4ème Journée et Prix de la Recherche Clinique

Jeudi 19 mai 2011
13h30 – 18h30

HUG – Site Cluse-Roseraie
Nouvel auditoire de pédiatrie, niveau 2

Programme final
et
Recueil des résumés

UNIVERSITÉ DE GENÈVE
FACULTÉ DE MÉDECINE

Centre de Recherche Clinique

HUG
Hôpitaux Universitaires de Genève

PROGRAMME

13h30 Introduction
Pr. Jean-Louis Carpentier, 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. Bernard Hirschel, Directeur du Centre de recherche clinique

13h45	Mme L. Allet:	**The gait and balance of patients with diabetes can be improved: a randomised controlled trial**
13h57	Pre C. Bouchardy:	**Risk of second breast cancer according to estrogen receptor status and family history**
14h09	Dre S. Carnesecchi:	**A key role for NOX4 in epithelial cell death during development of lung fibrosis**
14h21	Dr P. Gervaz:	**A prospective, randomized, single-blind comparison of laparoscopic versus open sigmoid colectomy for diverticulitis**
14h33	Dr I. Guessous:	**Health care renunciation for economic reasons in Switzerland**
14h45	Dre Albane Maggio :	**Long-term follow-up of cardiovascular risk factors after exercise training in obese children**

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

16h15 Présentations orales – Partie II
Modérateur: Pr. Osman Ratib, Chef du département d'imagerie et des sciences de l'information médicale

16h15	Dre B. MartinezTejada:	**Intrapartum group B streptococcus detection by rapid polymerase chain reaction assay for the prevention of neonatal sepsis**
16h27	Dre A. Quercioli:	**Elevated endocannabinoid plasma levels are associated with coronary circulatory dysfunction in obesity**
16h39	Dr F. Ris:	**Islet autotransplantation after extended pancreatectomy for focal benign disease of the pancreas**
16h51	Pre. C.-A. Siegrist:	**Influence de l'âge, de la maladie et de l'immunosuppression sur la sécurité et l'immunogénicité des vaccins contre la grippe A/H1N1/09 : étude transversale aux HUG**
17h03	Dr N. Vuilleumier:	**Anti-apolipoprotein A-1 IgG as an independent cardiovascular prognostic marker affecting basal heart rate in myocardial infarction**
17h15	Dr S. Vulliemoz:	**Localisation of focal epileptic activity with EEG-fMRI**

17h30 Conférence par **Monsieur Bernard Pécoul**, MD, MPH, directeur exécutif de DNDi Drugs for Neglected Diseases initiative :
De la molécule au médicament : un modèle innovant de recherche et développement contre les maladies négligées.

18h10 Remise des Prix de la présentation orale et du poster par le Pr Pierre Dayer, Directeur médical et qualité

Clôture de la journée par M. Bernard Gruson, Président du comité de direction des HUG

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. L'édition 2011 est particulièrement prometteuse : En comparaison avec les 50 à 60 contributions des années précédentes, nous en avons reçu 91 cette année !

Un jury dirigé par le Pr Th. Berney a choisi, parmi les 91, douze résumés qui seront présentés oralement. Un Prix rétribuera le meilleur travail parmi les présentations orales. 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 Docteur Bernard Pécoul, directeur de DNDi (Drugs for Neglected Diseases initiative) :

De la molécule au médicament : un modèle innovant de recherche et développement contre les maladies négligées.

DNDi est une organisation de recherche indépendante, à but non lucratif, basée à Genève, ayant pour objectif le développement de médicaments à potentiel commercial limité. Fondée en 2003, elle emploie 30 personnes à Genève et environ 400 dans divers pays en voie de développement. Elle a déjà à son actif la mise à disposition de plusieurs médicaments, notamment contre le paludisme et la leishmaniose.

Je me réjouis de vous voir nombreux le 19 mai 2011 !

Directeur du 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.
91 recherches provenant de services très variés ont été soumises pour cette quatrième édition.

Le jury :

Pr Thierry Berney, chirurgie (Président)
Pr Jacques Cornuz, 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

THE GAIT AND BALANCE OF PATIENTS WITH DIABETES CAN BE IMPROVED: A RANDOMISED CONTROLLED TRIAL

Lara Allet*°, Stéphane Armand§, Rob de Bie°, Alain Golay‡, Do minique Monnin*, Kamiar Aminian‡‡, Baart Staal°, Eling de Bruin#*

Care Services Directorate, Unit of Physiotherapy Research and Quality Assurance, Geneva University Hospital and University of Geneva, Geneva, Switzerland*° Department of Epid emiology, Maastricht University and Caphri Research School, Maastricht, the Netherlands° Willy Taillard Laboratory of Kines iology, Geneva University Hospital and University of Geneva,Geneva, Switzerland§ Service of Therapeutic Education for Chronic Diseases, WHO Collaborating Center, Geneva University Hospital and University of Geneva,Geneva, Switzerland‡ Laboratory of Movement Analysis and Measurement, EPFL, Lausanne, Switzerland‡‡ Institute of Human Movement Sciences and Sport, ETH, Zürich, Switzerland#

Introduction: Gait characteristics and balance are altered in diabetic patients. Little is known about possible treatment strategies. This study evaluates the effect of a specific training programme on gait and balance of diabetic patients.
Méthode: This was a randomised controlled trial (n=71) with an intervention (n=35) and control group (n=36). The intervention consisted of physiotherapeutic group training including gait and balance exercises with function orientated strengthening (twice weekly over 12 weeks). Controls received no treatment. Individuals were allocated to the groups in a central office. Gait, balance, fear of falls, muscle strength and joint mobility were measured at baseline, after intervention and at 6-month follow-up.
Résultat: After training, the intervention group increased habitual walking speed by 0.149 m/s ($p<0.001$) compared with the control group. Patients in the intervention group also significantly improved their balance (time to walk over a beam, balance index recorded on Biodex balance system), their performance-oriented mobility, their degree of concern about falling, their hip and ankle plantar flexor strength, and their hip flexion mobility compared with the control group. After 6 months, all these variables remained significant except for the Biodex sway index and ankle plantar flexor strength. Two patients developed pain in their Achilles tendon: the progression for two related exercises was slowed down.
Conclusion: Specific training can improve gait speed, balance, muscle strength and joint mobility in diabetic patients. Further studies are needed to explore the influence of these improvements on the number of reported falls, patients' physical activity levels and quality of life.

RISK OF SECOND BREAST CANCER ACCORDING TO ESTROGEN RECEPTOR STATUS AND FAMILY HISTORY

Christine Bouchardy *• Simone Benhamou • Gérald Fioretta • Helena M. Verkooijen • Pierre O. Chappuis • Isabelle Neyroud-Caspar • Monica Castiglione • Vincent Vinh-Hung • Georges Vlastos • Elisabetta Rapiti*

Le Registre genevois des tumeurs (Faculté de médecine / Département de santé et médecine communautaire)

Introduction: A recent study reported an increased risk of contralateral estrogen-negative breast cancer after a first primary estrogen-negative breast cancer. Our study aims to confirm this result and to evaluate how the risk of second breast cancer occurrence is affected by family history of breast cancer and anti-estrogen treatment.
Méthode: We included all 4,152 women diagnosed with breast cancer between 1995 and 2007, using data from the population-based Geneva Cancer Registry. We compared the incidence of second breast cancer among patients according to estrogen receptor (ER) status with that expected in the general population by age-period Standardized Incidence Ratios (SIRs).
Résultats: Among the cohort, 63 women developed second breast cancer. Patients with ER-positive first tumors had a decreased risk of second breast cancer occurrence (SIR: 0.67, 95% CI:0.48–0.90), whereas patients with ER-negative primary tumors had an increased risk (SIR: 1.98, 95% CI: 1.19–3.09)limited to ER-negative second tumors (SIR: 7.94, 95% CI:3.81–14.60). Patients with positive family history had a tenfold (SIR: 9.74, 95% CI: 3.57–21.12) higher risk of ERnegative second tumor which increased to nearly 50-fold(SIR: 46.18, 95% CI: 12.58–118.22) when the first tumor was ER-negative.
Conclusion: Treatment with anti-estrogen decreased the risk of second ER-positive tumors but not ER-negative tumors. The risk of second ER-negative breast cancer is very high after a first ER-negative tumor, in particular among women with strong family history. Surveillance and prevention of second cancer occurrence should consider both ER status of the first tumor and family history.

A KEY ROLE FOR NOX4 IN EPITHELIAL CELL DEATH DURING DEVELOPMENT

Stephanie Carnesecchi, *Christine Deffert, Yves Donati, Olivier Basset, Boris Hinz, Olivier Preynat-Seauve, Cecile Guichard, Jack L. Arbiser, Botond Banfi, Jean-Claude Pache, Constance Barazzone-Argiroffo* & Karl-Heinz Krause**
Departement de Pediatrie, Pathologie/Immunologie

Introduction: The pathogenesis of pulmonary fibrosis is linked to oxidative stress, possibly generated by the ROS generating NADPH oxidase NOX4. Epithelial cell death is a crucial early step in the development of the disease, followed only later by the fibrotic stage.
Méthode: To study expression of NOX4 in humans, we have performed immunohistochemistry with a NOX4 antibody in sections of IPF and of healthy lungs. To demonstrate a possible causative role of NOX4 in the epithelial cell death in lung fibrosis, we have generated NOX4-deficient mice and studied them in bleomycin model.
Résultats: We discovered a novel role for NOX4 in death of alveolar epithelial cells. We showed that NOX4 was highly expressed in hyperplastic alveolar type II cells in IPF patients. We also demonstrated that NOX4-deficient mice are protected from bleomycin-induced pulmonary fibrosis through modulation of epithelial cell death in vivo. Indeed, at day 7 after bleomycin, lungs of wild-type mice showed massive increase in epithelial cell apoptosis and inflammation. In NOX4 deficient mice, no increase in apoptosis was observed, whereas inflammation was comparable to wild-type. In vitro, NOX4-deficient primary alveolar epithelial cells exposed to TGF-β1 did not generate ROS and were protected from apoptosis. Acute treatment with the NOX inhibitors also blunted TGF-β1-induced apoptosis
Conclusion: Finally, we demonstrated that ROS generation by NOX4 is a key player in epithelial cell death leading to pulmonary fibrosis

A PROSPECTIVE, RANDOMISED, SINGLE-BLIND COMPARISON OF LAPAROSCOPIC VERSUS OPEN SIGMOID COLECTOMY FOR DIVERTICULITIS

Pascal Gervaz *MD*, Ihsan Inan MD*, Thomas Perneger MD†, Eduardo Schiffer MD§, Philippe Morel MD*
Chirurgie et Anesthésie, HUG

Introduction: The aim of this study was to compare open and laparoscopic sigmoid resection for diverticulitis with the patient and the nursing staff blinded to the surgical approach.
Méthode: 113 patients scheduled for an elective sigmoidectomy were randomised to receive either a traditional open (54 patients) or a laparoscopic (59 patients) approach. Postoperatively, an opaque wound dressing was applied and left in place for 4 days, and patients from both groups were managed similarly. The primary endpoints for analysis were; 1) postoperative pain; 2) duration of postoperative ileus; and 3) duration of hospital stay (ClinicalTrials.gov, number NCT 00453830).
Résultats: The median duration of procedure was 165 minutes (range 90-285) in the laparoscopy group and 110 minutes (range 70-210) in the open group ($p<0.0001$). The median delay between surgery and first bowel movement was 76 (range 31-163) hours in the laparoscopy group versus 105 (range 53-175) hours in the open group ($p<0.0001$). The median score for maximal pain (assessed by a Visual Analog Scale) was 4 (range 1-10) the laparoscopy group and 5 (range 1-10) in the open group ($p=0.05$). Finally, the median duration of hospital stay was 5 days [range 4-69] in the laparoscopy group versus 7 days (range 5-17) in the open group ($p<0.0001$).
Conclusion: Laparoscopic sigmoid resection is associated with a 30% reduction in duration of postoperative ileus and hospital stay; by comparison, benefits in terms of postoperative pain appear less impressive, when the patient is blinded to the surgical technique.

