera attribué au meilleur poster assorti d'une somme de 1'000.- francs, décerné par vote du public.

Pour toute information sur la Journée de la recherche clinique:
corinne.chaudet@hcuge.ch, tél. 022 372 98 08 / 91 34

RECUEIL DES RESUMES

PRESENTATIONS ORALES

ORDRE SELON LE PROGRAMME

FRACTURES DURING CHILDHOOD AND ADOLESCENCE IN HEALTHY BOYS: RELATION WITH BONE MASS, MICROSTRUCTURE AND STRENGTH

Thierry Chevalley *Jean-Philippe Bonjour Serge Ferrari René Rizzoli*
Service des maladies osseuses - HUG

Introduction: In healthy boys, fractures (fx) result from various severity trauma, suggesting contribution of an intrinsic biomechanical fragility. Objectives: To characterize bone mineral mass, microstructure and strength in boys with and without fx.
Méthode: Participants, Design: 176 healthy boys followed from 7.4±0.5 to 15.2±0.5 (±SD) yrs of age. Outcomes: Areal(a) bone mineral density(BMD) measured by DXA at radius(R) metaphysis and diaphysis, total hip, femoral neck(FN) and diaphysis, L2-L4 vertebrae. Volumetric(v) BMD and microstructure assessed by high resolution peripheral computerized tomography(HR-pQCT) at both distal tibia(DT) and radius(DR). Bone strength evaluated by micro-finite element analysis(µFEA).
Résultat: 156 fx were recorded in 87/176 boys with peak incidence between 10 and 13 yrs. At 7.4 yrs, subjects with fx had lower aBMD in all sites, and at 15.2 yrs in femoral and spinal, but not in R sites. At that age, boys with fx displayed lower trabecular (Tb) vBMD (P = 0.029) and number (P=0.040), stiffness (P=0.024) and failure load (P=0.016) at DT, but not DR. Odds ratios of fx risk per 1 SD decrease was 1.80 (P=0.006) for FN aBMD and 1.46 (P=0.038) for DT Tb vBMD, 1.59 (P=0.031) for Tb Number, 1.53 (P=0.072) for Stiffness, and 1.60 (P=0.056) for Failure Load.
Conclusion: In an homogeneous cohort of healthy boys, fractures recorded until 15.2±05 yrs of age were associated with lower femoral neck aBMD and with lower distal tibia trabecular vBMD and number, stiffness and failure load. These deficits in bone mineral mass, microstructure and strength could contribute to the occurence of fractures during growth.

GENETIC VARIANTS IN NOVEL PATHWAYS INFLUENCE BLOOD PRESSURE AND CARDIOVASCULAR DISEASE RISK

Georg B. Ehret *on behalf of ICBP.*
Service de Cardiologie - HUG

Introduction: Blood pressure is a heritable trait influenced by several biological pathways and responsive to environmental stimuli. Over one billion people worldwide have hypertension (>=140 mm Hg systolic blood pressure or >=90 mm Hg diastolic blood pressure). Even small increments in blood pressure are associated with an increased risk of cardiovascular events.
Méthode: This genome-wide association study of systolic and diastolic blood pressure, which used a multi-stage design in 200,000 individuals of European descent, identified sixteen novel loci.
Résultat: Six of these loci contain genes previously known or suspected to regulate blood pressure (GUCY1A3–GUCY1B3, NPR3–C5orf23, ADM, FURIN–FES, GOSR2, GNAS–EDN3); the other ten provide new clues to blood pressure physiology. A genetic risk score based on 29 genome- wide significant variants was associated with hypertension, left ventricular wall thickness, stroke and coronary artery disease, but not kidney disease or kidney function. We also observed associations with blood pressure in East Asian, South Asian and African ancestry individuals.
Conclusion: Our findings provide new insights into the genetics and biology of blood pressure, and suggest potential novel therapeutic pathways for cardiovascular disease prevention. (doi:10.1038/nature10405)

ADALIMUMAB IN ACUTE SCIATICA REDUCES THE LONG-TERM NEED FOR SURGERY: A THREE-YEAR FOLLOW-UP OF A RANDOMIZED DOUBLE BLIND PLACEBO CONTROLLED TRIAL

Stéphane Genevay *(1), Axel Finckh (1), Pascal Zufferey (2) Sébastien Viatte (3) Federico Balagué (4) Cem Gabay (1)*

1.- service de rhumatologie HUG 2.- service de rhumatologie CHUV 3.- Scool of translational medicine, UK 4.- Service de rhumatologie HFR

Introduction: Nous avions montré que 2 injections sous-cutanée d'adalimumab (Humira), administrée précocement chez des patients souffrant de lombosciatique aiguë sévère avait un effet favorable sur le nombre d'interventions chirurgicales effectuées à 6 mois. Un suivi à 3 ans de cette étude randomisée, contrôlée contre placebo a pour but de déterminer si cet effet persiste au cours du temps.
Méthode: L'issue primaire de cette étude est le recours à la chirurgie pour traiter la lombosciatique. En moyenne 3 ans après la randomisation, une information fiable a pu être obtenue chez 56/61 (93%) patients initialement randomisés. Les facteurs prédisposant à cette intervention ont été analysé à l'aide d'un modèle multivarié (Multivariate Cox proportional hazard models).
Résultat: 23 (41%) patients avait subit une chirurgie, 8/29 (28%) dans le groupe adalimumab versus 15/27 (56%) dans le groupe placebo, p= 0.036. L'adalimumab a réduit le risque de chirurgie de 61% [hazard ratio (HR) : 0.39 (95%CI: 0.17-0.92)]. En analyse multivariée, l'administration d'adalimumab reste le facteur le plus important déterminant le recours à la chirurgie (HR 0.17, p = 0.002). Les autres facteurs d'influence sont : la corrélation radio-clinique (HR = 11.6, p = 0.04), l'intensité initiale de la douleur de la jambe (HR = 1.3, p= 0.06) et du dos (HR = 1.4, p = 0.03), et la durée de l'arrêt de travail (HR=1.01 par jour, p = 0.03).
Conclusion: Un bref traitement d'adalimumab permet de diminuer le recours à la chirurgie chez les patients souffrant d'une lombosciatique aigüe sévère

BURNOUT IN ICU CAREGIVERS: A MULTICENTER STUDY OF FACTORS ASSOCIATED TO CENTERS

Paolo Merlani*, Mélanie Verdon, Adrian Businger*, Guido Domenighetti†, Hans Pargger*, Bara Ricou and the STRESI+ group*

Service of Intensive Care, Department of Anesthesiology, Pharmacology and Intensive Care, Geneva University Hospitals and the University of Geneva, *Division of Operative Intensive care, Department of Anesthesia and Intensive care, University Hospital of Basel, †Multidisciplinary intensive care, Regional Hospital of Locarno, Switzerland.

Introduction: The stressful work environment of ICUs can lead to burnout. Burnout can impact on the welfare and performance of caregivers, and may lead them to resign from their job. The shortage of ICU caregivers is becoming a real threat for health care leaders. The objective of this study was to investigate the factors associated with burnout on a national level in order to determine potential important factors.
Méthode: A prospective, multicenter, observational survey of all caregivers from 74 of the 92 Swiss ICUs was led from March 2006 to April 2007.
Résultat: Out of the 4322 questionnaires distributed, 3052 (71%) were returned, with a response rate of 72% by center, 69% from nurse-assistants, 73% from nurses and 69% from physicians. A high proportion of female nurses among the team was associated with a decreased individual risk of high burnout (OR 0.98, 95% CI:0.97-0.99 for every %). The caregiver-related factors associated with a high risk of burnout were being a nurse-assistant, being a male, having no children and being under 40 years old.
Conclusion: The findings of this study seem to open a new frontier concerning burnout in ICUs, highlighting the importance of team composition. Our results should be confirmed in a prospective multicenter, multinational study. Whether our results can be exported to other medical settings where team-working is pivotal remains to be investigated. Grants: This work was supported by the Swiss Society of Intensive Care Medicine and Departmental funds of Anesthesiology, Pharmacology and Intensive Care of Geneva University Hospitals.

PREVENTION OF PRETERM DELIVERY WITH VAGINAL PROGESTERONE IN WOMEN WITH PRETERM LABOR. RESULTS OF THE INTERMEDIARY ANALYSES.

B. Martinez de Tejada
Dept. Gynécologie obstétrique des HUG pour le groupe 4P

Introduction: Prematurity is a leading cause of neonatal morbidity and mortality. The medical, psychological, and economic burdens of preterm births are very important.
Progesterone (**P**) is the primary factor of uterine quiescence that permits the physical distension of the uterine muscle throughout pregnancy. The use of **P** for prevention of preterm birth in women with preterm labor has not been evaluated. Our main objective is to assess whether the use of vaginal **P** in women with preterm labor reduces the risk of preterm birth before 37 weeks of gestation. Secondary endpoints are to show that **P** 1) reduces preterm birth before 32 and before 34 weeks of gestation 2) reduces the number of recurring episodes of preterm labor and 3) reduces neonatal mortality and morbidity.
Méthode: International (Switzerland & Argentina), multicenter, prospective, double-blind randomized placebo-controlled trial comparing the administration of vaginal natural progesterone to the administration of placebo in women hospitalized and treated for preterm labor ($24^{0/7}$ to $33^{6/7}$ weeks). Estimated sample size: 626 women. An intermediate analysis will be performed after inclusion of 300 patients. The criteria to stop the study are those described by O'Brien and Fleming (p value < 0.015 for the primary outcome).
Résultat: We analyzed date from 302 women (Switzerland: 164 from 2006 and Argentina: 138 from 2010) with data concerning delivery: Rates of preterm delivery in the whole population were: 37% at <37 w., 16.2% at <34 w. and 9.8% at < 32 weeks. Rates of preterm at <37 w.,<34 w. and < 32 weeks in women on **P** compared to women on placebo were, 44.1% vs. 33.8%; *p*:0.07; 21.4% vs. 11.5%; *p*:0.03 and 13.1% vs. 7.6%; *p*:0.1, respectively. Neonatal morbidity-mortality [**P**: 38(26.5%) vs. Placebo: 34(22.4%): *p*:0.42] and local side effects [**P**:11(7.4%) vs Placebo: 12(7.5%); *p*: 1] were similar between groups. Using different scenarios, we have calculated that the probability to conclude, at the end of the study, to a positive effect of **P** in the prevention of preterm birth is 0%.
Conclusion: Based of these results, we have decided to interrupt the inclusion of cases in the study. We have shown that progesterone is not efficacious in preventing preterm delivery among women with preterm labor

GSTP1 HYPERMETHYLATION IS ASSOCIATED WITH REDUCED PROTEIN EXPRESSION, AGGRESSIVE DISEASE AND PROGNOSIS IN NEUROBLASTOMA

Fabienne Gumy-Pause1*, Bruno Pardo2, Mary Khoshbeen-Boudal, Marc Ansari1 Angele Gayet-Ageron3, Andre-Pascal Sappino4, Edward F. Attiyeh5, and Hulya Ozsahin1*
1Department of Pediatrics, University Hospital of Geneva, 2Department of Genetics and Laboratory Medicine, University Hospital of Geneva,3Clinical Research Center, Division of Clinical Epidemiology, Department of Community Health and Medecine, University Hospital of Geneva, 4Clinique des Grangettes, Geneva, 5Department of Pediatrics, University of Pennsylvania School of Medicine, Philadelphia, PA, USA

Introduction: Neuroblastoma (NB) is the most common malignant disease of infancy. The clinical hallmark of this tumor is the marked variability in prognosis depending on the age, stage and biological characteristics. Aberrant methylation of CpG-islands in tumor-suppressor genes has been associated with tumor development. The aim of this project was to determine the methylation status of 35 different genes in NB cell lines and tumor samples (NBs).
Méthode: Using MS-MLPA method, we analyzed 35 different genes in 16 NB cell lines and 50 NBs, and investigated whether specific hypermethylation was associated with biological/clinical parameters. The effect of GSTP1 hypermethylation on mRNA and protein expression was also explored.
Résultat: The median number of hypermethylated genes was higher in cell lines compared to NBs (5.5 vs. 2). For 8 genes, aberrant methylation of CpG-islands in NB was not (ESR1, PAX5, WT1, CADM1, MSH6, CDKN2B) or very rarely (CDH13, GSTP1) reported in literature. GSTP1 was found hypermethylated in 33% of the stage 4-11qLOH-nonMYCN-amplified high risk NBs. Hypermethylation was correlated with reduced mRNA and protein expression. In the whole NBs cohort, GSTP1 hypermethylation was less frequently detected (8%), but found to be associated with lower event-free (EFS) and overall survival. Hypermethylation of GSTP1 showed also association with lower EFS in high risk subgroups as stage 4 and older patients.
Conclusion: Our results suggest that, as in several adult cancers, aberrant methylation of GSTP1 may contribute to the carcinogenetic process in NB and could be potentially used as a new marker leading to define an ultra-high risk subgroup.

ELECTROENCEPHALOGRAPHIC SOURCE IMAGING: A PROSPECTIVE STUDY OF 152 OPERATED EPILEPTIC PATIENTS

*Verena Brodbeck , **Serge Vulliemoz**, Agustina Lascano, Laurent Spinelli, Maria-Isabel Vargas, Claudio Pollo, Karl Schaller, Christoph M Michel, Margitta Seeck*
Epilepsy Unit, Neurology Clinic, University Hospital and University of Geneva, Switzerland Department of Radiology, University Hospital of Geneva, Geneva, Switzerland Department of Neurosurgery, University Hospital (CHUV), Lausanne, Switzerland Department of Neurosurgery, University Hospital of Geneva, Geneva, Switzerland Functional Brain Mapping Laboratory, Neurology Clinic and Department of Fundamental Neuroscience, University Hospital and University Medical Centre, University of Geneva, Switzerland

Introduction: In patients with drug-resistant epilepsy who are candidate for surgery, non-invasive functional imaging methods are helpful in guiding surgical resections. Our main aim was to determine localisation precision of the epileptogenic focus with electric source imaging (ESI) and to compare it to other well-established imaging tools.
Méthode: 152 pharmaco-resistant epileptic patients with more than one year post-operative follow-up were included. Sensitivity (defined as % of seizure free patients with focus localization within the resected zone) and specificity (defined as % of patients with focus localization outside the operated area) of different techniques was assessed: ESI, magnetic resonance imaging (MRI), positron emission tomography (PET) and single-photon emission-computed tomography (SPECT).
Résultat: A total of 43 patients underwent all examinations. High-resolution ESI (>64 electrodes) using individual MRI as a head model rendered the highest sensitivity (80%) and, principally, specificity rate (88%), followed by MRI (71.4% and 50%), PET (62.9% and 37.5%) and SPECT (54.3% but a higher specificity as compared to MRI and PET of 62.5%). The sensitivity of ESI was high in both temporal and extratemporal lobe epilepsy (91 and 75%, resp). The chance ot becoming seizure-free if the focus source maximum is resected was 97%.
Conclusion: From a clinical perspective, ESI is a very attractive non-invasive technique with a high localization yield which provides high temporal resolution in the millisecond range, as compared to methods based on changes in metabolic or vascular correlates of neural activity. From a practical perspective, it does not require sedation, it can be performed at bedside and is suitable for the pediatric population and cognitively impaired patients.