HEALTH CARE RENUNCIATION FOR ECONOMIC REASONS IN SWITZERLAND

Hans Wolff, Jean-Michel Gaspoz, ***Idris Guessous***
Service de Médecine de premier recours

Introduction: Most societies elaborate ways to contain increasing health care expenditures. In Switzerland out of pocket payments and cuts in the catalogue of reimbursed services are used as cost-containment measures. The aims of the study were to estimate the extent of health care renunciation for economic reasons and to identify associated factors.
Méthode: A population-based cross-sectional survey (2008–2009) of a representative sample in the Canton of Geneva, Switzerland. Health care underuse, income level categories (13\'000), education, occupation, insurance status and cardiovascular comorbidities were collected using self-rated questionnaires.
Résultats: 765 men and 814 women aged 35–74 years participated. 14.5% (229/1579) (95%CI 12.7-16.2) renounced health care for economic reasons. Among those who renounced (N = 229), 74% renounced dental care, 37% physician consultation (22% specialist, 15% general practitioner), 26% health devices, 13% medication, and 5% surgery. Income was negatively correlated with renouncement (r = –0.18, p <.0001). Each decrease in income level category provided a 48% increased risk of renouncing health care for economic reasons (OR 1.48, 1.31–1.65). This association remained when dental care was excluded from the definition of health care renunciation.
Conclusion: In a region of Switzerland with a high cost of living, such as Geneva, socioeconomic status may influence the use of the health care system, and renunciation for economic reasons was not uncommon. More than 30% of the lowest income group renounced health care for economical reasons in the previous year. Health care underuse and renunciation may worsen the health status of a substantial part of society.

LONG-TERM FOLLOW-UP OF CARDIOVASCULAR RISK FACTORS AFTER EXERCISE TRAINING IN OBESE CHILDREN

Albane B.R. Maggio*, Yacine Aggoun, Xavier E. Martin, Laetitia M. Marchand, Maurice Beghetti, Nathalie J. Farpour-Lambert.*
Pediatric Cardiology Unit, Department of Child and Adolescent, University Hospitals of Geneva and University of Geneva

Introduction: We previously demonstrated beneficial effects of physical activity on cardiovascular disease (CVD) risk factors, body mass index (BMI) and fat mass in pre-pubescent obese children. The aim of this study was to determine whether these changes were maintained 2 years later.
Méthode: Two years after the RCT, we performed a follow-up study with 20 of 38 subjects (11.4±1.8 years). Outcomes included BP by ambulatory monitoring; arterial function and structure using high-resolution ultrasound, BMI, body composition by dual-energy x-ray absorptiometry (DXA), physical activity using accelerometer, and biological markers.
Résultats: During the 2-year follow-up period, mean 24-hour diastolic BP z-score significantly decreased (1.4±1.2 vs. 0.3±1.4, p=.04), while systolic BP z-score was slightly reduced (2.4±1.5 vs. 1.4±1.7, p=.067). Blood pressure changes was greater in children who diminished their BMI z-score compared to the ones who did not. Systolic hypertension rates dropped from 50 to 28% and diastolic hypertension from 42 to 6%. In addition, arterial intima-media thickness (0.51±0.03 vs. 0.51±0.06, p=.004), BMI z-score (2.9±0.8 vs. 2.9±1.1 kg.cm-2, p=.27), body fat (41.9±6.9 vs. 42.8±6.7 %; p=.39) and physical activity count (703±209 vs. 574±244 cpm, p=.30) were stable.
Conclusion: To our knowledge, this is the first study reporting that beneficial effects on adiposity and CVD risk factors of a physical activity centred intervention are sustained 2 years after the cessation of training in obese children. Subjects stabilized BMI z-score and maintained physic al activity with further improvement of BP and stabilization of arterial wall remodelling. We conclude that it is important to encourage physical activity in this population.

INTRAPARTUM GROUP B STREPTOCOCCUS DETECTION BY RAPID POLYMERASE CHAIN REACTION ASSAY FOR THE PREVENTION OF NEONATAL SEPSIS

Intrapartum Group B Streptococcus Detection by Rapid Polymerase Chain Reaction Assay for the Prevention of Neonatal Sepsis ***Begoña Martinez de Tejada****, Riccardo E. Pfister, Gesuele Renzi, Patrice François, Olivier Irion, Michel Boulvain, Jacques Schrenzel*

Department of Gynecology and Obstetrics, Department of Pediatrics, Department of Genetics and Laboratory Medicine, and Department of Internal Medicine of the University Hospitals of Geneva and Faculty of Medicine, University of Geneva, Switzerland

Introduction: Group B streptococcus (GBS) is a leading cause of infectious neonatal morbidity and mortality. Timely and accurate identification of colonized mothers is imperative to implement antibioprophylaxis during labor to reduce the risk of neonatal sepsis. We planned our study to analyze the diagnostic accuracy of an intrapartum PCR assay to identify GBS colonized women and to allow the implementation of correct (i.e. at least 4 hours) intrapartum antibiotic prophylaxis based on the PCR results.
Méthode: We included 695 women in labor who were tested for rectovaginal GBS carriage by culture and PCR. PCR were immediatly processed by the midwife. Women were also screened at 35-37 weeks of gestation following current recommendations.
Résultats: Intrapartum GBS colonization was 19.3%. Assay sensitivity was 81.0% for antenatal culture and 85.0% for intrapartum PCR; P = .72. GBS colonization (n=107) was known at least 4 hours before delivery in 68 (64%) and 73 (68%) women based on antenatal culture and intrapartum PCR, respectively. Among 43 women delivering preterm, correct status was known at least 4 hours before delivery in 10 (23%) and 32 (74%) women according to antenatal culture and intrapartum PCR, respectively.
Conclusion: These results support the concept that GBS screening can be performed routinely during labor in a clinical setting. The intrapartum approach is at least as accurate as the antenatal screening with the additional advantage of identifying women delivering preterm or not followed during pregnancy.

ELEVATED ENDOCANNABINOID PLASMA LEVELS ARE ASSOCIATED WITH CORONARY CIRCULATORY DYSFUNCTION IN OBESITY

Alessandra Quercioli*, Zoltan Pataky, Gabriella Vincenti, Vincent Makoundou, Vincenzo Di Marzo,Fabrizio Montecucco, Sebastian Carballo, Aure lien Thomas,Christian Staub, Sabine Steffens, Yann Seimbille, Alain Golay, Osman Ratib,Elisabetta Harsch, Francois Mach, and Thomas H. Schindler*

Service de Cardiologie, Service de Medecine Nucleaire, Service des Maladies Chroniques.

Introduction: We aimed to evaluate a possible association between endocannabinoid (EC) plasma levels, such as anandamide (AEA) and 2-arachidonoylglycerol (2-AG), and coronary circulatory function in obesity
Méthode: Myocardial blood flow (MBF) re! sponses to cold pressor test (CPT) and during pharmacologic vasodilation with dipyridamole were measured with 13N-ammonia PET/CT.
Résultats: Study participants (n=77) were divided into three groups based on their body mass index (BMI, kg/m2): control group 20≤ BMI <25 (n=21); overweight group, 25≤ BMI<30 (n=26); and obese group, BMI≥30 (n=30). Median of AEA but not of 2-AG plasma levels was significantly elevated in obesity as compared to controls, respectively [0.68 (0.53, 0.78) vs. 0.56 (0.47, 0.66) ng/ml, p=0.020, and 2.2 (1.21, 4.59) vs. 2.0 (0.80, 5.90) ng/ml, p=0.806)]. The endothelium-related change in MBF during CPT from rest (ΔMBF) progressively declined in overweight and obese as compared to control group [0.21 (0.10, 0.27) and 0.09 (-0.01, 0.15) vs. 0.26 (0.23, 0.39) ml/g/min; p=0.010 and p=0.0001, respectively). Compared with controls, hyperemic MBFs were significantly lower in overweight and obese individuals (! 2.39 (1.97, 2.62) vs. 1.98 (1.69,2.26) and 2.10 (1.76, 2.36), ! p=0.007 and p=0.042, respectively)] . In obese individuals, AEA and 2-AG plasma levels were inversely correlated with ΔMBF to CPT (r=-0.37, p=0.046 and r=-0.48, p=0.008) and hyperemic MBFs (r=-0.38, p=0.052 and r=-0.45, p=0.017), respectively.
Conclusion: Increased EC plasma levels of AEA and 2-AG are associated with coronary circulatory dysfunction in obese individuals. This observation might suggest increases in EC plasma levels as a novel endogenous cardiovascular risk factor in obesity, but needing further investigations.

ISLET AUTOTRANSPLANTATION AFTER EXTENDED PANCREATECTOMY FOR FOCAL BENIGN DISEASE OF THE PANCREAS

***Frédéric Ris**, Nadja Niclauss, Philippe Morel, Sandrine Demuylder-Mischler, Yannick Muller, Raphael Meier, Muriel Genevay, Domenico Bosco and Thierry Berney*
Service de Chirurgie Viscérale et de Transplantation, HUG, Genève

Introduction: Extended pancreatectomy is associated with the risk of surgical diabetes. Islet autotransplantation is successful in the prevention of diabetes after pancreas resection for chronic pancreatitis(CP), with insulin independence rates of 50% at 1 year. The aim of the present study is to demonstrate the safety and efficiency of islet autotransplantation after extended left pancreatectomy for benign disease.
Méthode: Between 1992 and 2009, 25 patients underwent extended pancreatectomy and islet autotransplantation for benign disease. Of these, 15 patients were operated for focal lesions located at the neck of the pancreas (14 benign tumors, 1 traumatic pancreatic section), the remainder being CP cases. After unequivocal diagnosis of benignity, the rest of the pancreas was processed and infused into the portal vein. Metabolic results were analyzed and isolation results were compared with those obtained from CP patients or donors with brain death (DBD).
Résultats: There was no mortality and a low morbidity (Str. mitis bacteremia in 1 patient), no portal thrombosis or pancreatic fistula occurred. Median follow-up was 90 months. Actuarial patient survival was 100% at 10 years. Actuarial insulin-independence was 94% at 10 years. All patients had positive basal and stimulated C-peptide levels and normal HbA1c. Mean islet yields were 5'455 IEQ/gram vs 1'457 in CP (p=0.001) and 3'738 in DBD (p=0.003).
Conclusion: Islet autotransplantation after extensive pancreatic resection for benign disease is a safe and successful procedure. Islet yields after isolation, which are equivalent to the live donor situation, are significantly better than those from DBD donors.

INFLUENCE DE L'AGE, DE LA MALADIE ET DE L'IMMUNOSUPPRESSION SUR LA SECURITE ET L'IMMUNOGENICITE DES VACCINS CONTRE LA GRIPPE A/H1N1/09 : ETUDE TRANSVERSALE AUX HUG.

***C.A. Siegrist**, M. Bel, S. Meier, K. Posfay-Barbe; L. Kaiser, W. Wunderli, S. Yerly, Y. Thomas; J. Desmeules, C. Combescure ; C. Gabay, P.A. Guerne, C. Ribi, J. Seebach, J. Villard ; P.Y. Dietrich, A.C. George, E. Roosnek, B. Mohty, M. Nagy; A. Calmy, A. Nguyen, B. Hirschel, J. Ambrosioni ; C. van Delden, K. Hadaya, P.Y. Martin, P. Soccal, T. Berney, S. Noble.*
Centre de Vaccinologie et Plateforme de recherche clinique pédiatrique; Laboratoire Central de Virologie; Centre de Recherche Clinique; Services de Rhumatologie et d'Immunologie et Allergologie; Services d'oncologie et d'hématologie; Service des maladies infectieuses; Services de transplantation, néphrologie, chirurgie thoracique, chirurgie viscérale, cardiologie.

Introduction: La crainte d'une pandémie grippale sévère a conduit à utiliser de nouveaux vaccins adjuvantés chez des patients immunocompromis. Une étude transversale multi-cohorte a analysé la tolérance et les réponses vaccinales de nos patients.
Méthode760 patients (rhumatologie: 173, VIH: 121, cancer: 192, transplantation de moelle allogénique (65) ou d'organe (216)),138 contrôles et 83 enfants ont été inclus! et suivis jusqu'à 4 semaines après 1 (contrôle) ou 2 (patients) doses de Pandemrix®. Les effets secondaires, les biomarqueurs d'activité des maladies de base et les taux d'anticorps ont été mesurés.
Résultats: Les réactions inflammatoires sont plus fréquentes chez les contrôles (88%) que les patients (73% - 81%) – sauf en rhumatologie (91%). L'âge diminue les réactions inflammatoires (OR par 10 ans : 0.7, 95%CI 0.6-0.7) mais aussi les réponses anticorps (-31% par 10 ans). Les scores d'activités et biomarqueurs sont restés inchangés - mais la vaccination a induit des anticorps anti-HLA chez 15% des greffés rénaux séronégatifs et une augmentation de virémie VIH chez 58% des patients avirémiques. Deux doses de vaccin ont permis à la plupart des patients – sauf parmi les greffés - d'atteindre les mêmes taux d'anticorps que les contrôles. Chez l'enfant immunocompétent, une dose de vaccin a induit les mêmes réponses que chez 60 enfants convalescents. Les analyses multivariées ont identifié pour chaque cohorte les! facteur s déterminants de l'immunogénicité vaccinale.
Conclusion: La recherche clinique transversale est possible aux HUG même en temps de crise (pandémie), notamment avec l'appui du Centre de Recherche Clinique.

ANTI-APOLIPOPROTEIN A-1 IGG AS AN INDEPENDENT CARDIOVASCULAR PROGNOSTIC MARKER AFFECTING BASAL HEART RATE IN MYOCARDIAL INFARCTION

Nicolas Vuilleumier *1, Michel F. Rossier 1,2, Sabrina Pagano 1, Magaly Python 2,Emmanuel Charbonney 3, Rene Nkoulou 4, Richard James 2, Guido Reber 5, Francois Mach 4, and Pascale Roux-Lombard 6*

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Introduction: Anti-apoA-1 IgG have been reported in MI without autoimmune disease, but their clinical significance remains undetermined.Therefore, we assess the prognostic value of anti-apolipoprotein A-1 (anti-apoA-1) IgG after myocardial infarction (MI) and its association with major cardiovascular events (MACEs) at 12 months, and we determined their association with resting heart rate (RHR), a well-established prognostic feature after MI.
Méthode: A total of 221 consecutive patients with MI were prospectively included, and all completed a 12-month follow-up. Major cardiovascular events consisted in death, MI, stroke, or hospitalization either for an acute coronary syndrome or heart failure. Resting heart rate was obtained on Holter the day before discharge under the same medical treatment. Neonate rat ventricular cardiomyocytes (NRVC) were used in vitro to assess the direct anti-apoA-1 IgG effect on RHR.
Résultats: During follow-up, 13% of patients presented a MACE. Anti-apoA-1 IgG positivity was 9% and was associated with a higher RHR (P ¼ 0.0005) and higher MACE rate (adjusted OR, 4.3; 95% CI, 1.46–12.6; P ¼ 0.007). Survival models confirmed the significant nature of this association. Patients with MACE had higher median anti-apoA-1 IgG values at admission than patients without (P ¼ 0.007). On NRVC, plasma from MI patients and monoclonal anti-apoA-1 IgG induced an aldosterone and dose-dependent positive chronotropic effect, abrogated by apoA-1 and therapeutic immunoglobulin (IVIG) pre-incubation
Conclusion: In MI patients, anti-apoA-1 IgG is independently associated with MACE at 1-year, interfering with a currently unknown aldosterone-dependent RHR determinant. Knowing whether anti-apoA-1 IgG assessment could be of interest to identify an MI patient subset susceptible to benefit from apoA-1/IVIG therapy remains to be demonstrated.

LOCALISATION OF FOCAL EPILEPTIC ACTIVITY WITH EEG-FMRI

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Introduction: In patients with medically refractory focal epilepsy who are candidates for epilepsy surgery, concordant findings from non-invasive multimodal imaging are needed to localise the epileptic focus and guide intracranial EEG recording and/or resective surgery. Simultaneous EEG-fMRI can map focal haemodynamic (BOLD signal) changes related to interictal epileptiform discharges (IED) detected on the EEG and helps to localise the epileptic focus. However, EEG-fMRI studies are negative in 40-70% of cases due to a lack of IED or absence of significant correlated BOLD changes. Here, we used EEG topographic features of the epileptic activity derived from long term clinical EEG monitoring (LTM) to inform EEG-fMRI analysis.
Méthode: After building the voltage map of averaged IED recorded during LTM, we calculated the timecourse of the correlation of this map with the intra-MR EEG topography. This timecourse was used as a regressor for fMRI analysis in a General Linear Model. In all cases, results were validated by concordance with the target area defined as seizure onset zone on intracranial recordings and/or resection zone in post-operatively seizure free patients. Concordance was labelled as good (maximal statistical BOLD change ($p<0.001$ uncorrected) or any corrected BOLD change (family-wise error correction $p<0.05$) located <15mm from the target area) or moderate (non-maximal uncorrected BOLD change <15mm from the target area).
Résultats: In 5/5 patients with IED-re! lated BOLD change on conventional analysis, concordant with th! e seizur e onset zone, the topographic analysis gave similar concordant results. In 14/18 (78%) patients with absent BOLD changes on conventional analysis, the topographic method showed good concordance (N=10) or moderate concordance (N=4) with intracranial EEG or resection area in post-operative seizure-free patients. All cases with lateral temporal or extratemporal lobe epilepsy showed concordance.
Conclusion: Pathological EEG topographic features have haemodynamic correlates and our method dramatically increased the yield of EEG-fMRI for estimating the localisation of the epileptogenic zone. These findings could have important implications for tailoring surgical resection in patients with pharmaco-resistant epilepsy

PRESENTATIONS POSTERS

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

P1

RITONAVIR INHIBITS THE TWO MAIN PRASUGREL BIOACTIVATION PATHWAYS IN VITRO: A POTENTIAL DRUG–DRUG INTERACTION IN HIV PATIENTS

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Introduction: Prasugrel is an antiplatelet prodrug used in patients with acute coronary syndrome. Prasugrel is mainly bioactivated by cytochromes P450 3A4/5 and CYP2B6. HIV patients are at risk of cardiovascular disease, and the protease inhibitor ritonavir is a potent inhibitor of these 2 CYPs. The aim of this in vitro study was to determine the impact of ritonavir in prasugrel metabolism.
Méthode: Human liver microsomes (HLMs) and recombinant microsomes were used to identify the enzymes responsible for the bioactivation of prasugrel. Prasugrel concentrations of 5 to 200 µM were used for Km determination. Inhibition by ritonavir was characterized using HLMs at concentrations of 0.1 to 30 µM. Prasugrel active metabolite determination was performed with a validated liquid chromatography-mass spectrometry method.
Résultats: Using recombinant microsomes, prasugrel biotransformation was mainly performed by CYP2B6, CYP2D6, CYP2C19, CYP3A4, and CYP3A5. With specific inhibitors of CYP3A, CYP2B6, CYP2D6, CYP2C9, and CYP2C19, active metabolite production was decreased by 38% ± 15% with 4-(4-chlorobenzyl) pyridine (CYP2B6 inhibitor) and by 45 ± 16% with ketoconazole (CYP3A inhibitor). The Km value for prasugrel metabolism in HLMs was determined to be 92.5 µM. Ritonavir at 0.1 to 30 µM was shown to be a potent dose-dependent inhibitor of prasugrel.
Conclusion: In this in-vitro study, we found a potent inhibition of prasugrel bioactivation by ritonavir compared to the specific inhibitors of CYP3A and CYP2B6 due to the simultaneous inhibition of CYP2B6 and CYP3A by ritonavir. This finding suggests a potential significant drug–drug interaction between these two drugs.

P2

DO NK CELLS CONTRIBUTE TO THE PATHOPHYSIOLOGY OF THROMBOTIC MICROANGIOPATHY POST HEMATOPOIETIC STEM CELL TRANSPLANTATION?

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Introduction: Transplant-associated microangiopathy (TAM) is a life-threatening complication after allogeneic hematopoietic stem cell transplantation (HSCT).The pathophysiology of TAM is caused by aggregation of platelets exposed to the thrombogenic subendothelial matrix of endothelial cells. Natural Killer (NK) cells lacking inhibitory receptors may contribute to TAM by damaging endothelial cells. Furthermore, as NK-cells produce platelet-activating factor upon activation, they may also promote TAM progression.
Méthode: We present a case of a 9-year-old girl with idiopathic aplastic anemia who received a HSCT from a mismatchdonor.The conditioning regimen included Fludarabine, ATG and cyclophosphamide with cyclosporine for GvHD prophylaxis. Donor CD34 cells treated with Campath-1H in the bag were infused followed the next day by 5x106 T cells/kg. On day +8 she developed a severe TAM andengrafted on day +13. CSA was replaced by methylprednisolone. Intestinal GvHD started on day 17. Despite treatment by plasma exchange, anti TNF, statins, heparin, and defibrotide, the patient worsened clinically. She reactivated CMV, cardiac and pleural effusion appeared with HHV-6 infection, respiratory failure, pulmonary arterial hypertension and she ultimately died on day +193.
Résultats: An important increase of NK-cell was detected in the blood at engraftment. Only few NK cells expressed an inhibitory KIR specific for one of the HLA-Cw16 and HLA-Cw17 KIR-ligands. Immunohistochemistry using the monoclonal antibody NKp46 revealed that the NK-cell population expanded in the blood analysis was present in the pericardial fluid and infiltrated the pericardium, kidneys and lungs coinciding with renal and pulmonary vasculopathy.
Conclusion: NK-cells that had infiltrated the lungs and kidney\'s may have contributed to the microangiopathy

P3

INCREASED PRODUCTION OF IL-22 BY T CELLS IN AN INDIVIDUAL WITH SEVERE CUTANEOUS AND SYSTEMIC INFLAMMATION AFTER BEING EXPOSED TO PURE DIOXIN.