PROSPECTIVE RANDOMISED STUDY COMPARING SCREW VERSUS HELICAL BLADE IN THE TREATMENT OF LOW-ENERGY TROCHANTERIC FRACTURES

***Hermes Miozzari**, Richard Stern, Anne Lübbeke, Domizio Suva, Pierre Hoffmeyer*
Service Orthopédie et traumatologie de l'appareil moteur - HUG

Introduction: The purpose of this study was to compare femoral head placement, rates of reoperation and cephalic implant cut-out of a screw versus a blade for patients over age 60 with low energy trochanteric fractures (AO/OTA 31-A1, A2, and A3) treated either with sliding hip screw or cephalomedullary nail.
Méthode: After surgeon selection of either hip screw or nail, hip screw patients were randomised to either a DHS (dynamic hip system screw) or DHS blade (dynamic hip system blade), while nail patients were randomised to either a Gamma3 Trochanteric Nail or a PFNA (proximal femoral nail antirotation). This resulted in a screw group (DHS and Gamma nail), and a blade group (DHS blade and PFNA). Outcome measures included tip-apex distance and zone location of the cephalic implant, as well as reoperation and implant cut-out within the first postoperative year.
Résultat: A total of 335 patients were randomised, 172 to a screw and 163 to a blade. There was no significant difference concerning mean tip-apex distance, percentage of patients with a tip-apex distance >25 mm, and patients with a centre–centre position of the cephalic implant. There were 137 patients in the screw group and 132 in the blade group available for follow-up. They did not differ regarding rates of reoperation or cut-out (screw group=2.9%; blade group=1.5%).
Conclusion: Both a screw and a blade performed! equally well in terms of implant placement in the femoral head and outcome

ANTIPLATELET DRUG RESPONSE STATUS DOES NOT PREDICT RECURRENT ISCHEMIC EVENTS IN STABLE CARDIOVASCULAR PATIENTS: RESULTS OF THE ADRIE STUDY

Jl Reny, P. Berdague, A. Poncet, I. Barazer, S. Nolli, P. Fabbro Peray, JF Schved, H. Bounameaux, F. Bach, P. De Moerloose, P. Fontana
SMIG ANGIOLOGIE HEMOSTASE CARDIOLOGIE

Introduction: The biological response to antiplatelet drugs has repeatedly been shown to predict the recurrence of major adverse cardiovascular events (MACE). However, most studies involved coronary artery disease patients with recent vessel injury, shortly after the initiation of antiplatelet therapy. Data on stable cardiovascular (CV) patients are scarce, and the added predictive value of specific assays (the VASP assay for the clopidogrel response and serum thromboxane B2 for the aspirin response) and aggregation-based assays relative to common predicto! rs has rarely been addressed.
Méthode: Stable CV outpatients participating in the ADRIE study (n=771) were tested twice, at two separate visits, with specific and aggregation-based assays. Follow-up lasted 3 years, and fewer than 1% of patients were lost to follow-up. MACE were adjudicated by an independent committee. Multivariate survival analyses included relevant variables identified in univariate analysis and platelet function test results. The C-index was used to express the prognostic value of various multivariate models.
Résultat: MACE, the primary endpoint, occurred in 16% of patients. Hypertension, smoking, older age and elevated LDL cholesterol were predictive of MACE recurrence, with a c-index of 0.63 (P
Conclusion: Biological antiplatelet drug responsiveness, measured with specific or aggregation-based assays, has no incremental predictive value over common CV risk factors for MACE recurrence in stable CV outpatients. These results do not support platelet function testing for MACE risk evaluation in stable CV patients. Circulation 2012, in press

A CAPILLARY BLOOD AMMONIA BEDSIDE TEST FOLLOWING GLUTAMINE LOAD TO IMPROVE THE DIAGNOSIS OF HEPATIC ENCEPHALOPATHY IN CIRRHOSIS

Saskia Ditishein, Emiliano Giostra, Pierre R Burkhard, Nicolas Goossens, Gilles Mentha, Antoine Hadengue, **Laurent Spahr**
Gastroentérologie, Neurologie, Transplantation - HUG

Introduction: L'encéphalopathie hépatique (EH) est une complication grave de la cirrhose affectant la qualité de vie. Le diagnostic peut être difficile dans les formes subcliniques. L'ammoniémie dans le sang veineux est peu fiable
Méthode: 57 patients atteints de cirrhose (âge 56 ans, cirrhose alcoolique n =42) sans signes évidents d'EH lors de l\'examen) et 13 sujets sains ont été étudiés. Des tests psychométriques et une mesure de l'ammoniémie dans le sang capillaire ont été effectués au temps 0', 30', et 60' après une charge orale en glutamine.
Résultat: L'ammoniémie capillaire était plus élevée à 0, 30 et 60' que chez les contrôles. Le test de provocation a permis de démasquer à 60' une EH chez 23% des patients. La performance diagnostique de l'ammoniémie capillaire à T0 montrait une AUC (aire sous la courbe) de 0.541, et à 60' de 0.727
Conclusion: L'hyperammoniémie provoquée par voie orale chez le cirrhotique sans signes cliniques d'EH améliore la performance diagnostique de l'EH subclinique. L'ammoniémie, même capillaire, reste toutefois un test peu performant pour faire le diagnostic d' une EH

CONSANGUINITY AS A MEANS TO IDENTIFY PATHOGENIC RECESSIVE MUTATIONS

P. Makrythanasis1, *M. Nelis1, M. Guipponi2, A. Vannier1, F.A. Santoni1, F. Béna2, S. Gimelli2, E. Stathaki2, G. Duriaux-Sail1, S. Temtamy3, A. Megarbane4, M. Aglan3, M.S. Zaki3, S. Fokstuen2, L. Gwanmesia2, A. Bottani2, K. Aliferis2, A. Masri5, S. Psoni6, S. Kitsiou6, H. Fryssira6, E. Kanavakis6, N. Al-Allawi7, A Sefiani8, S. Al-Hait9, S. Elalaoui8, N. Jalkh4, L. Al-Gazali10,11, F. Al-Jasmi10,11, H. Chaabouni Bouhamed 12 H. Hamamy1, S.E. Antonarakis1,2*

1Department of Genetic Medicine and Development, University of Geneva, Geneva, Switzerland, 2Service of Genetic Medicine, University Hospitals of Geneva, Geneva, Switzerland, 3Department of Clinical Genetics, National Research Centre, Cairo, Egypt, 4Medical Genetics Unit, Saint Joseph University, Beirut, Lebanon, 5Pediatric Department, Jordan University Hospital, Amman, Jordan, 6Department of Medical Genetics, University of Athens, Athens, Greece, 7Department of Pathology, College of Medicine, University of Dohuk, Dohuk, Iraq, 8Département de génétique médicale, Institut National d'Hygiène, Rabat ,Morocco, 9Genetic Clinic, Al Amal Maternity Hospital, Amman, Jordan, 10Department of Paediatrics, Faculty of Medicine and Health Sciences, United Arab Emirates University, Al-Ain, United Arab Emirates, 11Department of Pediatrics, Tawam Hospital, United Arab Emirates University, Al-Ain, United Arab Emirates, 12Department of Human Genetics, University Tunis El Manar, Faculty of Medicine, Tunis, Tunisia

Introduction: Consanguinity and inbreeding increase the sharing of alleles among individuals. We have initiated a project to collect samples from families with recessive phenotypes in consanguineous families, in order to identify the functional genomic variation responsible for the disease. Any phenotype and family history compatible with autosomal recessive inheritance (and unknown molecular defect) is candidate for participation in the study.

Méthode: Forty two families of different ethnic background have already been collected. From each family, blood DNA from the patient(s), all unaffected siblings, and the parents is extracted. Samples from one or more of the affected individuals per family are first analyzed by array-CGH 400K for the detection of homozygous deletions. Then the samples of all family members are genotyped with a dense SNP array in order to identify Runs of Homozygosity (ROH), allowing the definition of chromosomal regions likely to contain the responsible genes. Finally exome sequencing is performed in one affected individual per family. Variants are called using publically available tools and filtered according to polymorphic SNVs deposited in public databases and predicted pathogenicity.

Résultat: In the first part of our project we have analyzed twenty families using this approach. Causative variations of known disease genes have been identified in three families (VLDLR, FKTN and DMP1). In 8 additional families candidate genes have been identified.

Conclusion: Exome sequencing has become one of the main tools in the research of genetic disorders and the accumulating evidence from this and other studies shows that it will soon be available for clinical purposes.

PRESENTATIONS POSTERS

EN ORDRE ALPHABETIQUE SELON LE NOM DE L'AUTEUR QUI A SOUMIS

P1

PARAOXONASE-1 PATHWAY IS NOT A MAJOR BIOACTIVATION PATHWAY OF CLOPIDOGREL IN VITRO

Virginie Ancrenaz, *Jules Desmeules, Richard James, Pierre Fontana, Jean-Luc Reny, Pierre Dayer, Youssef Daali*
Pharmacologie et Toxicologie cliniques –Diabétologie - HUG

Introduction: Clopidogrel is a prodrug bioactivated by cytochrome P450s (CYPs). More recently, paraoxonase-1 (PON1) has been proposed as a major contributor for clopidogrel metabolism. The purpose of this study was to assess the relative contribution of CYPs and PON1 in clopidogrel metabolism in vitro.
Méthode: Clopidogrel metabolism was studied in human serum, recombinant PON1 enzyme (rePON1), pooled human liver microsomes (HLMs), HLMs with the CYP2C19*1/*1 genotype and HLMs with the CYP2C19*2/*2 genotype. Inhibition studies were also performed using specific CYP inhibitors and antibodies. Clopidogrel and its metabolites were measured using LC-MS/MS method.
Résultat: PON1 activity (mean ± SD) was 295 ± 28.5 U/mL, 2.01 ± 0.1 U/mg, 1.99 ± 0.04 U/mg and 2.0 ± 0.04 U/mg in human serum, pooled HLMs, HLMs with CYP2C19*1/*1genotype, and HLMs with CYP2C19*2/*2 genotype, respectively. Production of clopidogrel active metabolite (clopidogrel-AM) from 2-oxo-clopidogrel in pooled HLMs was approximately 500 times that in serum. When 2-oxo-clopidogrel was incubated with rePON1, clopidogrel-AM was not detected. Clopidogrel-AM production from 2-oxo-clopidogrel was lower in CYP2C19*2/*2 HLMs compared to CYP2C19*1/*1 HLMs (Vmax= 18.4 ± 0.96 pmol/min/mg vs. 4.1 ± 0.08 pmol/min/mg) while PON1 activity in HLMs with both genotypes was similar. Moreover, incubation with inhibitors of CYP3A, CYP2B6 and CYP2C19 significantly reduced clopidogrel bioactivation while a PON1 inhibitor, EDTA, had only a weak inhibitory effect.
Conclusion: This in vitro study shows that contribution by PON1 in clopidogrel metabolism is limited at clinically relevant concentrations. Moreover, CYP2C19, CYP2B6, and CYP3A play important roles in the bioactivation of clopidogrel.

P2

IMPACT OF MESENCHYMAL STEM CELLS TRANSFUSION ON THROMBOTIC MICROANGIOPATHY POST HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Introduction: Thrombotic microangiopathy (TAM) post hematopoietic stem cell transplantation (HSCT) has an incidence of 13%, and is a life-threatening complication. Manifestations include thrombocytopenia, microangiopathic hemolysis, renal dysfunction with neurological complications. The risk factors include: female gender, TBI, lymphoid malignancy, unrelated or mismatched donor, calcineurin inhibitors, presence of infection and graft-versus-host disease (GvHD). There is no consensus for treatment of post-transplantation TAM.
Méthode: 9-year-old girl with aplastic anemia received an HSCT (9/10) with HLA-Cw mismatch. The conditioning regimen included fludarabine, cyclophosphamide and ATG. Cyclosporine (CSA) was administered to prevent GvHD. The graft was T-cell depleted with Campath-1H in vitro followed by an addback of CD3+ cells. On day+2 she developed a Coomb's negative anemia, with schistocytes, elevate! d LDH, thrombocytopenia with an acute renal failure. The renal biopsy confirmed TAM. She developed a grade III intestinal GvHD. The TAM was treated with plasma exchange, basiliximab, anti-TNF, heparin, and defibrotide. CSA was replaced with methylprednisolone/sirolimus. None of these drugs decreased TAM intensity. The clinical status worsened with CMV, HHV-6 reactivation, cardiac and pleural effusions. Considering TAM as a form of GvHD, allogenic mismatched third pary mesenchymal stem cell (MSC) were infused.
Résultat: Two weeks later, the biological parameters went back to normal without any need of transfusional support. The biological signs of TAM reappeared 10 weeks after MSC infusion, associated with viral reactivation, pleural and cardiac effusions.
Conclusion: This case illustrates a possible benefit of MSC infusion for the treatment of TAM. The timing of administration, the quantity and the number of doses is not defined yet.

P3

LA SPONGIOSE EPIDERMIQUE RESULTE D\'UNE SURPRODUCTION DU HYALURONATE, DUE A UNE SURACTIVATION DE HYALURONATE SYNTHASE 3 (HAS3) ET DE CD44 DANS LES LESIONS ECZEMATIFORMES.

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Introduction: L'eczéma se traduit au niveau épidermique par une spongiose induisant une désolidarisation des kératinocytes à cause d'une accumulation de liquide dans l'espace intercellulaire dans l'épiderme. Cette infiltration laisse supposer que les enzymes de type hyaluronate synthase (HAS) 1,2,3 en sont à l'origine via le hyaluronate (HA), une molécule avec une forte capacité de rétention d'eau, qu'elles sécrètent dans le milieu intercellulaire.
Méthode: L'enzyme HAS3, le récepteur principal du HA, CD44, et le HA ont été marqués par immunohistochimie sur des coupes histologiques cutanées de patients sains et de patients atteints d'eczéma.
Résultat: Nos résultats montrent pour la première fois le pattern d'expression de la HAS3 dans la peau normale et pathologique. La spongiose épidermique semble de plus clairement imputable à une surproduction du HA essentiellement due à une surexpression de HAS3. En accord avec cette observation, l'expression du CD44 augmente également. L'expression de la HAS3 est connue pour être positivement régulée dans les phénomènes inflammatoires. Nos travaux suggèrent qu'une induction de l'expression du gène Has3 est à l'origine de la surproduction d'HA qui cause la spongiose.
Conclusion: La spongiose est principalement due à une suractivation inflammatoire de la production du HA imputable à une surexpression de HAS3. Les causes de la spongiose sont donc à rechercher dans la régulation du gène Has3 dans les kératinocytes.