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Introduction: Dioxins are ubiquitous environmental toxic chemicals known to have pleiotropic biological effects in animals. The activity of these compounds in humans, despite their daily exposition, is poorly known. We therefore investigated the long-term immunological effects induced by dioxins in an individual who developed a severe cutaneous and systemic syndrome after exposure to an extremely high dose of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD).
Méthode: T cells were studied via multiparameter flow cytometry for their capacity to produce cytokines and for the expression of chemokine receptors involved in skin homing. Transcription of the TCDD-target gene CYP1A1 was evaluated by RT- PCR.
Résultats: The supernatants from T cells of the exposed individual contained a substantially increased amount of interleukin (IL)-22 but not IL-17A, interferon-γ or IL-10 when compared to healthy controls. In vitro experiments demonstrate an enhancing effect of TCDD on IL-22 production via a mechanism involving the transcription factor aryl hydrocarbon receptor (AhR). However, the increased production of IL-22 in the exposed individual was not dependent on AhR occupancy by residual TCDD molecules. In contrast, it was due to an increased frequency of IL-22 single producing cells accompanied by an increased percentage of cells expressing the skin-homing chemokine receptors CCR6 and CCR4.
Conclusion: This case strongly supports the contention that exposure to dioxins in vivo induces a long-lasting effect on the human adaptive immune system and specifically polarizes T cells to produce IL-22. It is tempting to speculate that these cells may have been involved in the severe dermal manifestations observed after dioxin intoxication.

P4

RE-ENTRAINEMENT PRE-OPERATOIRES DES PATIENTS AVEC CANCER PULMONAIRE NON A PETITE CELLULE

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Introduction: La capacité d'effort mesuré par la consommation maximale d'O2 à l'ef! fort (VO2 max) prédit les complications post-opératoires et la mortalité à court et long terme pour les patients atteint de cancer pulmonaire (CP). L'effet d'un ré-entraînement supervisé (RS) en pré-opératoire et inconnu.
Méthode: Nous prévoyons d'inclure 390 patients CP dans un essai randomisé (1/1) multicentrique (HUG et RSV, Sion). Les patients alloués au groupe intervention (I) reçoivent un entraînement à l'effort supervisé et adapté à la VO2 max mesurée à l'inclusion. Après 90 j d'étude, 24 patients on été screenés et 22 ont été inclus. [I n=9, C n=13. Age 69 (DS10), homme 57%, BPCO 56%, diabète 25%, hypertension 43%, fumeur 95%.] Le VEMS ou la capacité de diffusion sont abaissés à moins de 80% de la valeur prédite chez 42% et 66% des patients respectivement. La VO2 max moyenne mesurée à l'inclusion est de 18 ml/min/kg (min 11, max 29).
Résultats: Dans le groupe I, après RS la VO2 augmente de 1.2ml/min/kg (C! I95% -12.0 à +14.8) et baisse de 6.8 ml/min/kg dans le groupe C (CI95 % -17.2 à +3.1).
Conclusion: Un essai clinique interdisciplinaire (pneumologie, anesthésie, physiothérapie, médecine du sport, oncologie et chirurgie) permet d'inclure 90% des patients screenés. Le ré-entraînement supervisé s'accompagne d'une tendance à l'augmentation de la VO2 max. Nos futures analyses compareront l'incidence de complications, l'effet sur la mortalité et la qualité de vie dans les groupes I et C à court et long terme. La capacité d'effort et la fonction pulmonaire à 1 an seront également mesurées.

P5a

POPULATION PERCEPTION OF SURGICAL SAFETY AND BODY IMAGE TRAUMA: A PLEA FOR SCARLESS SURGERY?

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Introduction: Background: Laparoendoscopic single-site (LESS) and natural orifice translumenal endoscopic (NOTES) surgery are prospected as the future of minimally invasive surgery. While scarless surgery, NOTES and LESS, is gaining increasing popularity, perception toward these approaches should be investigated.
Méthode: Materials and Methods: Anonymous questionnaire (describing laparoscopy, LESS, and NOTES) was given to medical staff (n=120), paramedical staff (n=100), surgical patients (n=100), and general population (n=100). Participants (median age 37, 18-81 years) were queried about their expectations from surgical treatment and approach preference.
Résultats: The first concern of survey responders is the risk of surgical complications (92%). When asked about the respective importance of surgical safety, cure, and cosmetics; 74% placed cure first, 33% safety, and 3% cosmetics. These results were not influenced by sex, age, prior surgery/endoscopy, and education. With similar operative risk, 90% of participants preferred scarless approach (75% LESS and 15% NOTES) to laparoscopy. Scarless approach preference was significantly higher in younger
Conclusion: Although cure and safety remains the main concern, the population has a favorable perception of scarless surgery, even in case of increased procedural risk. LESS is favored to NOTES. Such a popular adoption of scarless surgery should warrant us to promote further research, technological innovations, and establish surgeon training to improve its safety.

P5b

FEMALE POPULATION PERCEPTION OF CONVENTIONAL LAPAROSCOPY, TRANSUMBILICAL LESS, AND TRANSVAGINAL NOTES FOR CHOLECYSTECTOMY

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Introduction: Recent population survey has shown a preference for transumbilical LESS (U-LESS) compare to NOTES for cholecystectomy assuming similar surgical risk. Study aim was to evaluate perception and preference of women regarding conventional laparoscopy, U-LESS and transvaginal NOTES (TV-NOTES) with particular interest to access perception.
Méthode: Anonymous questionnaire on laparoscopic, U-LESS, and TV-NOTES cholecystectomy, without regards to risks or advantages, were given to female medical/paramedical staff (n=100), patients (n=100), and general population (n=100). Women participants (median age 35, 16-79 years) were queried about preference, perception of the different accesses, and personal informations. 54% had children, 79% had stable relationship, and 96% were sexually active (vaginal intercourse).
Résultats: With similar operative risk, 87% preferred U-LESS, 4% TV-NOTES and 8% laparoscopy. LESS/NOTES choice was influenced by a desire of improved cosmetics (82%) and lower pain (44%). 96% had worries regarding transvaginal access, among them: dyspaneuria (68%), decrease sensibility during intercourse (43%), refuse of short-term sexual abstinence (40%), and infertility (23%). Transumbilical access evocated worries in 35%: umbilical pain (19%), post-operative umbilical sensibility (15%), and incisional hernia (11%). Post-operative intercourse abstinence after TV-NOTES evocated worries in 76% (defined as 3 weeks in survey): feel less attractive (40%), less feminine (32%), tension with their intimate (35%), lover non-acceptation (20%), possible abortion of new relationship (26%), and feel less comfortable socially (16%).
Conclusion: The high acceptation rate for U-LESS approach compare to TV-NOTES may be related to fears regarding post-operative sexuality and fertility. The importance of temporary post-operative sexual abstinence (vaginal intercourse) is high and may be difficult to influence. Future research on TV-NOTES should focus on the access risk to be able to scientifically reinsure our patients. Whatever and until now, U-LESS seems to be favor to TV-NOTES for cholecystectomy in female patients.

P6

OXYGENATED HYPOTHERMIC PULSATILE PERFUSION VERSUS COLD STATIC STORAGE FOR KIDNEYS FROM NON HEART BEATING DONORS TESTED BY IN LINE ATP RESYNTHESIS TO ESTABLISH A STRATEGY OF PRESERVATION

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Introduction: The aim of this study was to find the best way for the preservation of the kidneys from Non Heart Beating Donors (NHBD): cold static storage (CSS) or perfusion. ATP production during their preservation has been retained as the measure of their energetic levels, consequently their viability. The presence of warm ischemia with both types of preservation was studied.
Méthode: Porcine kidneys presenting no warm ischemia or 30 minutes of warm ischemia have been submitted to immediate oxygenated hypothermic pulsatile perfusion or immediate cold static storage. ATP resynthesis was measured after 8 h. of perfusion. ATP has been acquired by 31P Nuclear Magnetic Resonance Spectroscopy in line during the preservations.
Résultats: Only oxygenated perfusion could restore ATP in organs with warm ischemia. Initial cold static storage seems deleterious on organs having suffered from warm ischemia.
Conclusion: Oxygenated perfusion must be introduced immediately after kidney removal from Non Heart Beating Donors. In organs without warm ischemia, any kind of preservation is equivalent.

P7a

ROBOT-ASSISTED GASTRECTOMY FOR CANCER

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Introduction: Minimally invasive approach for gastric cancer has gained increasing acceptance. Introduction of the da Vinci robotic system has allowed overcoming the technical limitations of standard laparoscopy. To date, several studies have been published reporting the feasibility of robot-assisted gastrectomy (RAG). The aim of this study is to extensively review all the published literature concerning RAG and to assess its value.
Méthode: Since 2003, this systematic review of the literature shows that 10 original studies reporting 199 RAG for cancer have been published worldwide. The authors' analyzed operative time, blood loss, conversion rate, lymph nodes retrieval, complications, mortality, length of hospital stay and follow up through a systematic review.
Résultats: Mean age was 63 years (range: 25-96). Mean operative times were 265 minutes and 334 minutes for total and subtotal gastrectomy respectively. Mean blood loss reported was 113 ml (range: 12-1400). Conversion rate was 2.5%. Average lymph nodes retrieval was 32 (range: 11-83). Twenty-nine complications were reported (14.6%). Mortality rate was 1.5%. Mean length of stay was 10 days (range: 3-175).
Conclusion: This review demonstrates that RAG for cancer is not only feasible but also seems to be safe, with low mortality and acceptable morbidity. However, due to the lack of long-term follow up and the limited number of published studies, it is relatively too early to draw definitive conclusions and/or to recommend the use of RAG for oncologic gastrectomy. Randomized controlled trials with long-term follow up are needed before this promising approach can eventually be generalized.

P7b

VALUE OF CONTRAST-ENHANCED FDG PET/CT IN DETECTION AND PRESURGICAL ASSESSMENT OF PANCREATIC CANCER: A PROSPECTIVE STUDY

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Introduction: Positron Emission Tomography (PET) using 18F-fluorodeoxyglucose (FDG) associated with Computed Tomography (CT) is increasingly used for the detection and the staging of pancreatic cancer, but data regarding its clinical added value in pre-surgical planning is still lacking. The aim of this study is to investigate the performance of FDG PET associated with contrast-enhanced CT in detection of pancreatic cancer.
Méthode: We prospectively evaluated FDG PET/CT studies obtained in patients with suspicion of operable pancreatic cancer between May 2006 and January 2008. Staging was conducted according to a standardized protocol, and findings were confirmed in all patients by surgical resection or biopsy examination.
Résultats: Forty-five patients with a median age of 69 (range 22 - 82) were included in this study. Thirty-six had malignant tumors and nine had benign lesions (20%). The sensitivity of enhanced versus unenhanced PET/CT in the detection of pancreatic cancer was 96% vs. 72% (p=0.076), the specificity 66.6% vs. 33.3% (p=0.52), the positive predictive value 92.3% vs. 80% (p=0.3), the negative predictive value 80% vs. 25% (p=0.2), and the accuracy 90.3% vs. 64% (p=0.085).
Conclusion: Our preliminary data obtained in a limited number of patients shows that contrast-enhanced FDG PET/CT offers a good sensitivity in the detection and assessment of pancreatic cancer, but at the price of a relatively low specificity. Enhanced PET/CT seems to be superior to unenhanced PET/CT. Further larger prospective studies are needed to establish its value for pre-surgical diagnosis and staging in pancreatic cancer.

P7c

ROBOT-ASSISTED ONCOLOGIC RESECTION FOR LARGE GASTRIC GASTROINTESTINAL STROMAL TUMOR: A PRELIMINARY CASE SERIES

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Introduction: Laparoscopic resection of gastric Gastrointestinal Stromal Tumor (GIST) has been shown as feasible and safe in terms of oncologic results. However, laparoscopic resection has been demonstrated to be mainly suitable for small and favorably localized GIST. Robotic approach may by its characteristics enable to perform atypical gastrectomies in unfavorable location (close to pylorus or cardia). Its use in oncologic gastric surgery has been poorly defined and never been reported for GIST.
Méthode: All patients who underwent robotic assisted gastric resection for GIST at a single institution from 2006 to 2009 were prospectively followed-up.
Résultats: There were five patients, 3 men and 2 women, with a median age of 39 years (range 32-74), who had a complete resection (R0). Two patients had a cardial GIST and three of the antrum. Median tumor sizes were of 5.5 cm (range: 4.2-7). According to Fletcher criteria, four tumors (80%) were classified as intermediate or high risk. No post-operative morbidity and mortality were noted. One patient had a conversion to open surgery because of a suspicion of diffuse adenocarcinoma on fresh frozen section and necessitated a total gastrectomy with radical lymph node dissection. The median operation time was 192 minutes (range: 132-285). With a median follow-up of 18 months (11-27), disease free survival rates was 100%.
Conclusion: Da Vinci robot is a valuable instrument for oncologically safe resection with oesogastric or duodenogastric junction preservation for unfavorably located gastric GIST. Moreover, the three dimensional high definition vision, the instrument mobility and the ease to perform difficult suture enable safe large atypical gastrectomy, close to pylorus or cardia.

P8

KINGELLA KINGAE OSTEOARTICULAR INFECTIONS IN YOUNG CHILDREN: CLINICAL FEATURES AND CONTRIBUTION OF A NEW SPECIFIC REAL-TIME PCR ASSAY TO THE DIAGNOSIS.

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Introduction: K. kingae is currently considered as the major bacterial cause of osteoarticular infections (OAI) in children less than 4 year-old. Unfortunately, this fastidious microorganism is difficult to isolate and osteoarticular samples remain culture-negative in a substantial proportion of patients. The main objective of this prospective study is to characterize the clinical and biological features of children with OAI caused by K. kingae. We also describe the benefit due to the usage of a new K. kingae-specific real-time PCR assay developped in the University Hospitals of Geneva.
Méthode: We prospectively collected all children less than 4 year-old admitted to our institution since January 2007 for suspected OAI. Biological evaluation and classical cultures (blood, joint fluid or bone aspirate sample) were ordered for each patient. A novel real-time PCR assay targeting the RTX toxin gene was used in this study.
Résultats: Routine blood and site aspiration cultures identified the causative organism in 11.5% of the cases. Classical isolation methods combined with specific qPCR assays yielded to a microbiologic diagnosis in 37 out of the 53 samples (69.8%) and identified K. kingae in a total of 31 cases, corresponding to 83.8% of the bacteriologically documented cases of OAI.
Conclusion: This study, using a new highly specific real-time PCR, confirms that K. kingae is the major bacterial cause of OAI in children less than 4 year-old. It demonstrates too that none of the 31 OAI due to K. kingae could have been detected without the contribution of the new K. kingae-specific real-time PCR assay.

P9

LES PARENTS DOIVENT ETRE INCLUS DANS LES PROGRAMMES DE THERAPIE DE L'OBESITE : RESULTAT D'UNE ETUDE QUALITATIVE

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Introduction: La dynamique familiale est fortement associée à l'obésité des adolescents. Le but de notre étude est de connaitre les perceptions des parents à la fin d'une thérapie comportementale familiale pour la prise en charge de l'obésité.
Méthode: La dynamique familiale est fortement associée à l'obésité des adolescents. Le but de notre étude est de connaitre les perceptions des parents à la fin d'une thérapie comportementale familiale pour la prise en charge de l'obésité.
Résultats et conclusion: Les parents rapportent que la participation à la thérapie leur a permis de lutter contre leur isolement : «On n'est pas les seuls à se battre, cela donne de la force et du courage». Partager leurs difficultés et leur épuisement face à la maladie chronique a fait diminuer leur sentiment de culpabilité. La thérapie de groupe les a également aidé à comprendre l'implication de la famille dans le processus de soin: «ce n'est pas une problématique liée juste à une personne». Elle les a soutenu dans la transition vers l'adolescence: "pouvoir séparer ma fille de sa problématique de poids, on ne voit plus que le poids, ça empêche de voir les autres problèmes

P10a

EARLY SERUM IGF-I RESPONSE TO ORAL PROTEIN SUPPLEMENTS IN ELDERLY WOMEN WITH A RECENT HIP FRACTURE

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Introduction: In patients with recent hip fracture, reduced serum IGF-I in relation to protein undernutrition is frequent. Elevation of circulating IGF-I in response to a daily oral supplement of 20 g of casein was observed after 6 months. This study determined if the response to casein as compared to whey protein can be observed as early as after one week.
Méthode: 45 Women were randomized after recent hip fracture in 3 groups receiving a preparation of 20 g of casein, an isocaloric supplement of 20 g of whey protein or an isocaloric supplement of 15 g of whey protein combined with 5 g of essential amino acids (a.a.).
Résultats: A similar significant elevation of serum IGF-I was already observed after 7 days for casein (þ37.3 mg/L), whey (þ29.4) and for wheyþ a.a. (þ34.3). From day 7–28, no further significant rise in IGF-I was recorded.
Conclusion:After one week of protein supplementation, the percent increase of IGF-I was of similar magnitude to that previously observed after 6 months of protein supplementation. It suggests that in hip fracture patients, long-term effects of various protein preparations on IGF-I could be predicted from changes observed as early as 7 days after the onset of supplementation.

P10b

PUBERTAL TIMING AND BODY MASS INDEX GAIN FROM BIRTH TO MATURITY IN RELATION WITH FEMORAL NECK BMD AND DISTAL TIBIA MICROSTRUCTURE IN HEALTHY FEMALE SUBJECTS

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Service des maladies osseuses

Introduction: Recent data point to a relationship between BMI change during childhood and hip fracture risk in later life. We hypothesized that BMI development is linked to variation in pubertal timing as assessed by menarcheal age (MENA) which in turn, is related to peak bone mass (PBM) and hip fracture risk in elderly.
Méthode: We studied in a 124 healthy female cohort the relationship between MENA and BMI from birth to maturity, and DXA-measured femoral neck (FN) aBMD at 20.4 year. At this age, we also measured bone strength related microstructure components of distal tibia by HR-pQCT.
Résultats: At 20.4±0.6 year, FN aBMD (mg/cm2), cortical thickness (µm), and trabecular density (mg HA/cm3) of distal tibia were inversely related to MENA (P=0.023, 0.015, and 0.041, respectively) and positively to BMI changes from 1.0 to 12.4 years (P=0.031, 0.089, 0.016, respectively). Significant inverse (P<0.022 to <0.001) correlations (R=−0.21 to –0.42) were found between MENA and BMI from 7.9 to 20.4 years, but neither at birth nor at 1.0 year. Linear regression indicated that MENA Z-score was inversely related to BMI changes not only from 1.0 to 12.4 years (R=−0.35, P=0.001), but also from 1.0 to 8.9 years, (R=−0.24, P=0.017), i.e., before pubertal maturation.
Conclusion: BMI gain during childhood is associated with pubertal timing, which in turn, is correlated with several bone traits measured at PBM including FN aBMD, cortical thickness, and volumetric trabecular density of distal tibia. These data complement the reported relationship between childhood BMI gain and hip fracture risk in later life.

P11

MONITORING OF NON-INVASIVE VENTILATION BY BUILT-IN SOFTWARE OF HOME BI-LEVEL VENTILATORS: A BENCH STUDY

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Introduction: Recent bi-level positive pressure ventilators for home non-invasive ventilation (NIV) provide clinicians with softwares which record items important for patient monitoring such as compliance, tidal volume (VT), leaks. However, validity of this information has not yet been independently assessed.
Méthode: Testing of seven home ventilators on a bench model, adapted to simulate NIV and generate unintentional leaks (i.e other than mask exhalation valve). Five levels of leaks were simulated with a computer driven so! lenoid valve (0 – 60L/min.) at different levels of inspiratory pressure (15 and 25 cmH2O), and at a fixed expiratory pressure (5 cmH2O), i.e. a total of 10 conditions. Bench data was compared to results retrieved from ventilator software for leaks and VT.
Résultats: For assessing leaks, three of the devices tested were highly reliable, with a small bias (0.3 – 0.9L/min), narrow limits of agreement (LA) and high correlations (R2: 0.993-0.997) when comparing ventilator software and bench results; conversely, for 4 ventilators, bias ranged from -6.0 to -25.9 L/min, exceeding -10L /min for 2 devices, with wide LA, and lower correlations (R2: 0.70 – 0.98). Bias for leaks increased markedly with importance of leaks in three devices. VT was underestimated by all devices and bias (range: 66 – 236 ml) increased with higher insufflation pressures. Only 2 devices had a bias < 100 ml, all testing conditions considered.
Conclusion: Clinicians monitoring patients with home ventilation must be aw! are of d ifferences in estimation of leaks and VT by ventilator softwares, and of different ways in reporting leaks according to device used.