P4

ROLE DE LA MANIPULATION HORMONALE DANS LE TRAITEMENT DU CANCER DU SEIN METASTATIQUE (CSM) HORMONOSENSIBLE.

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Introduction: Le traitement d'un CSm a principalement un caractère palliatif. La manipulation hormonale est une option thérapeutique importante lors de cancer hormonosensible, de faible masse tumorale.
Méthode: Des études de phase II/III, entre 1976-2010, ont été analysées. Les patientes inclues étaient des femmes pré ou post-ménopausées, souffrant d'un CSm hormonosensible. L'hormonosensibilité est définie par l'expression de récepteurs oestrogène et/ou progestérone par > de 1% des cellules tumorales. Nous avons analysé les résultats pour les patientes pré et post-ménopausées. Les principales issues de ces études étaient le taux de réponse (TR), la survie sans progression (SSP) et la survie globale (SG). Comme stratégie de recherche des sources nous avons utilisé Medline et Pubmed.
Résultat: Pré-ménopause: Pour les patientes n'ayant reçu de tamoxifen en adjuvant ou ayant récidivé plus de 12 mois après la fin de la thérapie adjuvante, l'association d'un agoniste GnRH et du tamoxifen apporte un petit bénéfice de SG, par rapport à l'approche séquentielle. En 2e ligne ou en cas de récidive précoce, l'association d'un agoniste GnRH et d'un inhibiteur de l'aromatase (IA) apporte un bénéfice en TR et SSP. Post-ménopauses : Un IA est supérieur au tamoxifen en terme de SSP, sans différence statistique en SG. En deuxième ligne le fulvestrant (antagoniste pure des récepteurs oestrogéniques) ou un autre IA permettent un TR entre 10-20%.
Conclusion: La manipulation hormonale est une approche thérapeutique importante des CSm hormonosensibles, sans cependant de bénéfice avéré en terme de SG.

P5

PROSTAGLANDIN I2 (PGI2) AGONISTS ENHANCE ALREADY EXUBERANT TH17 CELL RESPONSES IN SYSTEMIC SCLEROSIS FAVORING IL-23 PRODUCTION BY MONOCYTES

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Introduction: Prostaglandin I2 (PGI2) analogs are used to treat Systemic Sclerosis (SSc) vascular complications. Their capacity to affect adaptive immunity remains poorly characterized. We aimed at assessing whether PGI2 analogs impact on T helper (Th) cell responses in SSc patients and healthy donors (HD).
Méthode: Peripheral blood mononuclear cells (PBMC) were obtained from 33 SSc and 29 HD. Cytokine levels in T cells cultures were quantified by immunoassays and the frequency of IL-17A, IL-22, IFN-γ and IL-4-producing CD4+ T cells assessed by multicolor flow-cytometry. Selective receptor antagonists, cytokine-blocking antibodies and signaling protein inhibitors were used to unravel the mechanisms involved.
Résultat: Th17 ($p<0.04$) and Th22 ($p<0.02$) cells were more abundant in SSc than HD. PGI2 analogs (iloprost, treprostinil and beraprost) significantly increased IL-17A and IL-22 while decreasing IFN-& #947; production both in SSc and HD. These effects relied on the speci fic expansion of Th17 ($p<0.0001$) and Th22 ($p<0.0001$) and inhibition of Th1 cells ($p<0.0001$). The enhanced Th17 cell responses depended on increased IL-23 production by monocytes and relied on signals delivered by the IP-receptor in a PKA-dependent manner. Importantly, in vivo administration of iloprost in SSc individuals presenting with digital ulcers resulted in a significant increase in the frequency of Th17 cells.
Conclusion: Our findings demonstrate that PGI2 analogs affect Th cell differentiation/expansion programs in SSc resulting in enhanced Th17/Th22 and depressed Th1 cell responses. The clinical benefit observed in SSc under PGI2 analogs may imply that the Th cell modifications observed may play a favorable role in the disease course.

P6

FIRST RESULTS OF A COMPARATIVE 11C-ACETATE AND 18F-FLUOROCHOLINE PET/CT STUDY IN PROSTATE CANCER PATIENTS RELAPSING WITH LOW PSA AFTER INITIAL CURATIVE TREATMENT

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Introduction: 18F-fluorocholine (FCH) and 11C-acetate (ACE) PET/CTs have shown promise in the detection of recurrent prostate cancer (PC). We present preliminary results of a comparative PET/CT study of both radiotracers in the same patients presenting a recurrence with low PSA.
Méthode: We studied 12 patients with recurrent PC after surgery alone (N=5), radiotherapy (RT, N=2) or surgery with salvage RT (N=5). Both FCH and ACE PET/CTs were performed in a randomized sequence a mean of 4±3 days apart. FCH PET/CT (309±21 MBq) was started at injection with a 10 min dynamic acquisition on prostate region, followed by whole-body PET and late (45min) imaging of the pelvis. ACE PET/CT (986±82 MBq) was performed as dual whole-body PET starting 5 and 22 minutes post injection, respectively, and a late view (45min) on prostate region. PET/CTs were blindly reviewed by 2 independent groups of 2 experienced nuclear medicine physicians each.
Résultat: ACE and FCH findings were concordant for all patients concerning local status and distant (bone) metastases. Concordant positive, negative and doubtful local status were observed in 4, 7 and 1 patients, respectively. Two patients showed a single bone metastasis, confirmed by bone scintigraphy. Concordant lymph-node results were observed in 7 patients (4 positive, 2 negative, 1 equivocal, respectively) while differences between both PET/CTs were observed in 5 patients. Further concordant hyperactivities were observed in 2 patients concerning once the thyroid and once the pituitary gland (surgically removed macroadenoma).
Conclusion: ACE and FCH PET/CT performed equally regarding local recurrences. Bone metastases were positive in 2 patients. Discordant results were observed for lymph node status in 5 of 12 patients. Current follow-up is too short to provide a gold standard regarding the differences observed between ACE and FCH PET.

P7

PULSE TRANSIT TIME AS A MEASURE OF RESPIRATORY EFFORT UNDER NON-INVASIVE VENTILATION

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Introduction: Among respiratory events which may occur during nocturnal non-invasive ventilation (NIV), differentiating between central and obstructive events requires appropriate indicators of respiratory effort.
Méthode: Objective: To assess pulse transit time (PTT) as an indicator of respiratory effort under NIV in comparison with esophageal pressure (Pes). Methods: 1: During wakefulness, PTT was compared to Pes during spontaneous breathing and under NIV with or without induced leaks in 11 healthy individuals. 2: Contribution of PTT versus Pes for differentiating central from obstructive respiratory events occurring under NIV during sleep was evaluated in 10 patients with obesity hypoventilation syndrome (OHS).
Résultat: 1: From spontaneous breathing to NIV without leaks, respiratory effort decreased significantly whereas, with increasing level of leaks, there was a significant increase in respiratory effort. Changes in PTT accurately reflected changes in Pes. 2: In OHS patients during nocturnal NIV, intraclass correlation coefficients between Pes and PTT were 0.970 for total number of events and 0.970 for percentage of central events.
Conclusion: PTT accurately reflects the unloading of respiratory muscles induced by NIV and the increase in respiratory effort during leaks. PTT during sleep is also useful to differentiate central from obstructive respiratory events occurring under NIV.

P8

INTRAVENOUS LIDOCAINE HAS NO IMPACT ON ROCURONIUM-INDUCED NEUROMUSCULAR BLOCK. RANDOMISED STUDY

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Introduction: Intravenous lidocaine is increasingly used in surgical patients. As it has neuromuscular blocking effects, we tested the impact of an intravenous lidocaine infusion on the time course of a rocuronium-induced neuromuscular block.
Méthode: Fifty-two adults undergoing surgery were randomly allocated to intravenous lidocaine 1.5 mg/kg followed by a continuous infusion of 2 mg/kg/h or physiological saline (control) throughout surgery. Anaesthesia was induced and maintained with a target-controlled propofol infusion and sufentanil. After loss of consciousness, rocuronium 0.6 mg/kg was given. Neuromuscular transmission was measured using train-of-four (TOF)-watch SX (Organon, Swords Co., Dublin, Ireland) acceleromyography.
Résultat: Onset time (to 95% depression of first twitch) was on average 113.9 s (standard deviation 35.3) with lidocaine and 119.5 s (44.9) with saline (P = 0.618). Total recovery time (TOF ratio 0.9) was on average 58.1 min (15.1) with lidocaine and 54.3 min (16.9) with saline (P = 0.394). Clinical duration (until first twitch has recovered to 25%) was on average 33.3 min (7.2) with lidocaine and 30.6 min (8.1) with saline (P = 0.21). Recovery index (time between 25% and 75% recovery of the first twitch) was on average 11.5 min (5.0) with lidocaine and 10.6 min (4.1) with saline (P = 0.458). Recovery time (between 25% recovery of the first twitch and TOF ratio 0.9) was on average 24.8 min (9.3) with lidocaine and 23.2 min (9.2) with saline (P = 0.541).
Conclusion: A continuous intravenous infusion of lidocaine has no impact on the time course of the neuromuscular blockade induced by a standard intubation dose of rocuronium.
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P9

PRESERVED VISUAL LANGUAGE IDENTIFICATION DESPITE SEVERE ALEXIA

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Introduction: Patients with letter-by-letter alexia may have residual access to lexical or semantic representations of words despite severely impaired overt word recognition (reading). Here, we report a multilingual patient with severe letter-by-letter alexia who rapidly identified the language of written words and sentences in French and English while he had great difficulty in reading them, judging their lexical status or extracting semantic information.
Méthode: The study started 3 months after the stroke and lasted for 6 months. During this period the patient's reading def! icit remained stable. Evaluation of reading was performed in French and English. The patient's performance was compared to three age- and gender- matched healthy volunteers (3 males, mean age, 71 ± 2.7 years). All were native French speakers with excellent knowledge of written English which had been acquired after the age of 7 years and not spoken every day.
Résultat: Lexical decision was strongly influenced by the orthographic structure of stimuli: whereas he easily determined the lexical status of illegal nonwords (e.g., 'rsdo'), he had random performance with legal pseudowords (e.g., 'binus'). When asked to determine the language of meaningless letter trigrams with high frequency in the English or French orthography (e.g., 'oth' or 'iqu') his performance was significantly above chance. In contrast, similarly to healthy participants his language decision was at chance with low-frequency trigrams.
Conclusion: These findings suggest that written language identification relies on sublexical processing of orthographic rules specific to each language.

P10

LA CIGARETTE ÉLECTRONIQUE; UNE NOUVELLE FORME GALÉNIQUE RÉVOLUTIONNAIRE?

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Introduction: La cigarette électronique (e-cigarette) permet d\'inhaler une vapeur parfumée, chargée de nicotine ou d\'autres médicaments. Nous avons conduit quelques-unes des premières études publiées réalisées auprès d\'utilisateurs de ce produit.
Méthode: Enquête par questionnaires auprès de 3587 utilisateurs de cigarettes électroniques. Analyse de la cotinine (un métabolite de la nicotine) dans la salive de 30 utilisateurs de ce produit.
Résultat: Nous avons montré pour la première fois que les utilisateurs de e-cigarettes obtiennent autant de nicotine de ce produit que les fumeurs en obtiennent des cigarettes, et 2 fois plus que les utilisateurs de gommes ou patches de nicotine. Le plus souvent, la e-cigarette était utilisée comme aide pour arrêter de fumer.
Conclusion: Cette nouvelle manière d\'administrer des médicaments fournit de grandes quantités de nicotine et aide sans doute les fumeurs à arrêter de fumer. Des applications pour d\'autres médicaments devraient être développées.

P11

TOOTH LOSS IS ASSOCIATED WITH SWOLLEN JOINTS IN A COHORT OF HEALTHY INDIVIDUALS AT INCREASED RISK OF DEVELOPING RHEUMATOID ARTHRITIS

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Introduction: Background: Evidence suggests an association between periodontitis/tooth loss and rheumatoid arthritis (RA). Periodontitis, a common chronic inflammatory process of the tooth supporting tissues, is a major cause of tooth loss; thus, the number of teeth is considered a surrogate marker for periodontitis. Whether periodontitis/tooth loss n healthy individuals at increased risk of developing RA, is associated with joint inflammation is unknown. The aim of this study is to determine the prevalence of tooth loss, as a proxy for periodontitis, and to evaluate its association with joint involvement in a cohort of first degree relatives (FDRs) of patients with RA.
Méthode: The study sample is an ongoing, prospective cohort of 366 healthy FDRs of patients with RA,. Participants are followed annually to assess the development of signs and symptoms of arthritis. Additional data collected include smoking status, number of teeth, morning stiffness (MS) lasting more than one hour during at least 6 weeks, tender and swollen joint counts , and blood tests including antibodies (positive RF , ACPA,and shared epitope. The primary outcome was objective swollen joints, dichotomized at presence of at least one swollen joint with no joint swelling as the reference group. The exposure was the number of present teeth at baseline, which was categorized as ≤20, 21-27, 28-31, and 32 teeth. Multivariate regression models were fit to test the association between tooth loss and swollen joints, adjusting for potential confounders such as age, sex, shared epitope, body mass index (BMI) and smoking status. A secondary analysis model used morning stiffness as the endpoint.
Résultat: The cohort is 73% female, 93% Caucasian with a mean age of 41 (SD±14) years. 15% were RF positive and/or ACPA positive. The mean number of teeth at baseline was 28 (SD±4). Six percent of the group had ≤20 teeth, 20% had 21-27 teeth), 46% had 28-31, and 28% 32 teeth. FDRs with at least one swollen joint on examination had less teeth compared with those with no swollen joints (mean number of teeth 29 vs. 26, respectively; p=0.004). Compared to FDRs with no tooth loss, those in the lowest category of present teeth (<20 teeth) were more likely to have at least one swollen joint on examination (OR 8.1; 95% CI 1.1, 60) and morning stiffness (OR 5.3; 95% CI 1.1, 26), independent of potential confounders.
Conclusion: In this large cohort of FDRs of patients with RA , individuals who have lost teeth are significantly more likely to have at least one swollen joint. While ascertainment of periodontal status is needed to confirm the role of periodontitis in this association, these results suggest that tooth loss is an independent predictor of joint swelling in individuals at increased risk of RA. Longitudinal studies are needed to establish the causal involvement of periodontitis on RA development.