P12

TRANSCUTANEOUS NICOTINE DOES NOT PREVENT POSTOPERATIVE NAUSEA AND VOMITING: A RANDOMIZED CONTROLLED TRIAL

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Introduction: There is empirical evidence that smokers are less likely to suffer from postoperative nausea and vomiting (PONV).We sought to investigate whether transcutaneus nicotine prevents PONV.
Méthode: Non-smokers receiving general anaesthesia for surgery were randomly allocated to Nicotinell® Patch 10 cm2 (TTS 10), containing 17.5 mg of nicotine (average delivery rate, 7mg 24 h-1) or matching placebo patch. Patches were applied 1 h before surgery and were left in situ until 24 h after surgery (or until the first PONV symptoms occurred).
Résultats: We randomized 90 patients (45 nicotine, 45 placebo). In the post-anaesthetic care unit, the incidence of nausea was 22.2% with nicotine and 24.4% with placebo (P = 0.80), and the incidence of vomiting was 20.0% with nicotine and 17.8% with placebo (P = 0.78). Cumulative 24 h incidence of nausea was 42.2% with nicotine and 40.0% with placebo (P = 0.83), and of vomiting was 31.1% with nicotine and 28.9% with placebo (P = 0.81). PONV episodes tended to occur earlier in the nicotine group. Postoperative headache occurred in 17.8% of patients treated with nicotine and in 15.6% with placebo (P = 0.49). More patients receiving nicotine reported a low quality of sleep during the first postoperative night (26.7% vs. 6.8% with placebo; P = 0.01).
Conclusion: Non-smokers receiving a prophylactic nicotine patch had a similar incidence of PONV during the first 24 h and tended to develop PONV symptoms earlier compared with controls. They had a significantly increased risk of insomnia during the first postoperative night

P13

CYP2C9 PHENOTYPING USING A SINGLE-POINT DRIED BLOOD SPOT AFTER ORAL ADMINISTRATION OF FLURBIPROFEN

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Introduction: Flurbiprofen (FLB) is widely accepted as a reliable probe for CYP2C9 activity assessment. However, only urinary measures of metabolism have been validated using an over-night or 8 hours urine collection which is tedious, time consuming and uncomfortable for the patients and for the medical staff. In this study, we investigated whether a single blood measurement using a new and minimally invasive technique (dried blood spot) consisting of a 5 ul blood sampling using a small finger prick would be suitable for CYP2C9 phenotyping.
Méthode: Ten healthy volunteers genotyped for the CYP2C9 received flurbiprofen (50 mg) alone in session 1, flurbiprofen and the CYP2C9 inhibitor fluconazole(200 mg) in session 2 and in session 3 they were pretreated for 4 days with rifampicin (600 mg) and at day 5 they received flurbiprofen (50 mg) with the last dose of rifampicin. Plasma and DBS samples were obtained at 0, 0.5, 1, 2, 4, 6 and 8 hours after drug administration and urine was collected from 0 to 8 hours. FLB and OH-FLB were determined in DBS, plasma and urine using validated analytical methods.
Résultats: Urine mean metabolic ratios were 1.73 (0.45) in session 1, 0.79 (0.35) after fluconazole and 2.18 (0.44) after rifampicine. Statistically significant differences in the OH-FLB/FLB metabolic ratios in urine (8h), plasma (2h) and DBS (2h) were observed between the three sessions (p
Conclusion: Single-point method using a DBS provides a reliable and a minimally invasive method of predicting CYP2C9 activity. This new phenotyping method is particularly suitable for pediatric patients since only 5 ul of blood are needed for CYP2C9 phenotype.

P14

ELECTROPHYSIOLOGICAL PATTERNS DISTINGUISH MULTIPLE- FROM SINGLE-DOMAIN AMNESTIC MILD COGNITIVE IMPAIRMENT AT RETRIEVAL, BUT NOT AT ENCODING

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Introduction: Amnestic mild cognitive impairment (aMCI) is characterized by memory deficits alone (single-domain) or with other cognitive impairments (multiple-domain). The present study assessed the patterns of electroencephalographic (EEG) activity during the encoding and retrieval phases of short-term memory in single- and multiple-domain aMCI, to identify potential functional differences according to the aMCI subtype.
Méthode: 79 elderly subjects (64.7 ± 5.9 years) underwent complete neuropsychological assessment and were classified as cont! rols (EC, N=36), single-domain (S-aMCI, N=16), and multiple-domain (M-aMCI, N=27) amnestic MCI. Continuous EEG was recorded using 32 surface electrodes during sequential presentation of two faces and two letters in random order, followed by a delayed face probe. Subjects attended faces while ignoring letters, deciding if the probe belonged to the presented set. Event-related alpha desynchronization/synchronization (ERD/ERS) and probe-evoked responses were analyzed during successful encoding and retrieval, respectively.
Résultats: At encoding, attended faces elicited parietal activation (alpha ERD), whereas ignored letters were associated with inhibition at central sites (alpha ERS). This inhibition was significantly reduced in M-aMCI compared to EC, showing intermediate level in S-aMCI. At retrieval, the N250 component indexing covert recognition was absent in M-aMCI as compared to S-aMCI and EC.
Conclusion: A differential alteration of working memory cerebral processes for faces was observed in the two aMCI subtypes. M-aMCI showed EEG inhibition deficit for distracting letters during face encoding and altered EEG activation during face retrieval. In contrast, S-aMCI displayed preserved EEG activation at retrieval counteracting the moderate alteration of inhibitory activity observed at encoding.

P15

ELECTRONIC CIGARETTE: USERS PROFILE, UTILIZATION, SATISFACTION AND PERCEIVED EFFICACY

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Introduction: Electronic cigarettes are an entirely new way of administering medications to the lung. They are popular, but little is known about users, their experience of this product and how much nicotine they obtain from it. The objective of this study was to assess users' profile, utilization patterns, cotinine levels, satisfaction and perceived effects of electronic cigarettes.
Méthode: We conducted an Internet survey in English and French in 2010. Participants were visitors of websites and online discussion forums dedicated to electronic cigarettes and to smoking cessation. Saliva samples for cotinine analysis were collected by mail.
Résultats: There were 3587 participants (70% ex-tobacco smokers, 61% men, mean age 41 years). The median duration of electronic cigarette use was 3 months, users drew 120 puffs/day and used 5 refills/day. Almost all (97%) used e-cigarettes containing nicotine. They spent $33 per month on these products. Most (96%) said the e-cigarette helped them quit smoking or reduce their smoking (92%). Reasons for using the e-cigarette included the perception it was less toxic than tobacco (84%), to deal with craving for tobacco (79%) and withdrawal symptoms (67%), to quit smoking or avoid relapsing (77%), because it was cheaper than smoking (57%) and to deal with situations! where smoking was prohibited (39%). Most ex-smokers (79%) feared they might relapse to smoking if they stopped using the e-cigarette. Users of nicotine-containing e-cigarettes reported better relief of withdrawal and more effect on smoking cessation than users of non-nicotine e-cigarettes. The median cotinine level was 322 ng/ml.
Conclusion: E-cigarettes were used much as people would use nicotine medications: by former smokers to avoid relapse or as an aid to cut down or quit smoking. Because it may be difficult to conduct clinical trials of a product for which the safety profile is unknown, online surveys such as this are useful in tracking user attitudes and behavior. Cotinine levels in e-cigarette users were similar to levels observed, in previous reports, in smokers, and higher than levels observed in users of nicotine medications. Further research should evaluate the safety and efficacy of e-cigarettes for administration of nicotine and other substances.

P16a

EVALUATION OF CARDIOVASCULAR RISK IN PATIENTS WITH RHEUMATOID ARTHRITIS. WHAT IS THE ADDED PREDICTIVE ABILITY OF NEW CARDIOVASCULAR BIOMARKERS OVER ESTABLISHED CLINICAL RISK SCORES?

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Introduction: Rheumatoid arthritis (RA) is associated with an increased risk of major cardiovascular events (MACE). Quantification of cardiovascular (CV) risk can be performed using well established clinical risk scores, such as the Framingham 10-years Global Cardiovascular Disease Score (FCVDS). Furthermore, emergent biomarkers of CV risk have been identified. It remains unclear whether the prognostic accuracy of the FCVDS can be improved by adding emergent biomarkers of CV risk, such as anti-apolipoprotein A-1 (anti-ApoA-1) IgG, N-terminal pro-Brain Natriuretic peptide (NT-proBNP) or oxidised LDL (oxLDL). Objectives: To determine whether the adjunction of 3 emergent CV biomarkers (anti-ApoA-1 IgG, NT-proBNP, oxLDL) to the FCVDS could improve its prognostic accuracy for MACE prediction in RA patients.
Méthode: We performed an ancillary study (n=118) derived from a single center prospective RA cohort published earlier (1). Patients had no cardiovascular disease at baseline and were assessed for incident MACE during follow-up. MACE was defined as fatal or non-fatal stroke or acute coronary syndrome. We measured the levels of anti-ApoA-1 IgG, NT-proBNP and oxLDL on baseline serum samples and computed the FCVDS. We assessed discriminatory ability using the area under the ROC curve (AUC) and the integrated discrimination improvement (IDI) statistic (2). The added predictive ability of the aforementioned biomarkers was assessed by the increase in discrimination obtained by combining the biomarker and the FCVDS and compared to discrimination of the FCVDS alone.
Résultats: During a median follow-up of 9 years, MACE incidence was 16% (19/118). Individually, all 3 biomarkers were modestly predictive of MACE, with AUCs between 0.68 – 0.73 (Table). However, adding these biomarkers to established clinical risk factors (FCVDS) resulted in significant increase of predictive ability only for anti-Apo A1 IgG (Table). The AUC improved from 0.72 (0.61 – 0.84) for FCVDS alone to 0.82 (0.72 – 0.92) for FCVDS + anti-ApoA-1 IgG, and the IDI by 0.98 (<0.001).
Conclusion: Among the emergent prognostic biomarkers tested in this study, anti-ApoA-1 IgG was the only independent predictor of MACE and the only biomarker that significantly improved the predictive ability of the Framingham CV risk score in RA. Whether deriving a new score from the anti-ApoA-1 IgG and FCVDS combination could yield a valuable CV risk stratification tool in RA remains to be demonstrated.

P16b

A NOVEL SCREENING STRATEGY FOR PRECLINICAL RHEUMATOID ARTHRITIS (RA) IN FIRST DEGREE RELATIVES OF PATIENTS WITH RA

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Introduction: The pathophysiology of rheumatoid arthritis (RA) is believed to begin with a pathologic activation of the adaptive immune system (or 'immune onset of the disease'), followed by an asymptomatic period (or 'preclinical phase'), which eventually leads to the 'clinical onset of the disease'. Biomarkers and clinical risk factors of pre-symptomatic disease exist and suggest that screening at risk populations for early detection of RA and treatment is possible. Objective: To assemble a prospective multicenter cohort of a population at increased risk of developing RA in first-degree relatives (FDRs) of RA patients.
Méthode: This is an ongoing, prospective cohort study of individuals at increased risk of developing RA in FDRs of patients with active RA without clinical evidence of joint effusion or active synovitis. The individuals are then followed yearly to determine the development of symptoms and signs of arthritis. The clinical and immunochemical characteristics of the cohort are described.
Résultats: We present the first consecutive FDRs of RA patients enrolled between 1st January 2009 to 31st December 2010: 302 FDRs from 5 centers have been identified. At inclusion, mean age is 41 years (SD 15), 75% are female, 93% are Caucasian, median duration of education is 13 years (IQR:12 – 16), median BMI is 23 (IQR: 21 – 26). On average, these individuals have 1.3 direct relatives with RA and 15% present at least one tender joint on examination. 18% of FDRs had at least one positive auto-antibody associated with RA (auto-AB): 14% were positive for rheumatoid factor IgM, 3% were positive for rheumatoid factor IgA, and 1% had anti–cyclic citrullinated peptide antibodies (anti-CCP 2 or 3.1). High levels of auto-AB or simultaneous positivity of several auto-AB were rare in this population (N=1). Individuals with at least one positive auto-AB were at higher risk of having tender joints on examination (OR: 3.23, 95% CI: 1.10 - 9.52).
Conclusion:The prevalence of auto-AB positivity and subtle signs of joint inflammation (joint tenderness) is somewhat higher among asymptomatic FDRs than what would be expected in a younger general population, suggesting that FDRs are indeed a group at higher risk of developing RA. The association between positive auto-Ab and joint tenderness suggests that auto-Ab are a valid intermediate marker of RA development in this population. FDR cohorts can be a valuable resource to decipher RA development and the relationship between genetic and environmental risk factors.