P12

EVALUATION OF CARDIOVASCULAR RISK IN PATIENTS WITH RHEUMATOID ARTHRITIS. DO CARDIOVASCULAR BIOMARKERS OFFER ADDED PREDICTIVE ABILITY OVER ESTABLISHED CLINICAL RISK SCORES?

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Introduction: Rheumatoid arthritis (RA) is associated with an increased risk of cardiovascular (CV) disease. CV risk can be estimated using established clinical risk scores; however traditional risk factors do not perform as well in RA patients. Reliable CV risk stratification remains an unmet clinical need in the RA population. It is unknown whether emergent biomarkers increase the predictive ability of clinical scores for CV risk in RA. The objective of this study is to determine whether adding C-reactive protein, anti-citrullinated peptide antibodies, rheumatoid factor, N-terminal pro-Brain Natriuretic peptide (NT-proBNP), oxidized LDL (oxLDL) or anti-apolipoprotein A-1 IgG (anti-apoA-1) to the 10 year-Framingham cardiovascular risk score (FRS) could improve its CV prognostic accuracy in RA.
Méthode: We performed an ancillary study derived from a prospective single center cohort including 118 RA patients without cardiovascular disease at baseline. The FRS and the various biomarkers were assessed at enrollment and their prognostic accuracy was determined using receiver operating characteristic (ROC) curve analysis. The incremental predictive ability of biomarkers was assessed using the integrated discrimination improvement (IDI) statistics.
Résultat: During a median follow-up of 9 years, the incidence of CV events was 16%. Both the FRS and 3 of the biomarkers (NT-proBNP, oxLDL, anti-apoA-1) were significant predictors of subsequent CV events (area under the ROC curve (AUC) between 0.68 – 0.73). Anti-apoA-1 was the only biomarkers to improve significantly the FRS's prognostic ability, with AUCs increasing from 0.72 to 0.81 and the IDI improving by 175% (p<0.001).
Conclusion: Among the biomarkers tested, only anti-apoA-1 significantly improved the FRS predictive ability.

P13

USE OF BRAIN NATRIURETIC PEPTIDE TO DETECT PREVIOUSLY UNKNOWN LEFT VENTRICULAR DYSFUNCTION IN PATIENTS WITH ACUTE EXACERBATION OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Introduction: Up to 30% of patients with chronic obstructive pulmonary disease (COPD) simultaneously suffer from often-unrecognised chronic heart failure (HF). Their timely identification is challenging as both conditions share similar clinical presentations
Méthode: Retrospective medical records analysis of all patients hospitalised between January 2003 and May 2009 with the final diagnosis of acute exacerbation of COPD, and who had undergone BNP dosage at admission followed by an echocardiography.
Résultat: Among the 57 patients included, 13 had left ventricular systolic dysfunction. There was a statistically significant difference of mean BNP values between patients with or without systolic dysfunction (mean 689 pg/ml vs. 340 pg/ml, p = 0.007). For the detection of systolic dysfunction, a BNP level inferior to 100 pg/ml yielded a sensitivity of 92% and a negative predictive value of 91%, whereas BNP higher than 500 yielded a sensitivity of 80% and a positive predictive value of 47%. In a multivariate logistic regression analysis, a BNP value ≥500 (odds ratio 8.5, 95% confidence interval 1.9 to 38.2, p = 0.005) and history of coronary heart disease (odds ratio 5.9, 95% confidence interval 1.01 to 34.7, p = 0.048) remained as independent and mutually adjusted predictors of left ventricular systolic dysfunction
Conclusion: Our study confirms that BNP can help physicians in identifying heart failure in patients suffering from an acute exacerbation of COPD

P14

CLINICAL APPLICATIONS OF HYBRID PET/MRI IN NEUROIMAGING

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Introduction: PET and MRI are the modalities of choice for neuroimaging. One major challenge of a new technology available, hybrid PET/MR, is the optimization of acquisition protocols! in order to obtain diagnostic quality images in clinically acceptable time frame for both modalities, including specific MR sequences, such as spectroscopy, diffusion tensor imaging and functional MRI. We tested the performance and clinical applicability of combined diagnostic protocols.
Méthode: 15 patients (6 males; 9 females, mean age and range: 51±30, 6-89) were scanned on a Philips Ingenuity TF PET/MR. Standard imaging protocols of both modalities were combined. The clinical indications evaluated are: patients with cognitive disturbance of suspected neurodegenerative origin (4), pre-surgical evaluation of drug-refractory epilepsy (6) and brain tumor staging (5). For the first two indications, FDG PET imaging was performed, whereas for the last, fluoro-ethyl-tyrosine (FET), an aminoacidic tracer, was used.
Résultat: In all cases we obtained full diagnostic quality of both modalities and the total duration of the exam remained within a tolerable range (< 2h). 12 subjects had pathological findings, 11/12 confirmed by clinical follow-up as true positive, and 1 false positive result. For the three normal studies, the clinical follow-up confirmed the imaging findings as true negative.
Conclusion: Acquiring both PET and MR in a single session on a hybrid system minimized patient discomfort while maximizing clinical information and optimizing registration of both modalities. In additio! n, in comparison to PET/CT, the effective dose (related to CT), was reduced, and this is particularly beneficial in the paediatric population.

P15

CAN BILATERAL VARICOSE VEIN SURGERY BE PERFORMED SAFELY IN AN AMBULATORY SETTING?

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Introduction: Surgery for varicose veins is still the method of choice worldwide. When varicose veins require bilateral surgery, a single procedure often is the preferred choice by the patient. Today, unilateral varicose vein surgery is frequently performed as an outpatient procedure, while in many institutions bilateral surgery is done as an in-hospital procedure.
Méthode: Between 1 October 2004 and 31 October 2006, 433 patients underwent surgery for the great saphenous vein as in-patient procedure (303 unilateral and 130 bilateral), period 1. From 1 November 2006 until 31 December 2009, 825 patients had ambulatory great saphenous vein surgery (550 unilateral and 275 bilateral), period 2. We have compared unilateral and bilateral varicose vein surgery (high ligation and stripping of the great saphenous vein) and in-hospital procedures with ambulatory surgery, with regard to postoperative complications, postoperative pain and midterm follow-up.
Résultat: Operation time and total length of stay in the institution following varicose vein surgery were significantly shorter for period 2 compared with period 1 for both unilateral and! bilateral surgery, without other differences between the groups. There were few postoperative complications without differences between periods, and between unilateral and bilateral surgery (wound infection 0.5%, haematoma requiring drainage 0.2%, transient paraesthesia 1.1%, superficial localised thrombophlebitis 0.6% and deep vein thrombosis in one unilaterally operated case only
Conclusion: Bilateral varicose vein surgery can be safely performed as an outpatient procedure, without increased risk of postoperative complications, increased postoperative discomfort or midterm adverse effects compared with unilateral surgery

P16 – NON AFFICHE

P17

SATISFACTION MATERNELLE DE LA PRISE EN CHARGE ANESTHESIQUE DURANT L'ACCOUCHEMENT: UNE ETUDE DE COHORTE RETROSPECTIVE

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Introduction : Les facteurs qui contribuent à la satisfaction maternelle de la prise en charge anesthésique pendant l'accouchement restent peu connus. L'objectif de cette étude était d'évaluer ces facteurs.
Méthode: Nous avons réalisé une étude de cohorte rétrospective sur les parturientes admises entre janvier 2004 et décembre 2008. Nous avons extrait du dossier les données démographiques, les co-morbidités, les interventions anesthésiques et obstétricales réalisées, et différents éléments du vécu de l'anesthésie. La satisfaction maternelle a été mesurée au moyen d'une échelle numérique de 0 à 10 (0=pas satisfait du tout, 10=entièrement satisfait) 24 h après l'accouchement. Une valeur ≤ 6 a été utilisée comme indiquant l'insatisfaction. Nous avons ainsi identifié dans une analyse multivariée les différents prédicteurs de la satisfaction maternelle, notamment la douleur, le vécu global de la technique, les délais d'attente et la présence de complications anesthésiques, obstétricales ou néonatales.
Résultat: Des 15386 parturientes admises, 10034 avaient un dossier complet et de ce nombre, 761 (7,6%) étaient insatisfaites de leur prise en charge. Parmi les facteurs diminuant la satisfaction, on retrouvait la grossesse à risque (rapport de cotes (RC):0,59 et intervalle de confiance (IC) à 95%:0,34-1,02) et l\'accouchement difficile (RC:0,62, IC:0,52-0,74). La douleur, le vécu global négatif de l\'intervention, le retard, la mauvaise coordination dans la prise en charge et la présence de complications diminuaient la satisfaction (RC:0.07 à 0,71, p<0,001.
Conclusion: La satisfaction maternelle de l'anesthésie est largement déterminée par l'efficacité et le bon déroulement de l'intervention tant sur le plan technique qu'humain. Néanmoins d\'autres facteurs tels que la bonne coordination de la prise en charge des parturientes et l'absence de complications influencent également la satisfaction.

P18

ECG SCREENING OUTCOME IN PSYCHIATRY (THE ESOP STUDY): DRUG-INDUCED LONG QT SYNDROME >500 MS IS ASSOCIATED WITH HYPOKALEMIA, T-WAVE ABNORMALITIES, HIV AND HCV INFECTIONS IN ADULT PSYCHIATRIC INPATIENTS

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Introduction: The corrected QT interval (QTc) is a surrogate marker to assess the propensity to polymorphic arrhythmias named *Torsades de Pointe* (TdP), which are associated with ventricular fibrillation and fatal outcome. The ESOP study focuses on ECG recordings performed at admission in all inpatients entering the public psychiatric hospital to detect drug-induced long QT syndrome (diLQTS) and related risk factors
Résultat: Among 6'790 adult patients, 27.3% had abnormal ECG recordings. Long QT syndrome (LQTS), defined as QTc values >500 ms, was diagnosed in 107 patients (1.6%), of whom 62 (0.9%) were classified as diLQTS cases. Sudden cardiac death was recorded in five patients and TdP in seven other patients. Patients with diLQTS (n=62) were compared with a sample of patients who had normal ECG recordings at admission (n=143).
Drug-induced LQTS patients had significantly higher frequencies of hypokalemia (19.4% vs. 5.6%, p=0.004), HCV infection (41.9% vs. 9.8%, p<0.001), HIV infection (24.2% vs. 6.3%, p=0.001) and abnormal T-wave morphology (35.5% vs. 15.4%, p=0.003). Number of prescribed drugs was higher in diLQTS patients (median 4 vs. 3, p=0.002). Among antipsychotic drugs, haloperidol, sertindole, clotiapine and phenothiazines were significantly more frequent in diLQTS patients. The serotonin-specific reuptake inhibitors fluoxetine and citalopram/escitalopram, as well as methadone, were also associated with diLQTS. In a multivariable logistic regression model adjusted for hypokalemia (OR=6.5, p=0.005), HCV infection (OR=4.4, p=0.009), HIV infection (OR=3.9, p=0.036) and abnormal T-wave morphology (OR=4.0, p=0.004), effects of haloperidol, clotiapine, phenothiazines and citalopram/escitalopram remained statistically significant, whereas effects of sertindole, fluoxetine and methadone did not (p<0.10). ROC curve analysis based on the number of endorsed risk factors per patient (AUC 0.89; 95% CI 0.84-0.94) indicated that best cutoff was 2 risk factors, with sensitivity at 85.5% (% of diLQTS patients with ≥ 2 risk factors) and specificity at 81.1% (% of non-diLQTS patients with <2 risk factors).
Conclusion: The ESOP study emphasizes the multiplicity of factors that contribute to LQTS in psychiatric inpatients. DiLQTS and arrhythmias propensity substantially increase when particular psychotropic drugs are administered to patients presenting with conditions, such as abnormal T-wave morphology, hypokalemia, HCV infection and HIV infection.

P19

THE "BRODY EFFECT" TO DETECT HYPOVOLEMIA IN CLINICAL PRACTICE

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Introduction: Electrocardiogram (EKG) is a common monitoring in intensive care medicine. Several studies suggest that changes in EKG morphology may reflect changes in volume status. The ''Brody effect'', a theoretical analysis of left ventricular (LV) chamber size influence on QRS-wave amplitude is the key element of this phenomenon. It is characterized by an increase in QRS-wave amplitude induced by an increase in ventricular preload [1]. This study investigated the influence of changes in intravascular volume status on respiratory variations of QRS-wave amplitude (EKG) compared with respiratory pulse pressure variations (PP).
Méthode: In 17 pigs, EKG and arterial pressure were recorded. QRS-wave amplitude was measured from the Biopac recording ensuring that in all animals EKG-electrodes were always at the same location. Maximal QRS amplitude (EKGmax) and minimal QRS amplitude (EKGmin) were determined over one respiratory cycle. EKG was calculated as 100x[(EKGmax-EKGmin)/(EKGmax+EKGmin)/2]. EKG and PP were simultaneously recorded. Measurements were performed during normovolaemic conditions, after haemorrhage and following re-transfusion with constant tidal volume (10mL/kg) and respiration rate (15/min).
Résultat: At baseline, PP and EKG were both < 12%. ΔPP were significantly correlated with EKG ($r^2=0.89$, $p<0.001$). Volume loss induced by haemorrhage increased significantly PP and EKG. Moreover, during this state, PP were significantly correlated with EKG ($r^2=0.86$, $p<0.001$). Retransfusion significantly decreased both PP and EKG and PP were significantly correlated with DEKG ($r^2=0.90$, $p<0.001$).
Conclusion: Available correlations between PP and EKG at each time of the study were observed, meaning that EKG is a reliable parameter to estimate the changes in intravascular volume status and provide experimental confirmation of the "Brody effect."