P17

LA LEVOBUPIVACAINE PROCURE UNE DUREE D'ANALGESIE APRES BLOC SCIATIQUE POSTERIEUR SELON LA TECHNIQUE DE LABAT SUPERIEURE A CELLE PROCUREE PAR LA MEME DOSE DE ROPIVACAINE

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Introduction: Le lévobupivacaine et la ropivacaine sont 2 molécules énantiomères et lévogyres fréquemment utilisées dans les blocs périphériques au vu de leur excellente marge de sécurité. La lévobupivacaine est très lipophile et théoriquement plus puissante que la ropivacaine. Cependant, la controverse règne dans la littérature à ce sujet. Notre hypothèse est que l'analgésie relevant de la levobupivacaine est de plus longue durée.
Méthode: Nous avons comparé les caractéristiques analgésiques de 20 ml de lévobupivacaine par rapport à 20 ml de ropivacaine 0.5% lors d'un bloc sciatique postérieur dans la chirurgie de pied et de cheville. Quatre-vingt patients randomisés en double aveugle et de manière prospective ont bénéficié de l'administration de l'un ou l'autre des anesthésiques locaux. Nous avons procédé à la récolte de différentes données sur 24h (délai, durée, taux de succès du bloc, recours analgésiques, problèmes techniques ou complications neurologiques).
Résultats: Le délai d'action (min) s'est avéré semblable dans les groupes levobupivacaine et ropivacaine (15 (5-40) vs 15 (5-60) min respectivement) de même que le taux de succès (90% vs. 92.5%). Le temps écoulé jusqu'au premier recours analgésique est significativement plus long dans le groupe levobupivacaine que dans le groupe ropivacaine (1605 (575-2400) min vs. 1035 (590-1500) min, $p< 0.001$).
Conclusion: Vingt ml de levobupivacaine injectés lors d'un bloc sciatique postérieur selon la technique de Labat procurent une analgésie après chirurgie de pied ou de cheville d'environ 570 min supplémentaires par rapport à l'administration de la même dose de ropivacaine 0.5%.

P18

STATUS EPILEPTICUS IN FRAGILE X SYNDROME

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Introduction: Fragile X syndrome (FXS) is the most common cause of inherited mental retardation. The clinical spectrum includes dysmorphological signs, behavioral peculiarities, and epilepsy. Seizures are rare and EEG findings resemble those found in benign epilepsy with centro-temporal spikes (BECTS). Status epilepticus (SE) seems exceptional in FXS.
Méthode: Case series.
Résultats: We report the clinical features, EEG and MRI findings of five FXS children who presented with SE as their initial seizure. Interestingly, two of our patients had clinical manifestations and EEG findings more suggestive of Panayiotopoulos syndrome than of benign rolandic epilepsy.
Conclusion: Despite this initial severity, our patients did not evolve to refractory epilepsy, and presented only rare additional seizures, suggesting that long-term antiepileptic drugs might not be necessary. Epilepsy is a frequent manifestation in FXS (prevalence 13% -50%). Various mechanisms have been proposed. Various seizure types may be noted. The EEG frequently reveals a pattern found in BECTS. The natural course is often favorable. Two of our patients and one of the previously reported children, had clinical seizures and EEG findings more suggestive of Panayiotopoulos syndrome (PS) than of BECTS (prolonged seizures with vegetative symptoms). The etiology of PS is unknown, but some authors suspect it to be genetic. The link with FXS remains to be demonstrated. As observed in PS, one of our patients exhibited severe respiratory complications after receiving rectal Diazepam, suggesting that a reduction in the dosage of emergency benzodiazepines may be necessary in FXS patients presenting with predominantly vegetative ictal symptoms.

P19

WHAT DIFFERENCES ARE DETECTED BY SUPERIORITY TRIALS OR RULED OUT BY NONINFERIORITY TRIALS? A CROSS-SECTIONAL STUDY ON A RANDOM SAMPLE OF TWO-HUNDRED TWO-ARMS PARALLEL GROUP RANDOMIZED CLINICAL TRIALS

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Introduction: The smallest difference to be detected in superiority trials or the largest difference to be ruled out in noninferiority trials is a key determinant of sample size, but little guidance exists. The objectives were to examine the distribution of differences used by researchers and to verify that those differences are smaller in noninferiority compared to superiority trials.
Méthode: Cross-sectional study based on a random sample of 200 two-arm, parallel group superiority (100) and noninferiority (100) randomized clinical trials published between 2004 and 2009 in 27 leading medical journals. The main outcome measure was the smallest difference in favor of the new treatment to be detected (superiority trials) or largest unfavorable difference to be ruled out (noninferiority trials) used for sample size computation, expressed as standardized difference in proportions, or standardized difference in means. Student test and analysis of variance were used.
Résultats: In superiority trials, the standardized difference in means ranged from 0.007 to 0.87, and the standardized difference in proportions from 0.04 to 1.56. On average, superiority trials were designed to detect larger differences than noninferiority trials (standardized difference in proportions: mean 0.37 versus 0.27, P=0.001; standardize d difference in means: 0.56 versus 0.40, P=0.006). Standardized differences were lower for mortality than for other outcomes, and lower in cardiovascular trials than in other research areas.
Conclusion: Superiority trials are designed to detect larger differences than noninferiority trials are designed to rule out. The variability between studies is considerable and partly explained by the type of outcome and the medical context.

P20a

CHICKENPOX IN A SWISS PRISON: SUSCEPTIBILITY, POST-EXPOSURE VACCINATION AND CONTROL MEASURES

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Introduction: Chickenpox can cause severe complications in adults and measures to protect contacts are indicated, particularly in overcrowded prisons. After occurrence of a case of chickenpox in Switzerland's largest pre-trial prison (Champ-Dollon, Geneva)), we aimed to estimate the susceptibility to chickenpox in such a population and to assess the efficacy of control measures implemented to limit the spread of chickenpox.
Méthode: A serology for chickenpox was carried out to all inmates in contact with the index case. We implemented control measures, listed logistical facilitating or hindering parameters and estimated the predictive positive value of a history of chickenpox.
Résultats: Serological susceptibility to chickenpox was found in 14 prisoners out of 110 (12.7%; CI 95% 6.5-18.9). The positive predictive value of a history of chickenpox was 90%. Protective measures included vaccination of 80 inmates and quarantine of susceptible contacts; no secondary case of chickenpox was diagnosed.
Conclusion: In this predominantly migrant population, susceptibility to chickenpox was approximately 6 times higher than in the general Swiss adult population. Since the attack rate among susceptible household contacts is usually high, preventive measures such as vaccination and quarantine probably allowed containing the spread of infection.

P20b

IMPROVEMENT OF MEASLES IMMUNITY AMONG MIGRANT POPULATIONS: LESSONS LEARNED FROM A PREVALENCE STUDY IN A SWISS PRISON.

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Introduction: Measles persists worldwide despite the implementation of general vaccination campaigns. The environmental and demographic characteristics in many prisons increase the risk of measles epidemics. An important proportion of inmates come from countries where immunization coverage is low. We aimed to estimate the susceptibility to measles among prisoners in order to implement preventive measures.
Méthode: A serology screening for measles was carried out among 116 inmates in Switzerland's largest pre-trial prison (Champ-Dollon, Geneva). Socio-demographic characteristics were collected through a structured questionnaire. Risk factors for lack of measles immunity were examined.
Résultats: Seven of 116 (6%) inmates were not immune to measles. All 37 inmates from sub-Saharan Africa were immune. Considering only people native from regions other than sub-Saharan Africa, 7 of 40 inmates born after 1981 were susceptible (18.5%), whereas none of the 39 inmates born in 1981 or before were susceptible (p=0.006).
Conclusion: Susceptibility to measles is fairly low in this prison population composed mainly of migrants. Living in sub-Saharan Africa during childhood and birth before 1982 are protective factors associated with the presence of immunity against measles. The heterogeneity of vaccination campaigns in the various regions of the world, particularly in terms of timing of their introduction and scale of diffusion, explains epidemiological variability. Targeted vaccination in accordance to the origin and age would offer excellent herd immunity and would substantially reduce risks of outbreaks as well as costs.

P20c

HEPATITIS B: PREVALENCE, RISK FACTORS AND KNOWLEDGE OF TRANSMISSION MODES AMONG INMATES IN A SWISS PRISON

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Introduction: This study aimed to estimate the prevalence of HBV infection and its associated factors as well as the knowledge of transmission modes among inmates in Champ-Dollon prison,
Méthode: A total of 116 individuals were interviewed using a standardized questionnaire on sociodemographic characteristics and HBV knowledge. HBsAg, HBsAb and HBcAb were detected by enzyme immunoassay.
Résultats: Prevalence for HBcAb indicating past or current infection was 44% (95%CI: 34.9-53.0) and 4.3% (95%CI: 1.4-9.8) had HBsAg indicating current infection. Region of origin is significantly associated with HBV infection (p
Conclusion: The high prevalence combined with the ignorance of infection and the lack of knowledge of transmission modes underlines the need for preventive actions in prison. A serological screening of populations characterized by high HBV prevalence would enable the implementation of an intensive educational program targeting contagious and susceptible inmates. Persons tested positive for HBV could be excluded from vaccination thus leading to substantial reduction of costs. Prison settings provide unique opportunities to vaccinate this high risk population. Vaccinating incarcerated persons protects not only those individuals, but also the community at large.

P21

A PSYCHOLOGIST FOR NURSES AND NURSE-ASSISTANTS IN AN ICU: IMPACT ON THE BURNOUT AND THE ANXIETY OF THE CAREGIVERS

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Introduction: ICU caregivers are facing a demanding job (high level of technology and work load, stressful environment). They are at high risk of developing anxiety, depression and a burnout syndrome (BOS), which can impact on their welfare, performances and patients' care. BOS favours absenteeism and job-leave, whereas the shortage of ICU caregivers already started.
Méthode: Randomised, controlled, single blind study to evaluate the impact of the intervention of two psychologists leading weekly sessions in small groups of caregivers (9 months). Individual meetings were optional. Anxiety (HA)-depression (HD) assessed by HADS, BOS by MBI, before and after the intervention.
Résultats: 170 caregivers, 99(58%) responded the questionnaires before and after. Nurses: 77/99(78); Men:24(24); Age<40yo:72(73); Occupational rate 100%:54(55); Intervention Group(IG):41(41); Control Group(CG):58(59). IG: Scores mean(SEM):HA:before 7(17)/after 5(13); HD:0/2(5); MBI:-14.5(2.98)/-19.4(2.61)p<0.05; Exhaustion:16.3(1.83)/13.4(1.54); Depersonalisation:6.49(.87)/4.7(.65)p<0.01; Accomplishment:36.8(.98)/37.5(1.06). ProportionsN(%) of severe Anxiety (HA>8):7(17)/5(13); Severe Depression(HD>8):3(5)/2(4); Severe BOS(MBI>-9):15(27)/14(25). CG: Scores mean (SEM):HA: before 6.5(.43)/after 6.7(.45); HD:4.2(.45)/3.8(.41); MBI:-15.8(2.33)/-18.5(2.07); Exhaustion:16.9(1.45)/15.1(1.35); Depersonalisation:5.3(.77)/5.0(.58); Accomplishment:38.1(.87)/38.7(.78). ProportionsN(%) of severe Anxiety:7(13)/11(19); Severe Depression:0/2(5); Severe BOS:15(41)/9(22). The ICU activities during the 3 time periods of 3 months, Before, During, After were: Mortality(%): 8.8,8.3,13.0(p=0.009); ICU admissions:272,242,173; Mean SAPS:39,37,37; Mean PRN:166,167,166, respectively.
Conclusion: Up to 32% of ICU nurses and nurse-assistants show high risk of BOS. Up to17/4% show signs of anxiety/depression. After the intervention, the scores of BOS decreased significantly whereas it was unchanged in the CG. The anxiety-depression scores tended to decrease more in the IG(no statistical significance). The presence of psychologists might help to care for caregivers. Further investigation is needed for physicians.