P20

PRE-EJECTION PERIOD TO ESTIMATE CARDIAC PRELOAD DEPENDENCY IN MECHANICALLY VENTILATED PIGS SUBMITTED TO SEVERE HEMORRHAGIC SHOCK

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Introduction: Respiratory change in pre-ejection period (PEP) has been described as a potential parameter for monitoring cardiac preload dependency in critically ill patients. This study was designed to describe the relationship between PEP and pulse pressure variation (PPV) in pigs submitted to severe hemorrhagic shock.
Méthode: In 17 paralyzed, anesthetized mechanically ventilated pigs, electrocardiography, arterial pressure, and cardiac output derived from pulmonary artery catheter were recorded. Hemorrhagic shock was induced by removal of blood volume followed by restoration. PEP was defined as the time interval between the beginning of the Q wave on the electrocardiogram and the upstroke of the invasive radial arterial pressure curve.
Résultat: At baseline, PEP and PPVs were both <12% with PPV significantly correlated with PEP ($r = 0.96$, $p < 0.001$). Volume loss induced by hemorrhage significantly increased PPV and PEP values ($p < 0.05$). During severe hemorrhage, PPV correlated well with PEP ($r = 0.88$, $p < 0.001$) with PPV values significantly higher than PEP ($p < 0.05$). However, the reproducibility of PEP measurements was significantly better than PPV during this step ($p < 0.05$). Retransfusion significantly decreased PPV and PEP ($p < 0.05$) with PPV significantly correlated to PEP ($r = 0.94$, $p < 0.001$).
Conclusion: Available correlations between PPV and PEP at each time of the study were observed, meaning that PEP is a reliable parameter to estimate and track the changes in cardiac preload dependency. Moreover, during the severe hemorrhagic shock period, PEP measurements were more reproducible than PPV values.

P21

SCVO2 AS A MARKER TO DEFINE FLUID RESPONSIVENESS

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Introduction: Definition of the hemodynamic response to volume expansion (VE) could be very useful in shocked critically ill patients in absence of cardiac index (CI) measurements. The aim of the present study is to evaluate if central venous oxygen saturation variations (ScvO2) after VE could be an alternative to classify responders (R) and non responders (NR) to volume therapy.
Méthode: A total of 30 patients requiring VE were included in this prospective cohort study, all equipped with radial arterial line and pulmonary artery catheters. CI, mixed venous oxygen saturation (SvO2) and ScvO2 were measured before and after VE. CI, SvO2 and ScvO2 changes following volume were analyzed using linear regression. Receiver operating characteristics (ROC) curve analysis was used to test their ability to distinguish responders (R) and non responders (NR).
Résultat: ScvO2 and SvO2 variations following VE (SvO2) were significantly correlated with CI changes (CI) following VE ($r=0.67$ and $r=0.49$, $p<0.001$ respectively). A ScvO2 threshold value of 4% allowed the definition of R and NR patients with 86% sensitivity (95%CI; 57-98%) and 81% specificity (95%CI; 54-96%).
Conclusion: ScvO2 variations following VE was able to categorise VE efficiently and could be suggested as an alternative marker to define fluid responsiveness in absence of invasive CI measurement.

P22

VALIDATION OF A NEW TRANSPULMONARY THERMODILUTION SYSTEM TO ASSESS GLOBAL ENDDIASTOLIC VOLUME AND EXTRAVASCULAR LUNG WATER

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Introduction: A new system has been developed to assess global end-diastolic volume (GEDV), a volumetric marker of cardiac preload, and extravascular lung water (EVLW) from a transpulmonary thermodilution curve. Our goal was to compare this new system with the system currently in clinical use.
Méthode: Eleven anesthetized and mechanically ventilated pigs were instrumented with a central venous catheter and a right (PulsioCath; Pulsion, Munich, Germany) and a left (VolumeView™; Edwards Lifesciences, Irvine, CA, USA) thermistor-tipped femoral arterial catheter. The right femoral catheter was used to measure GEDV and EVLW using the PiCCO2™ (Pulsion) method (GEDV1 and EVLW1, respectively). The left femoral catheter was used to measure the same parameters using the new VolumeView™ (Edwards Lifesciences) method (GEDV2 and EVLW2, respectively). Measurements were made during inotropic stimulation (dobutamine), during hypovolemia (bleeding), during hypervolemia (fluid overload), and after inducing acute lung injury (intravenous oleic acid).
Résultat: One hundred and thirty-seven paired measurements were analyzed. GEDV1 and GEDV2 ranged from 701 to 1,629 ml and from 774 to 1,645 ml, respectively. GEDV1 and GEDV2 were closely correlated ($r2 = 0.79$), with mean bias of -11 ± 80 ml and percentage error of 14%. EVLW1 and EVLW2 ranged from 507 to 2,379 ml and from 495 to 2,222 ml, respectively. EVLW1 and EVLW2 were closely correlated ($r2 = 0.97$), with mean bias of -5 ± 72 ml and percentage error of 15%.
Conclusion: In animals, and o ver a very wide range of values, a good agreement was found between the new VolumeView™ system and the PiCCO™ system to assess GEDV and EVLW.

P23
IMPLANT VESTIBULAIRE : OÙ EN SOMMES-NOUS?

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Introduction: Le système vestibulaire concourt au maintien de l'équilibre corporel et à la stabilisation du regard lors des mouvements. Les patients souffrant d'un déficit vestibulaire bilatéral (DVB) se plaignent de déséquilibre constant et d'une diminution de l'acuité visuelle à la marche. Après avoir développé les approches chirurgicales des différentes branches du nerf vestibulaire, nous développons une neuroprothèse vestibulaire pour la réhabilitation de ces patients, pour lesquels n'existe aucun traitement.
Méthode: (1) Stimulation électrique (SE) aiguë des nerfs ampullaires postérieur et latéral chez 6 patients candidats à une vestibulectomie ; (2) SE chronique chez 4 patients sourds souffrant d'un DVB et ayant reçu un implant cochléaire modifié avec une électrode placée au contact du nerf ampullaire postérieur. L'effet de la SE a été quantifié en enregistrant les mouvements oculaires (MO). L'acuité visuelle a été mesurée avec et sans SE.
Résultat: Nos résultats démontrent qu'avec une SE du système vestibulaire il est possible : (1) de générer des mouvements oculaires (MO) horizontaux et verticaux, (2) de restaurer une activité neurale de base du système vestibulaire, (3) de piloter des MO par une modulation de la SE (4) ayant un effet significatif sur l'acuité visuelle.
Conclusion: Il est possible de piloter des MO par SE du système vestibulaire dont l'amplitude est comparable à celle des MO compensateurs des mouvements de tête. La prochaine étape consistera à évaluer le bénéfice de ce pilotage sur l'acuité visuelle des patients à la marche. Ce serait la démonstration claire du bénéfice d'une prothèse vestibulaire.

P24
ABCB1 POLYMORPHISMS AND NEUROPSYCHIATRIC ADVERSE EVENTS IN OSELTAMIVIR-TREATED CHILDREN DURING INFLUENZA H1N1/09 PANDEMIA

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Introduction: The aim of this study was to examine the safety profile of oseltamivir in children and evaluate the impact of P-glycoprotein polymorphisms on the incidence of neuropsychiatric adverse events (NPAE) in oseltamivir-treated children.
Méthode: This prospective cohort study was conducted in our tertiary care pediatric hospital (University Hospitals of Geneva, Switzerland) during the H1N1 pandemia, between 1 October 2009 and 31 January 2010. All newborn to 18 year-old patients presenting at the emergency department with a flu-like illness were eligible for inclusion. Adverse events were systematically recorded by pediatricians and/or by parents at home using a diary card, with a 30-day follow-up period. The causality assessment of oseltamivir in NPAE was performed by two clinical pharmacologists. After informed consent, enrolled patients were also genotyped for ABCB1 3435C>T (rs1045642) and 2677G>T/A (rs203258 2) polymorphisms.
Résultat: Among the 42 H 1N1-infected, oseltamivir-treated children who were genotyped for ABCB1 3435C>T and 2677G>T/A variants, 36% presented NPAE. When examining the association between the diplotype and the development of NPAE, we observed that the frequency of NPAE displayed a 'genotype-trend effect' with the variant and the wild-type subgroups at the two far ends. A total of 11% of the 2677GG–3435CC individuals (wild-type homozygous) presented NPAE, compared with 39% of the individuals being heterozygous for at least one variant allele and 67% of the 2677TT–3435TT individuals (homozygous variants) ($p = 0.149$, nonsignificant).
Conclusion: These observations suggest a potential influence of ABCB1 polymorphisms in oseltamivir-related NPAE, maybe as a result of an enhanced permeability of the blood–brain barrier to oseltamivir.

P25

MRI OF OLFACTORY DYSFUNCTION: HOW TO DO IT AND WHAT TO REPORT?

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Introduction: This poster reviews the essential MRI technique to investigate patients with olfactory dysfunction. After a short section about anatomy of the olfactory tracts, we expose the basic MRI technique and then the most frequent conditions associated with olfactory dysfunction.
Méthode: Retrospective analysis of 68 consecutive patients investigated with MRI for olfactory dysfunction during the past 5 years. All patients were imaged on a 3T or 1.5T unit according to a standard protocol consisting of four sequences with high matrix (512x512) centred on the anterior skull base: FSET2-weighted and SET1-weighted pre- and post-contrast in the coronal plane (3mm slices) and an isovoxel millimetric or submillimetric heavily T2-weighted three-dimensional sequence (CISS, SPACE or DRIVE). Volumetry of the bulbs was made using manual contouring in the coronal plane on the 3DT2 sequence.
Résultat: The most common clinical complaints were anosmia (n=38) and phantosmia (n=19). MRI was totally normal in 10 cases. Pathologic findings were: olfactive bulbs aplasia (n=5) or atrophy (n=47), mucosal naso-ethmoidal inflammation (n=22), traumatic fronto-basal brain sequelae (n=4) and tumoral mass of the olfactory groove (2 meningiomas, 1 lipoma). Mean volume of olfactive bulbs was 22.2+8.5mm3.
Conclusion: Because only a minority of MRI examinations was normal, a strict protocol with specific sequences is mandatory for a valuable assessment of the olfactory system. Aplasia/atrophy of olfactive bulbs and sinonasal mucosal thickening were the most common findings. The low volume of the bulbs in comparison to those published in the literature probably reflects the population of our collective including only patients with olfactory dysfunction.

P26

DIAGNOSTIC PERFORMANCE OF ULTRASOUND GUIDED FINE NEEDLE ASPIRATION CYTOLOGY IN THE ASSESSMENT OF MAJOR SALIVARY GLAND MASSES: A RETROSPECTIVE ANALYSIS

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Introduction: To evaluate the diagnostic performance of ultrasound guided fine needle aspiration cytology (USFNAC) in salivary gland masses.
Méthode: The Institutional Ethics Committee approved this retrospective study on a consecutive series of 184 patients addressed to our department for USFNAC of salivary glands lesions. The radiology records of 114 males and 70 females (mean age 59.6 years, range 16-99 years) were reviewed and findings from cytopathological and bacteriological analysis were compared to subsequent histology (n=72), or clinical and radiological follow-up of > 6 months (n=91).
Résultat: 90.4% of USFNAC procedures were performed in the parotid and 9.6% were performed in the submandibular glands on an outpatient basis using 22G and 21G needles. No major complications were noted. 90.8% of all samples were diagnostic and 9.2% were non-diagnostic. In the 137 procedures meeting inclusion criteria, the definitive diagnosis was infectious/inflammatory in 29.2% (n=40), benign tumors in 48.9% (n=67) and malignant tumors in 21.9% (n=30) of cases. The sensitivity and specificity for differentiating benign from malignant salivary gland masses were 86.7% and 97.2%, respectively. The positive and negative predictive values were 89.7% and 96.3%, respectively. With a total of 3 false positive and 4 false negative findings, USFNAC had some difficulties to differentiate benign tumors from low-grade malignances, mainly mucoepidermoid carcinoma.
Conclusion: USFNAC is a safe and reliable technique with a high negative predictive value for differentiating benign from malignant salivary gland pathologies.
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P27

INTERET DE L'ANALYSE QUANTITATIVE DE LA MARCHE EN DOUBLE TACHE POUR L'IDENTIFICATION D'UNE DEMENCE REVERSIBLE

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Introduction: L'hydrocéphalie à pression normale (HPN) est une des rares causes de démence réversible. Elle se caractérise par des déficits cognitifs, des troubles de la marche et une incontinence urinaire. Cependant, cette symptomatologie est peu spécifique car retrouvée dans d'autres pathologies neurodégénératives et cérébrovasculaires. Nous avons récemment montré la pertinence de l'utilisation du paradigme de double tâche (marcher et réaliser une tâche cognitive simultanément) pour l'évaluation de l'HPN. L'objectif de cette étude est de comparer les paramètres de marche de l'HPN à ceux observés dans des pathologies neurodégénératives ou cérébrovasculaires.
Méthode: L'analyse quantitative de la marche en condition de simple et de double tâche a été comparée avant et après une ponction lombaire (PL) soustractive parmi 49 sujets répartis entre un groupe de patients avec HPN et un groupe de patients avec un diagnostic alternatif.
Résultat: Une amélioration statistiquement significative de la largeur du pas, de la longueur du pas et de la vitesse de marche en condition de double tâche après la PL soustractive a été observée chez les patients avec un diagnostic d'HPN par rapport au groupe avec un diagnostic alternatif.
Conclusion: L'analyse quantitative de la marche évaluée en condition de double tâche avant et après une PL soustractive pourrait être un marqueur de choix pour différencier les patients avec une HPN des patients dont la présentation clinique mime ce diagnostic.

P28

NON-INVASIVE LOCALIZATION OF SOMATOSENSORY CORTEX WITH PNEUMATIC STIMULATION USING HIGH DENSITY EVOKED POTENTIALS AND FUNCTIONAL MRI

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Introduction: To non-invasively and precisely localise the primary somatosensory cortex (SI) in the individual brain by means of high-resolution somatosensory evoked potentials (SEP) using selective mechanical stimulation.
Méthode: SEP was elicited by tactile stimuli (distal phalanx of the first digit), applying fingerclips with diaphragms driven by compressed air, in a ! group of healthy subjects ("group 1" n=31; "group 2" n=17) and patients with intractable epilepsy (n=6). In all cases, data was recorded using 256-channel electroencephalogram (EEG) and analysed using electrical source imaging (ESI) techniques. Afterwards, patients were implanted with electrodes covering SI and intracranial SEP was recorded. Direct cortical stimulation (DCS) was also applied in all patients. We validated ESI localization in patients with intracranial SEP and DCS. Additionally, we compared localization precision of SI by means of SEP source imaging versus functional magnetic brain imaging (fMRI) in "group 2" and in all patients; and versus electrical stimulation of the median nerve in "group 1".
Résultat: Mechanical stimulation rendered a more accurate localization and a lower inter-subject variability, while comparing with electrical stimulation in "group 1". This result allowed us to take an extra step by contrasting electromagnetic and hemodynamic techniques. Relatively similar results were obta ined while assessing spatial precision of ESI versus fMRI after mechanical stimulation in "group 2" and in epileptic patients. The outcome after surface and intracranial SEP recordings were comparable. Moreover, gold standard DCS confirmed clear-cut localization of SI by means of ESI and fMRI.
Conclusion: Mechanical SEP is a painless stimulation technique that, if combined with high-resolution ESI, allows for precise localisation of SI, which is critical in a clinical setting (i.e. presurgical evaluation). The method can easily be applied to all type of patients (including children), in different situations (fMRI compatible) and locations (bedside).

P29

TEN-YEAR RESULTS WITH THE MORSCHER PRESS-FIT CUP: AN UNCEMENTED, NON-MODULAR, POROUS-COATED CUP INSERTED WITHOUT SCREWS

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Introduction: Total hip arthroplasty (THA) with well designed cementless acetabular implants has shown excellent results. The purpose of this study was to assess our clinical and radiological outcomes using an uncemented cup.
Méthode: We conducted a prospective cohort study including all consecutive primary THAs performed with the Morscher press-fit cup, an uncemented non-modular acetabular component, between March 1996 and December 1998. Patients were evaluated at ten years with clinical and radiological followup, patient satisfaction and questionnaire assessment using the Harris hip score (HHS), Merle d'Aubigné and Postel score, the UCLA score, the 12-item short-form health survey (SF-12) and a visual analog scale.
Résultat: Five hundred sixty-one THAs were performed in 518 patients. At 120 months (± 7.3 months), 303 patients with 335 THAs were still available for follow-up. None of the patients had required cup revision for aseptic loosening. At ten years, the cup survivorship was 98.8% (95% CI 97.4–99.5) with cup revision for any cause as an endpoint. No radiolucencies were seen around the cups, but osteolytic defects involved 21 stems (8.3%). Mean total linear polyethylene wear was 0.9 mm.
Conclusion: The Morscher acetabular replacement cup provides excellent results at ten years. There were no revisions for aseptic loosening of the cup, and no osteolytic defects were found around the cup. Patient satisfaction was high and the clinical results were very good.
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P30

INFLUENCE OF PATIENT ACTIVITY ON FEMORAL OSTEOLYSIS AT FIVE AND TEN YEARS FOLLOWING HYBRID TOTAL HIP REPLACEMENT

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Introduction: Following total hip arthroplasty patient participation in athletic activity may compromise implant survival. Literature concerning sports activity and implant survival is limited. Our objective was to evaluate the influence of patient activity on the occurrence of femoral osteolysis five to ten years after primary total hip arthroplasty.
Méthode: We conducted a longitudinal study including patients with the same type of primary hybrid total hip replacement and evaluated patient activity and femoral osteolysis at either five or ten years post-operatively. Activity was measured using the University of California, Los Angeles scale. The primary outcome was the radiological assessment of femoral osteolysis. Secondary outcomes were revision of the femoral component for aseptic loosening and the patients' quality of life.
Résultat: Of 503 hip replacements in 433 patients with a mean age of 67.7 years (30 to 91), 241 (48%) were seen at five and 262 (52%) at ten years post-operatively. Osteolytic lesions were identified in nine of 166 total hip replacements (5.4%) in patients with low activity, 21 of 279 (7.5%) with moderate activity, and 14 of 58 (24.1%) patients with high activity. The risk of osteolysis increased with participation in a greater number of sporting activities. In multivariate logistic regression adjusting for age, gender, body mass index and the inclination angle of the acetabular component, the adjusted odds ratio for osteolysis comparing high vs moderate activity was 3.6 (95% confidence interval 1.6 to 8.3). Stratification for the cementing technique revealed that lower quality cementing increased the effect of high activity on osteolysis. Revision for aseptic loosening was most frequent with high activity. Patients with the highest activity had the best outcome and highest satisfaction.
Conclusion: In conclusion, of patients engaged in high activity, 24% had developed femoral osteolysis five to ten years post-operatively.

P31

RISK FACTORS FOR POST-TRAUMATIC OSTEOARTHRITIS OF THE ANKLE: AN EIGHTEEN YEAR FOLLOW-UP STUDY

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Introduction: Unlike hip or knee osteoarthritis (OA) ankle OA is more frequently of post-traumatic origin. However, long-term studies evaluating risk factors for developing ankle OA following malleolar fractures are sparse.
Méthode: We conducted a retrospective cohort study including consecutive patients treated with open reduction internal fixation for malleolar fracture between 1/1988 and 12/1997. Peri-operative information was obtained retrospectively. Patients were evaluated clinically and radiographically 12-22 years postoperative. Radiographic ankle OA was determined on standardized radiographs using the Kellgren & Lawrence scale (grade 3-4 = advanced OA). Uni- and multivariable regression analyses were performed to determine risk factors for OA.
Résultat: 373 fractures (372 patients; 9% Weber A, 58% Weber B, 33% Weber C) were operated during the inclusion period. Mean age at operation was 42.9 years. There were 102 patients seen at follow-up (mean follow-up 17.9 years). Those not available did not differ in demographics and fracture type from those seen. Advanced radiographic OA was present in 37 patients (36.3 %). Significant risk factors were: Weber C fracture, associated medial malleolar fracture, fracture-dislocation, increasing BMI, age ≥ 30 years, and length of time since surgery.
Conclusion: Advanced radiographic OA was common 12-22 years after malleolar fracture. The probability of developing post-traumatic OA among patients having three or more risk factors was 60-70%.
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P32

REVISION TOTAL HIP ARTHROPLASTY IN PATIENTS 80 YEARS OR OLDER

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Introduction: Orthopaedic surgeons are frequently facing the decision whether to revise a total hip arthroplasty (THA) in a patient over 80 years of age. With the overall increase of revision THAs predicted for the next decades their number is expected to increase even more. Our objective was first to evaluate short- and mid-term complications, mortality, clinical results and patient satisfaction up to five years after revision total hip arthroplasty (THA) in patients ≥80 years of age and to compare them to outcomes in patients <80 years of age. Second, we investigated time trends in complication rates and mortality for the two age groups.
Méthode: We evaluated all revisions performed from March 1996 to December 2008 and compared complications, mortality, clinical outcomes and satisfaction between patients ≥80 and <80 years of age. All data and radiographs were collected prospectively through our hip registry. Merle d'Aubigné and Harris Hip scores, SF-12 and patient satisfaction were assessed.
Résultat: There were 325 revisions, 84 (25.8%) in patients ≥80, 241 in patients <80 years (62% revision for aseptic loosening in both groups). Mean follow-up was 4.3 years. The results, ≥80 vs. <80 years, revealed: Mortality 5% vs. 0% three months postoperative; Medical complications in 23.8% vs. 6.2%; Postoperative fractures 9.5% vs. 2.5%; Merle d'Aubigné score improved from 9.6 to 13.0 vs. 10.4 to 14.3.
Conclusion: evision THA in patients ≥80 years was associated with substantial clinical improvement and patient satisfaction. However, medical complications and 90-day mortality were higher, and postoperative fractures occurred more frequently.

P33

THE ACTIVATION OF THE CANNABINOID RECEPTOR TYPE 2 REDUCES NEUTROPHILIC PROTEASE-MEDIATED VULNERABILITY IN ATHEROSCLEROTIC PLAQUES

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Introduction: The activation of cannabinoid receptor type 2 (CB2)-mediated pathways might represent a promising anti-atherosclerotic treatment. Here, we investigated the expression of the endocannabinoid system in human carotid plaques and the impact of CB2 pharmacological activation on markers of plaque vulnerability in vivo and in vitro.

Méthode: The study was conducted using all available residual human carotid tissues (upstream and downstream the blood flow) from our cohort of patients symptomatic (n = 13) or asymptomatic (n = 27) for ischaemic stroke. In addition, the role of CB2 ac! tivation was assessed in a mouse model of atherosclerosis and in vitro in cultured inflammatory cells.

Résultat: Intraplaque levels of 2-arachidonoylglycerol, anandamide N-arachidonoylethanolamine, N-palmitoylethanolamine, N-oleoylethanolamine, and their degrading enzymes (fatty acid amide hydrolase and monoacylglycerol lipase) were not different in human plaque portions. In the majority of human samples, CB1 (both mRNA and protein levels) was undetectable. In downstream symptomatic plaques, CB2 protein expression was reduced when compared with asymptomatic patients. In these portions, CB2 levels were inversely correlated ($r = -0.4008$, $P = 0.0170$) with matrix metalloprotease (MMP)-9 content and positively ($r = 0.3997$, $P = 0.0174$) with collagen. In mouse plaques, CB2 co-localized with neutrophils and MMP-9. Treatment with the selective CB2 agonist JWH-133 was associated with the reduction in MMP-9 content in aortic root and carotid plaques. In vit! ro, pre-incubation with JWH-133 reduced tumour necrosis factor! (TNF)-a lpha-mediated release of MMP-9. This effect was associated with the reduction in TNF-α-induced ERK1/2 phosphorylation in human neutrophils.

Conclusion: Cannabinoid receptor type 2 receptor is down-regulated in unstable human carotid plaques. Since CB2 activation prevents neutrophil release of MMP-9 in vivo and in vitro, this treatment strategy might selectively reduce carotid vulnerability in humans.

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NEURAL ACTIVATION TO SEEING ADULT MALE-FEMALE INTERACTIONS AMONG WOMEN WHO ARE MOTHERS OF YOUNG CHILDREN IN THE CONTEXT OF INTERPERSONAL VIOLENCE-RELATED PTSD.

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Introduction: This study tested how mothers with male-perpetrated interpersonal violence-related Posttraumatic Stress Disorder (IPV-PTSD) differed in their brain activation from healthy controls (HC) when exposed to scenes of male-female interaction. It has been suggested that PTSD involves impaired regulation of the fear response to traumatic reminders (i.e. decreased ventromedial prefrontal [vmPFC] activation).

Méthode: Mothers of 21 children, 12-42 months of age, participated; 8 diagnosed with IPV-PTSD and 13 HC. Well-val! idated clinical measures were used for diagnosis. During MRI, mothers watched epochs of male-female interaction, which were neutral, menacing or positive.

Résultat: IPV-PTSD mothers showed greater vmPFC deactivation than HC in response to menacing vs. neutral scenes. While both groups deactivated the ventral anterior cingulate (vACC) when viewing menacing scenes, only IPV-PTSD mothers deactivated it during positive ones. IPV-PTSD mothers showed greater dorsomedial prefrontal (dmPFC) activation only in response to menacing scenes. IPV-PTSD mothers showed greater activation of the dACC and dmPFC, and stronger deactivations in the vmPFC and the anterior caudate in response to menacing vs. positive scenes.

Conclusion: IPV-PTSD mothers showed less cortico-limbic regulation than HC in response to menacing vs. other “Hollywood” film scenes. Neural activation patterns in response to clear “traumatic reminders” are similar to th! e same IPV-PTSD mothers’ response to seeing their own toddlers! in a st ressful, helpless interpersonal condition (Schechter et al., 2011). Going beyond reference to traumatic reminders, IPV-PTSD mothers compared to HC tended to hypoactivate the vACC during all emotional scenes, independent of their valence/arousal which we interpret possibly as a response to male-female interactions overall.

P35

MATERNAL NEURAL ACTIVATION TO SEEING TODDLERS IN SEPARATION VS. PLAY IN THE CONTEXT OF INTERPERSONAL VIOLENCE-RELATED PTSD AND PARENTING STRESS

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Introduction: This study tested in what way mothers with interpersonal violence related Posttraumatic Stress Disorder (IPV-PTSD) compared with healthy controls (HC) have altered activity in brain areas related to emotion regulation and parenting when viewing distress among their own and unfamiliar children during separation compared to play. We expect that IPV-PTSD mothers compared to HC will show less cortico-limbic regulation when seeing videos of toddlers.

Méthode: Mothers of 21 children, 12-42 months of age, participated; 8 mothers with a diagnosis of IPV-PTSD and 13 HC. During MRI, mothers watched silent epochs of play alternating with separation involving their own and unfamiliar children. Mothers were clinically assessed using well-validated clinical measures for IPV-PTSD diagnosis and subjective report of parenting stress.

Résultat: IPV-PTSD mothers showed less ventromedial PFC (vmPFC) activity and more dorsal mPFC activity than HC when viewing their own children during separation; Greater parenting stress was also associated with less vmPFC activation. When watching unfamiliar children IPV-PTSD mothers had stronger activation in the both bilateral amygdala and vmPFC.

Conclusion: Preliminary findings suggest that the functioning of self-regulatory circuits is altered in IPV-PTSD mothers. IPV-PTSD mothers in response to their own children activate the vmPFC less than controls, but, in response to unfamiliar children, a ctivate both limbic and vmPFC more than controls. Subjective parenting stress is also associated with less cortico-limbic regulation in response to own children. These preliminary findings converge with prior behavioral findings that IPV-PTSD mothers have more difficulty in reading and responding sensitively to child cues following separation-stress

P36

AN FMRI STUDY OF THE BRAIN RESPONSES OF TRAUMATIZED MOTHERS TO VIEWING THEIR TODDLERS DURING SEPARATION AND PLAY.

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Introduction: This study tested whether mothers with interpersonal violence-related posttraumatic stress disorder (IPV-PTSD) vs healthy controls (HC) would show greater limbic and less frontocortical activity when viewing young children during separation compared to quiet play.
Méthode: Mothers of 20 children (12-42 months) participated: 11 IPV-PTSD mothers and 9 HC with no PTSD. During fMRI, mothers watched epochs of play and separation from their own and unfamiliar children. The study focused on comparison of PTSD mothers vs HC viewing children in separation vs play, and viewing own vs unfamiliar children in separation.
Résultat: Both groups showed distinct patterns of brain activation in response to viewing children in separation vs play. PTSD mothers showed greater limbic and less frontocortical activity (BA10) than HC. PTSD mothers also reported feeling more stressed than HC when watching own and unfamiliar children during separation. Their self-reported stress was associated with greater limbic and less frontocortical activity. Both groups also showed distinct patterns of brain activation in response to viewing their own vs unfamiliar children during separation.
Conclusion: PTSD mothers\' may not have access to frontocortical regulation of limbic response upon seeing own and unfamiliar children in separation. This converges with previously reported associations of maternal IPV-PTSD and atypical caregiving behavior following separation.

P37

RPO (RESPIRATORY PHASE OPTIMIZER): UN LOGICIEL DE TRAITEMENT DE L'IMAGE 4D POUR MIEUX TRAITER LE CANCER DU POUMON.

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Introduction: Les tumeurs pulmonaires sont mobiles avec la respiration. La radiothérapie asservie à la respiration (RAR) permet d'en tenir compte et de traiter à une phase respiratoire donnée, réduisant ainsi le volume traité donc la toxicité, tout en augmentant les chances de guérison. Néanmoins, pour un patient donné, le meilleur moment respiratoire reste à ce jour inconnu. Nous avons créé le logiciel RPO de traitement de l'image de CT4D pour le déterminer.
Méthode: 19 premiers patients avec cancers pulmonaires ont eu un CT4D, soit l'équivalent de 10 scanners pour 10 phases respiratoires. RPO, développé pour traiter ces données informatiques sur la base de critères morphologiques de comparaison des phases, a permis au médecin de choisir la meilleure phase d'irradiation parmi les 10. Une étude dosimétrique a ensuite déterminé le gain d'une RAR délivrée pendant cette phase optimale.
Résultat: Dans 1/19 patients (5%), pas de mouvements détectés suggérant l'absence de bénéfice d'une RAR. Pour 18/19 patients (95%), un déplacement significatif a été identifié, avec détermination d'une phase optimale, se transformant en gain dosimétrique dans plus de 75% des cas. Les paramètres de toxicité pulmonaire peuvent être ainsi réduits de 35%, la dose à la moelle épinière de 26%, et la dose moyenne reçue par le cœur de 24%.
Conclusion: Les HUGs disposent avec RPO du 1er outil capable de sélectionner les patients pouvant bénéficier d'une RAR et même d'identifier le moment respiratoire idéal d'irradiation. Il ouvre la perspective d'une radiothérapie moins toxique et plus efficace sur la 1ère cause de mortalité par cancer.

P38

CORONARY VASOMOTOR CONTROL IN OBESITY AND MORBID OBESITY:CONTRASTING FLOW RESPONSES WITH ENDOCANNABINOIDS, LEPTIN, AND INFLAMMATION

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Introduction: There is increasing evidence that altered plasma levels of ECs, leptin, and CRP may affect coronary circulatory function in OB and MOB. We aimed to investigate abnormalities in coronary circulatory function in two different disease entities of obese (OB) and morbidly obese (MOB) individuals, and to evaluate whether these would differ in severity with different profiles of endocannabinoids (EC), leptin, and CRP plasma levels.

Méthode: Myocardial blood flow (MBF) responses to cold pressor test (CPT) from rest and during pharmacologically-induced hyperemia were measured with 13N-ammonia PET/CT. Study participants (n=111) were divided into four groups based on their body mass index(BMI, kg/m2): control group (CON, BMI 20-24.9, n=30); overweight group (OW, BMI 25-29.9, n=31), obese group (OB, 30-39.9, n=25); and morbidly obese group (MOB, BMI ≥40, n=25).

Résultat: The CPT induced change in endothelium-related MBF response (ΔMBF) progressively declined in OW and OB when compared with CON [0.19 (0.08, 0.27) and 0.11 (0.03, 0.17) vs. 0.27 (0.23, 0.38) mL/g/min; p≤0.01, respectively)], while it did not differ significantly between OB and MOB [0.11 (0.03, 0.17 and 0.09 (-0.01, 0.19) mL/g/min; p=0.93]. Compared with CON, hyperemic MBFs comparably declined in OW, OB and MOB [2.40 (1.92, 2.63) vs. 1.94 (1.65, 2.30), 2.05 (1.67, 2.38) and 2.14 (1.78, 2.76) mL/g/min; p≤0.05, respectively)]. In OB individuals, ΔMBF was inversely correlated with increase in the EC anandamide (AEA) (r=-0.45, p=0.044), but neither with leptin (r=-0.02, p=0.946) nor with CRP (r=-0.33, p=0.168). Conversely, there was a significant and positive correlation between ΔMBF and elevated leptin (r=0.43, p=0.031) and CRP (r=0.55, p=0.006), respectively, in MOB individuals, while not observed for AEA (r=0.07, p=0.740).

Conclusion: Contrasting associations of altered coronary endothelial function with increases in AEA, leptin, and CRP plasma levels identify and characterize OB and MOB as different disease entities affecting coronary circulatory function

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INFLUENCE OF THE PARAOXONASE-1 Q192R GENETIC VARIANT ON CLOPIDOGREL RESPONSIVENESS AND RECURRENT CARDIOVASCULAR EVENTS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: A poor biological response to clopidogrel is associated with an increased risk of major cardiovascular ischemic events (MACE). Paraoxonase 1 (PON1) enzyme activity is modulated by the PON1-Q192R variant (rs662) and was recently suggested to be strongly involved in clopidogrel bioactivation, but the influence of the PON1-Q192R variant on the risk of MACE in clopidogrel-treated patients is controversial. The aim was to determine whether the PON1-Q192R variant influences clopidogrel biological responsiveness and the r! isk of MACE in patients treated with clopidogrel.

Méthode: Systematic review and meta-analysis of studies of the association between the PON1-Q192R polymorphism and the biological response to clopidogrel and/or the risk of MACE during clopidogrel administration.

Résultat: Seventeen studies were included. In the 12 studies of the biological response to clopidogrel (n=5302 patients), there was no significant difference between 192QQ and 192QR+192RR subjects, whatever the laboratory method used (global mean standardized difference=0.10 [-0.06;0.25], p=0.22). Eleven studies assessed the risk of MACE, four using a case-control design (n=2739 patients) and seven a prospective design (n=5353 patients). Overall, MACE occurred in 19% of patients in case-control studies and in 6% of patients in prospective cohort studies, with no significant difference between 192QQ and 192QR+192RR patients (OR=1.28 [0.97;1.68], p=0.08). Simila! r results were obtained when study design was taken into account. Hete rogeneity was mainly driven by one publication.

Conclusion: This meta-analysis suggests that the PON1-Q192R polymorphism has no major impact on the risk of MACE and does not alter the biological response to clopidogrel in clopidogrel treated patients. Journal of Thrombosis and Haemostasis 2012 in press

P40

IMPACT OF LOW-LEVEL GLYCOPEPTIDE RESISTANCE ON TREATMENT FAILURE IN ORTHOPAEDIC DEVICE-RELATED METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS (MRSA) INFECTION

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Introduction: Reduced susceptibility to glycopeptides in methicillin-resistant Staphylococcus aureus (MRSA) clinical isolates is considered a risk factor for failure of glycopeptide therapy. We evaluated the prevalence of glycopeptide-intermediate S. aureus (GISA) in a previously described (Ferry et al., 2010) retrospective cohort of 41 patients treated for MRSA orthopedic device-related infections (ODRI) at the University Hospital of Geneva between 2000 and 2008.
Méthode: GISA isolates were detected by elevated vancomycin or/and teicoplanin MICs (≥ 4 mg/L), using a modified macrodilution assay of improved sensitivity (Vaudaux et al., 2010).
Résultat: MRSA isolates with elevated teicoplanin MICs were detected in 20/41 (49%) ODRI patients at the onset or during the course of glycopeptide therapy, namely in 10 of 20 patients with prosthetic joint and 10 of 21 patients with osteosynthesis infections. Only one isolate developed a concomitant increase in vancomycin MIC during therapy. All GISA isolates belonged to the widely prevalent clonotype ST228, which caused 85% of MRSA ODRI. 13/20 (65%) GISA-infected patients, including 7/10 (70%) with prosthetic joint and 6/10 (60%) with osteosynthesis, experienced treatment failure. In contrast, therapy failed in only 5/21 (24%) ODRI patients with non-GISA isolates (P = 0.012), including 2/10 (20%) with prosthetic joint and 3/11 (27%) with osteosynthesis infections. Emergence of low-level teicoplanin resistance could not be explained by teicoplanin administration since only 4 patients received teicoplanin.
Conclusion: Evaluation of low-level teicoplanin resistance may improve the detection of GISA isolates. Further studies are warranted to evaluate the impact of low-level teicoplanin resistance on the outcome of glycopeptide therapy.

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HYPEREOSINOPHILIA IN PATIENTS WITH MULTIPLE SCLEROSIS TREATED WITH NATALIZUMAB

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Introduction: To report asymptomatic hypereosinophilia as a potential side effect in patients treated with natalizumab, an α-4 integrin blocking agent
Méthode: A case series of 3 patients treated with natalizumab for relapsing-remitting multiple sclerosis including functional and phenotypic characterization of their peripheral blood lymphocytes and eosinophils is presented
Résultat: Marked peripheral blood eosinophilia with more than 2,000 cells/mm(3) emerged in all 3 patients after the fourth natalizumab infusion and was asymptomatic. Hypereosinophilia was associated with enhanced Th2 activity, ceased with drug discontinuation, and in 2 of 3 patients recurred with drug resumption. Despite persistently high eosinophil counts, there were no signs of end-organ damage
Conclusion: Hypereosinophilia may occur during treatment with natalizumab. It seems to reflect enhanced Th2 activity and recedes with systemic corticosteroids. If the patient is asymptomatic, natalizumab may be continued, provided that other causes of eosinophilia are excluded and the patient is carefully monitored.

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UNUSUAL MANIFESTATIONS OF BILATERAL CAROTID ARTERY DISSECTION DEEP MONOCULAR PAINS

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Introduction: A 44-year-old man in good general health presented with a 1-week history of deepseated, moderate right eye pain without exacerbation on eye movement, the rest of the examination was unremarkable
Méthode: Fluorescein and indocyanine green angiography were performed without delayed arterial filling. Cranial MRI with fat-saturated sequences and magnetic resonance angiography (MRA) were also done
Résultat: MRI and MRA revealed bilateral acute internal carotid artery (ICA) dissections without fibromuscular dysplasia
Conclusion: ICA unilateral or bilateral dissection can be asymptomatic. Why symptomatology from ICA is so variable is not understood; it was recently suggested that the number and distribution of activated intracranial collateral vessels may predict the gravity of ICA. A prospective study analyzing predisposing factors that predict ICA poor outcome would be interesting.

P43

PRESENTATION D'UN CAS D'OCCLUSION DE L'ARTERE CENTRALE DE LA RETINE (OACR) SUITE A UN COUP DE POING

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Introduction: Les traumatismes oculaires suite à une agression par coup de poing sont des consultations fréquentes aux urgences d'ophtalmologie. Nous rapportons un cas très inhabituel d'une OACR suite à un coup! de poing.
Méthode: Un patient de 51 ans, en bonne santé habituelle, a reçu un coup de poing dans l'œil gauche suivi d'une perte de vision presque totale en 15 minutes.
Résultat: Le fond d'oeil réalisé 8 heures après le traumatisme met en évidence une OACR avec un saignement péripapillaire. Le CT-scan cérébral montre un saignement rétrobulbaire sans syndrome des loges ni fracture orbitaire. L'IRM confirme un saignement important au niveau de la tête du nerf optique. L'acuité visuelle, limitée à la perception lumineuse, fut stable durant le suivi.
Conclusion: La physiopathologie de ce cas peu commun d'OACR post-traumatique reste encore à clarifier; cependant la perte visuelle progressive en 15 minutes ainsi que l'IRM penchent plus pour un phénomène compressif par un saignement au niveau de la tête du nerf optique que pour une rupture de l'artère centrale de la rétine au niveau de sa portion intra-oculaire.

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CROSS-LINKING DU COLLAGENE CORNEEN AVEC RIBOFLAVINE ET UVA POUR TRAITER LES ECTASIES RECURRENTES APRES KERATOPLASTIE PENETRANTE

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Introduction: Evaluer l'efficacité, la securité préliminaire et faisabilité du traitement des patients souffrant d'une éctasie cornéenne récurrente suite une kératoplastie pénétrante pour un kératocone avec cross-linking du collagène cornéen à l\'aide UVA et riboflavine (CXL) dans une série de cas interventionnel.
Méthode: Trois yeux de trois patients (deux hommes et une femme) avec une récurrence d'éctasie cornéenne après une greffe transfixiante de cornée ont bénéficié d'un traitement de cross-linking selon le protocole pour le CXL avec la modification suivante: l'aire d'irradiation a été augmentée à 11mm en diamètre et le limbus cornéen a été protegé de l'irraditation UVA avec une éponge circulaire.
Résultat: Chez tous les patients, la progression des éctasies s'est stoppée avec un suivi de 19 mois.
Conclusion: Le CXL pourrait stopper la progression des éctasies récurrentes après une kératoplastie transfixiante pour kératocône

P45

DEPIST : DEPISTAGE PAR AUTO-PRELEVEMENT POUR LES FEMMES QUI NE PARTICIPENT PAS AU DEPISTAGE DU CANCER DU COL DE L'UTERUS.

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Introduction: Entre 30 et 40% des femmes ne participent pas au dépistage du cancer du col de l'utérus en Suisse. Cette population est plus à risque de développer un cancer. Les raisons d'une non participation au dépistage sont multiples : refus de l'examen gynécologique, manque de temps, "ne se sent pas à risque", etc. Plusieurs études montrent que l'autoprélèvement HPV permet d'identifier la présence d'un pré-cancer avec une sensibilité similaire au frottis cytologique effectué par un professionnel de la santé. Le but de notre étude est d'évaluer si l'autoprélèvement HPV permet d'améliorer la participation au dépistage et si la méthode est acceptée par les femmes.
Méthode: Un total de 1 100 femmes âgées de 25 à 69 ans, n'ayant pas eu de dépistage depuis trois ans ou plus sont invitées à participer à l'étude. La communication est effectuée à l'aide d'un site internet (www.depist.ch), des media et des réseaux de santé (médecins de vilee, pharmacie, associations). L'étude est proposée en trois langues (français, anglais, espagnol) et comporte un questionnaire visant à comprendre les raisons de la non participation au dépistage ainsi que l'acceptabilité de l'autoprélèvement HPV.
Résultat: attendus : améliorer la participation au dépistage chez des femmes qui le négligent grâce à l\'introduction de pratiques innovantes : l'autoprélèvement HPV.
Conclusion: Etude en cours

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LEFT SPATIAL NEGLECT PATIENTS ALSO NEGLECT THE LEFT (PAST) SIDE OF TIME

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Introduction: Previous research suggests people construct mental timelines to represent and reason about time.
Méthode: However, are spatial representations truly necessary for representing events in time?
Résultat: Our results show for the first time that deficits in spatial representation (as a function of left hemi-spatial neglect) also result in deficits in representing events along the mental timeline. Specifically, we show that patients with left hemi-spatial neglect have difficulty representing events that are associated with the past and thus fall to the left on the mental time-line.
Conclusion: These results demonstrate that representations of space and time share neural underpinnings and that representations of time have specific spatial properties (e.g., a left and a right side). Further, it appears that intact spatial representations are necessary for at least some types of temporal reasoning.

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MATCHING BETWEEN REGIONAL CORONARY VASODILATOR CAPACITY AND CORRESPONDING CIRCUMFERENTIAL STRAIN IN INDIVIDUALS WITH NORMAL AND INCREASING BODY WEIGHT

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Introduction: To define the relationship between regional coronary vasodilator capacity and myocardial circumferential strain at rest in normal weight, overweight and obese individuals with normal global left-ventricular function.
Méthode: Myocardial blood flow (MBF) at rest and during pharmacologic vasodilation was measured with 13N-ammonia PET/CT in ml/g/min in normal weight control (CON, n=12), overweight (OW, n=10), and obese individuals (OB, n=10). In addition, resting myocardial function was evaluated as circumferential strain (Єc, %) by MRI
Résultat: Global myocardial flow reserve (MFR) did not differ significantly between CON and OW (2.98±0.96 vs. 2.70±0.66, p=0.290), whereas it declined significantly in OB (1.98±1.04,p=0.030). Further, global Єc (%) was comparable between CON, OW, and OB (-0.24±0.03, -0.23±0.02, and -0.23±0.04) but it was lowest in OB when normalized to the rate-pressure product (NЄc: -0.31±0.06, -0.32±0.05, and -0.26±0.08). When MFR of the three major coronary territories was correlated with corresponding Єc, a positive association was observed in CON (r=0.36,p=0.030), in OW (r=0.54, p=0.002), and also in OB when relating NЄc to coronary vascular resistance during pharmacologic vasodilation (r=-0.46, p=0.010).
Conclusion: Higher coronary vasodilator capacity is related to corresponding regional circumferential strain at rest in non-obese individuals, while this is also observed for reduced MFR in obesity. This observations are first to suggest a conditioning of the coronary vasodilator capacity by resting regional circumferential strain but needing further confirmatory investigations.

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LA CHOLESTASE EST UN MARQUEUR HISTOLOGIQUE DE MAUVAIS PRONOSTIC LORS D'HEPATITE ALCOOLIQUE: UNE ETUDE DE 163 CAS

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Introduction: L'hépatite alcoolique (HA) est une maladie grave du foie. La biopsie hépatique est requise pour établir le diagnostic, mais la signification pronostique des lésions observées n'est pas connue.
Méthode: Nous avons inclus 163 patients (âge moyen 55 ans, 97% de cirrhose) dont la biopsie hépatique pratiquée 3 jours [0-10] après l'admission montrait une HA avec un score de Maddrey de 39 [13-200]. Une analyse semi-quantitative a été faite (stéatose, ballonisation hépatocytaire, inflammation, réaction ductulaire, cholestase intraparenchymateuse, sidérose) et déterminé la mortalité à 3 mois.
Résultat: 43 patients sont décédés à 3 mois post biopsie (taux de survie 74%). En analyse univariée, la mortalité était associée à l\'âge, le score de Maddrey, le score de MELD et la cholestase parenchymateuse. En multivariée, seuls l\'âge (p=0.029), la cholestase parenchymateuse (p=0.001), et le score de Maddrey (p=0.027) étaient des prédicteurs indépendants de mauvais pronostic.
Conclusion: Chez ces patients atteints de cirrhose compliquée d'HA histologiquement prouvée, la biopsie hépatique a identifié la présence d'une cholestase intraparenchymateuse comme élément pronostic indépendant de mortalité à 3 mois, avec l'âge et le score de Maddrey. Cette variable histologique pourrait ainsi être incorporée dans les modèles pronostiques de l'HA

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A MODEL FOR DROPOUT ASSESSMENT OF CANDIDATES WITH OR WITHOUT HEPATOCELLULAR

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Introduction: In many countries, the allocation of liver grafts is based on the Model of End-stage Liver Disease (MELD) score and the use of exception points for patients with hepatocellular carcinoma (HCC). With this strategy, HCC patients have easier access to transplantation than non-HCC ones. In addition, this system does not allow for a dynamic assessment, which would be required to picture the current use of local tumor treatment on the waiting list.
Méthode: This study was based on the Scientific Registry of Transplant Recipients and included 5'498 adult candidates of a liver transplantation for HCC and 43'528 for non-HCC diagnoses. A proportional hazard competitive risk model was used.
Résultat: The risk of drop-out of HCC patients was independently predicted by MELD score, HCC size, HCC number and alpha fetoprotein (AFP). When combined in a model with age and diagnosis, these factors allowed for the extrapolation of the risk of drop-out. While this model and MELD did not share compatible scales, a correlation between both models was computed according to the predicted risk of drop-out, and drop-out equivalent MELD (deMELD) points were calculated.
Conclusion: The proposed model, with the allocation of deMELD, has the potential to allow for a dynamic and combined comparison of opportunities to receive a graft for HCC and non-HCC patients on a common waiting list. Such a strategy would allow a fairer liver graft allocation between transplant candidates with and without HCC.

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QUANTIFICATION OF SULFOLANE, A METABOLITE OF BUSULFAN, IN PLASMA BY GAS CHROMATOGRAPHY AND TANDEM MASS SPECTROMETRY: A NEW METHOD FOR EVALUATING THE ROLE OF SULFOLANE AND METABOLIC FATE OF BUSULFAN

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Introduction: Busulfan (Bu) is commonly used as a component of conditioning regimen in pediatric patients before hematopoietic stem cell transplantation (HSCT). The role of Bu metabolites on the events seen during Bu therapy is not completely known due to the lack of analytical methods. Hence, a strategy for the measurement of Sulfolane (Su), a stable metabolite of Bu, by gas chromatography/tandem mass spectrometric assay (GC/MS/MS) was developed.
Méthode: Bu and Su were simultaneously extracted from 100 microliters of plasma by ethyl acetate. Two aliquots of the extract were treated and injected separately into the GC/MS/MS system for Bu and Su quantification.
Résultat: The method was validated for the concentration range of 50–2000 ng/mL for Bu and 40–400 ng/mL for Su. Detectable levels of Su in plasma were observed 4 hours after the 1st dose, and levels above 200 ng/mL were observed after the 9th dose. Su was also measured in EBMT cohort plasma samples collected 4 hours after 1st dose (n=46), before 7th dose (n= 57) and after 9th dose infusion (n=54). The mean Su (Bu) levels measured at these three time points were 25 (266), 181 (393) and 250 (1271) ng/mL, respectively.
Conclusion: Clinical studies may adopt this novel method for investigating Bu metabolic fate and its mechanisms of toxicity. Understanding the kinetics of Su in subjects undergoing Bu infusion and its role in the adverse events seen! with Bu is now possible with this method.

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AUTOANTIBODIES AGAINST APOLIPOPROTEIN A-1 ANDPHOSPHORYLCHOLINE FOR DIAGNOSIS OF NON-ST-SEGMENT ELEVATION MYOCARDIAL INFARCTION

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Introduction: Aims: to explore the predictive accuracies of the anti-apolipoproteinA-1 (anti-ApoA-1) IgG and anti-phopshorylcholine (anti-PC) IgM alone, expressed as a ratio (anti-ApoA-1 IgG/anti-PC IgM, and combined to the NSTEMI-TIMI score to create a new risk stratification algorithm -the clinical autoantibody ratio (CABR) score- for non-ST elevation myocardial infarction (NSTEMI) diagnosis and subsequent cardiac troponin I (cTnI) elevation in patients with acute chest pain (ACP).
Méthode: In this single centre prospective study, 138 patients presented at the emergency room for ACP without ST-elevation MI.Anti-ApoA-1 IgG, and anti-PC IgM were assessed by ELISA upon admission. Post-hoc determination of CABR score cut-off was performed by receiver operating characteristics (ROC) analyses.
Résultat: The adjudicated final diagnosis was NSTEMI in 17% (24/138). Both auto-antibodies alone were found to be significant NSTEMI diagnosis predictors, but the CABR score had the best diagnostic accuracy (area under the curve [AUC]: 0.88; 95%Confidence Interval [CI]:0.82-0.95). At the optimal cut-off of 3.3, the CABR score negative predictive value (NPV) was 97% (95%CI:90-99). Logistic regression analysis showed that a CABR score above 3.3 increased the risk of subsequent NSTEMI diagnosis by 19-fold (Odds ratio: 18.7; 95%CI:5.2-67.3). For subsequent cTnI positivity, only anti-ApoA-1 IgG and CABR score displayed adequate predictive accuracies with AUCs of 0.80 (95%CI:0.68-91) and 0.82 (95%CI:0.70-0.94), respectively. NPV were 95 % (95%CI:90-98) and 99% (95%C! I:94-100), respectively.
Conclusion: The CABR score derived from adding anti-ApoA-1 IgG/anti-PC IgM ratio to NSTEMI-TIMI score could be promising for timely NSTEMI rule-out in ACP patients presenting at the emergency department without electrocardiographic changes.

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SUCCESSFUL USE OF BISPHOSPHONATE AND CALCIMIMETIC IN NEONATAL SEVERE PRIMARY HYPERPARATHYROIDISM

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Introduction: Neonatal primary hyperparathyroidism (NPHT) is associated with an inactivating homozygous mutation of the calcium sensing receptor (CaSR). The CaSR is expressed most abundantly in the parathyroid glands and the kidney and regulates calcium homeostasis through its ability to modulate parathormone secretion and renal calcium reabsorption. NPHT leads to life threatening hypercalcemia, nephrocalcinosis, bone demineralization, and neurologic disabilities. Surgery is the treatment of choice. While waiting for surgery, bisphosphonates offer an alternative to deal with hypercalcemia. Cinacalcet (calcimimetic of class II) increases CaSR affinity for calcium, leading to parathormone suppression and increased calcium renal excretion. At present, there is little evidence as to whether cinacalcet could improve the function of mutant CaSR in NPHT. We report a case of NPHT treated successfully with bisphosphonates and cinacalcet after surgery failure. To our knowledge, it is the first time cinacalcet has been used for NPHT.
Méthode: Case report
Résultat: Under cinacalcet therapy, we observed normalization of PTH and phosphate and near normalization of calcium.
Conclusion: In our patient, a mutation was found in the extracellular domain of the CaSR. This mutation should not change the chemical characteristics of the region, but it could modify the steric shape of the receptor, leading to calcium binding difficulties. In this mutation, cinacalcet worked successfully and was able to normalize PTH and calcium levels. More than 200 mutations of the CaSR are described in NPHT. It is difficult to predict which ones will respond to cinacalcet therapy. However, it seems reasonable and worth trying as an alternative to surgery.

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DUAL LOYALTY IN PRISON HEALTH CARE

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Dual loyalty is an ethical dilemma commonly encountered by health care professionals caring for persons in custody. It is defined as a role conflict between professional duties to a patient and obligations, express or implied, to the interests of a third party. National and international rules state that the sole task of health care professionals working in prisons is the care of physical and mental health of detainees. Despite large dissemination of these rules, most prison health care professionals and prison systems still struggle with dual loyalty and continue to infringe fundamental principles of prison health care. The most spectacular violations in recent history involved force-feeding of hunger strikers by health care professionals, participation in carrying out the death penalty, and complicity in torture. However, many subtle, much less spectacular situations in daily prison life cause health care professionals to forsake loyalty to their patients. For example, the medical supervision of certain punitive or security measures is clearly outside the scope of health care to prisoners.
A barrier to the respect of ethical standards in prison is related to organization. Health care professionals working under the hierarchies of justice or prison authorities receive little if any training in medical ethics regarding health care in prison. Despite the declarations regarding ethics of health care in prison, national professional organizations have largely failed to advocate on this issue. The relevant documents belong to what is called soft law: no legal sanctions apply to violators. If not covered by national law, deviation from principles of medical ethics can only be sanctioned by national professional boards and licensing bodies, which generally have no strongly developed interest in health care in prison.
Prison and law authorities frequently consider that “medical ethics apply to private doctors but not to prison doctors.” Furthermore, in times of scarcity of public resources, prison health care may not be given priority, particularly if prison health care is dependent of prison or justice authorities.
Proposals for improvement: First, we need to train medical and nonmedical professionals in human rights, medical laws and ethics, and skills to identify dual loyalty. Second, national and international professional boards of health care professionals should increase their involvement in both active support and oversight of health care professionals working in prisons. Third, professionals caring for prisoners should strictly and exclusively adhere to their role as caregivers to their inmate patients. Professionally, an authority other than the prison authorities, for example, the public health service or their professional association, should supervise them. Prison administrations and health authorities, although serving the same government, have different and often conflicting interests. The prison administration’s main task is safety and security; the health authority’s is health care. As long as health care professionals working in prisons are employed by the prison administration, they are vulnerable to pressures to serve medical purposes other than patient care. Therefore, responsibility for the provision of health care should be transferred from the prison administration to the public health authorities to avoid dual loyalty.

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COMPARATIVE METHODS FOR PET IMAGE SEGMENTATION IN PHARYNGOLARYNGEAL SQUAMOUS CELL CARCINOMA

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Introduction: Several methods have been proposed for the segmentation of (18)F-FDG uptake in PET. In this study, we assessed the performance of four categories of (18)F-FDG PET image segmentation techniques in pharyngolaryngeal squamous cell carcinoma ! using clinical studies where the surgical specimen served as the benchmark.
Méthode: Nine PET image segmentation techniques were compared including: five thresholding methods; the level set technique (active contour); the stochastic expectation-maximization approach; fuzzy clustering-based segmentation (FCM); and a variant of FCM, the spatial wavelet-based algorithm (FCM-SW) which incorporates spatial information during the segmentation process, thus allowing the handling of uptake in heterogeneous lesions. These algorithms were evaluated using clinical studies in which the segmentation results were compared to the 3-D biological tumour volume (BTV) defined by histology in PET images of seven patients with T3-T4 laryngeal squamous cell carcinoma who underwent a total laryngectomy. The macroscopic tumour specimens were collected \"en bloc\", frozen and cut into 1.7- to 2-mm thick slices, then digitized for use as reference.
Résultat: The clinical results suggested that four of the threshol ding methods and expectation-maximization overestimated the average tumour volume, while a contrast-oriented thresholding method, the level set technique and the FCM-SW algorithm underestimated it, with the FCM-SW algorithm providing relatively the highest accuracy in terms of volume determination (-5.9 ± 11.9%) and overlap index. The mean overlap index varied between 0.27 and 0.54 for the different image segmentation techniques. The FCM-SW segmentation technique showed the best compromise in terms of 3-D overlap index and statistical analysis results with values of 0.54 (0.26-0.72) for the overlap index.
Conclusion: The BTVs delineated using the FCM-SW segmentation technique were seemingly the most accurate and approximated closely the 3-D BTVs defined using the surgical specimens. Adaptive thresholding techniques need to be calibrated for each PET scanner and acquisition/processing protocol, and should not be used without optimization.

NOTES