P22

LIVER KIDNEY MICROSOMES TYPE 1 ANTIBODIES ARE ASSOCIATED WITH A SIX-FOLD REDUCTION OF THE CYP2D6 ACTIVITY IN PATIENTS WITH CHRONIC HEPATITIS C

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Introduction: In vitro, Liver Kidney Microsomal type 1 antibodies (LKM-1) have been associated with a reduction of CYP2D6 activity in patients with autoimmune hepatitis type 2. We considered chronic hepatitis C patients with and without LKM-1 antibodies and investigated whether LKM-1 antibodies were associated with reduced CYP2D6 activity.
Méthode: All anti-HCV-positive patients enrolled in the Swiss Hepatitis C Cohort Study who had LKM-1 antibodies were compared to a control group of patients without LKM-1 antibodies. Among 2\'569 patients, 1\'723 (67.1%) were tested for LKM-1 antibodies. Twenty-three patients (1.3%) had anti-CYP2D6 antibodies that persisted during at least one-year follow-up. CYP2D6 activity was evaluated by a specific substrate and both groups were genotyped for CYP2D6. CYP2D6 allelic variants were detected by AmpliChip® CYP450 test to exclude individuals with poor metabolizer genotype. Liver insufficiency (INR <0.9 or albumin <35g/L), concomittant interferon therapy or CYP2D6 inhibitors, ascites, liver transplantation were further exclusion criteria. CYP2D6 activity was assessed with the metabolic ratio dextromethorphan/dextrorphan (DEM/DOR) to classify patients in four phenotypic categories. We compared metabolic activity in both groups and determined the concordance between CYP2D6 activity and CYP2D6 genotype.
Résultats: Among LKM-1 positive HCV patients, ten fulfilled inclusion criteria (mean age 59 years, range 38-77, 60% male) and were included from January 2008 to July 2009. The median CYP2D6 metabolic activity was six-fold lower in LKM-1 positive compared to LKM-1 negative patients (median DEM/DOR ratios 0.096 vs. 0.016, p=0.004). CYP2D6 phenotype predicted from genotype was EM for all patients and controls. Whereas phenotype measured from the DEM/DOR ratio was concordant with predicted phenotype for 70% of LKM-1 negative patient, only 30% of LKM-1 positive patients had a concordant phenotype and 70% showed a phenotypic offset (60% classified as IM and 10% as PM). CYP2D6 activity was not significantly associated with gender, age, BMI, viral genotype, duration since hepatitis C diagnosis and biochemical parameters.
Conclusion: CYP2D6 activity drastically decreased in the presence of LKM-1 antibodies. The mechanism and clinical consequences deserve to be further investigated.

P23

FUNCTIONAL MAPPING OF CORTICAL LANGUAGE AREAS WITH FUNCTIONAL MRI IN INDIVIDUAL PATIENTS

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Introduction: In the last two decades, several tasks for fMRI-based non-invasive mapping of brain language areas for presurgical evaluation have been proposed. However, while hemispheric lateralization of language is obtained fairly reliably with fMRI, individual localization of the major language areas remains challenging. In the present study, we aimed to evaluate the localization reliability of a short and efficient auditory language paradigm in individual subjects.
Méthode: An auditory semantic decision task including congruent, incongruent and non-sense short sentences (Astesano, Besson et al. 2004) was presented to 22 right-handed, healthy subjects in an fMRI event-related design. 16 patients with epilepsy (N=14) or tumor (N=2) in temporal lobe were also included. For two of these patients the fMRI results in this task were compared to language mapping during electrical cortical stimulation (ECS).
Résultats: The group analysis revealed left hemispheric dominance, including activations in the superior middle temporal gyrus and the inferior frontal gyrus corresponding to the main language regions, namelay Broca and Wernicke's areas. These areas were detected in 100% (Broca) and in 86% (Wernicke) at the individual level using restrictive statistical constraints. ECS results in the two epileptic patients showed excellent concordance with their preoperative fMRI results.
Conclusion: This auditory semantic decision paradigm appears to provide a robust localization of language areas in fMRI at the individual level. The short duration (~8 minutes) and the simplicity make it particularly suitable in clinical settings.

P24a

IMPACT OF CYP2C9 POLYMORPHIMS AND/OR INHIBITORS ON THE RISK OF OVERANTICOAGULATION IN PATIENTS STARTING AN ACENOCOUMAROL TREATMENT

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Introduction: Acenocoumarol is an oral anticoagulant commonly prescribed in Switzerland. As warfarin, the response to treatment varies widely and is affected by genetic and environmental factors, bleeding being the most frequent serious adverse event. Drug-drug interactions (DDIs) or CYP2C9 polymorphisms are among the factors known to affect the risk of overanticoagulation. The objective of this study was to investigate the impact of CYP2C9 polymorphisms and drug interactions on overanticoagulation risk in patients treated with acenocoumarol.
Méthode: A prospective observational study was performed on patients starting acenocoumarol. CYP2C9 genotypes were assessed and data on INR, comedications, comorbidities, and doses of acenocoumarol were collected during the first 35 days of therapy. Drugs known to inhibit CYP2C9 were considered as relevant DDIs. Overanticoagulation was defined as the occurrence of at least one INR≥4.
Résultats: The CYP2C9 genotype of 107 subjects was assessed: 63.5% were wild-type subjects, 26.2% were carriers of CYP2C9*2 and 10.3% of CYP2C9*3. 42.1% had at least one INR≥4. Patients taking CYP2C9 inhibitors (31%) had an increased risk of overanticoagulation ($p<0.05$). The presence of a CYP2C9 inhibitor or CYP2C9 mutations statistically increased the risk of overanticoagulation (HR=3.2, $p<0.05$ and HR=2.4, $p<0.05$; respectively).
Conclusion: In the first month of acenocoumarol treatment, the presence of at least one allelic variant of CYP 2C9 and/or prescription of CYP2C9 inhibitors expose patients to an inc reased risk of overanticoagulation.These findings support that CYP2C9 genotyping could be useful to identify patients requiring a closer monitoring.

P24b

A RETROSPECTIVE STUDY OF CLINICAL PHARMACOLOGY CONSULTATIONS EVALUATING DRUG-DRUG INTERACTIONS IN PATIENTS TREATED WITH ACENOCOUMAROL

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Introduction: Acenocoumarol (ACO) is the most commonly used oral anticoagulant in the French-speaking part of Switzerland. Due to its narrow therapeutic margin and its metabolism, the response to ACO varies widely and is affected by genetic and environmental factors, bleeding being the most frequent serious adverse event. ACO is mainly metabolised by CYP2C9. CYP1A2 and CYP2C19 are minor metabolic pathways. Numerous drugs interact with ACO and are frequently involved in the occurrence of ACO-related adverse events. To identify the most frequent drug interactions occurring with ACO, that had required a clinical pharmacology consultation.
Méthode: A retrospective study of all clinical pharmacology consultations over the past 14 years (1994-2007). Every consultation, in which ACO was mentioned, was included in the study. Drug interactions clinically relevant (supratherapeutic or infratherapeutic INR, bleeding) with ACO were collected and classified as pharmacokinetic or pharmacodynamic. Pharmacokinetic interactions were further divided according to the metabolic pathway involved in the interaction.
Résultats: Among the 407 consultations identified (3% of all consultations), 225 were addressed to the clinical pharmacology to check interactions with ACO: - In 74% of these consultations, a real potential interaction with ACO was detected - In 70% of the cases, the question was addressed after the interaction had happened - 52% were due to a difficulty to settle the INR (supratherapeutic, infratherapeutic, fluctuation) - In 8% a bleeding was observed 74% of the potential interactions were pharmacokinetic and 26% pharmacodynamic. 60% of the drugs implied in the pharmacokinetic interactions had an effect on CYP2C9, CYP1A2 or CYP2C19 with 38% of the interactions due to a CYP substrate, 44% to a CYP inhibitor, and 18% to a CYP inducer. The most frequent drugs implied in a clinical relevant interaction were amiodarone, fluconazole, valproate, esomeprazole, rifampicine and carbamazepine. Acetylsalicylic acid was the drug most frequently implied in the pharmacodynamic interactions (antiagregant effect).
Conclusion: The drugs that most frequently interacted clinically with ACO and that had required specialised advice in a university hospital setting were identified. Interactions were mostly pharmacokinetic and usually due to substrates, inhibitors and inducers of CYP2C9, CYP2C19 or CYP1A2. A better detection of these interactions might decrease the ACO-related adverse events.

P25

THE NADPH OXIDASE NOX2 CONTROLS GLUTAMATE RELEASE: A NOVEL MECHANISM INVOLVED IN PSYCHOSIS-LIKE KETAMINE RESPONSES

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Introduction: Subanesthetic doses of NMDA receptor antagonist ketamine induce schizophrenia-like symptoms in humans and behavioral changes in rodents. Subchronic administration of ketamine leads to loss of parvalbumin-positive interneurons through reactive oxygen species (ROS), generated by the NADPH oxidase NOX2. However, ketamine induces very rapid alterations, in both mice and humans.
Méthode: Mice were intraperitoneally injected with subanesthetic doses of ketamine. Behavioral, neuropathological and neurochemical changes were then compare! d between wild-type and NOX2 deficient mice.
Résultats: In wild-type mice, ketamine caused rapid (30 min) behavioral alterations, release of neurotransmitters, and brain oxidative stress, whereas NOX2-deficient mice did not display such alterations. Decreased expression of the subunit2Aof theNMDAreceptor after repetitive ketamine exposure was also precluded byNOX2 deficiency. However, neurotransmitter release and behavioral changes in response to amphetamine were not altered in NOX2 deficient mice.
Conclusion: Our results suggest that NOX2 is a major source of ROS production in the prefrontal cortex controlling glutamate release and associated behavioral alterations after acute ketamine exposure. Prolonged NOX2-dependent glutamate release may lead to neuroadaptative downregulation of NMDA receptor subunits.

P26

TRANSPLANTATION PULMONAIRE ET VIRUS RESPIRATOIRES : ETUDE DE COHORTE

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Introduction: Les sujets transplantés pulmonaires ont un risque élevé de complication au cours d'une infection respiratoire. Ces infections favorisent des potentielles complications, telles que le rejet et la bronchiolite oblitérante, cette dernière étant la principale cause de décès.
Méthode: Nous avons conduit une étude prospective qui recrutait l'ensemble des patients suivis au Centre de transplantation Lausanne-Genève de juillet 2008 à mars 2011. Une détection de tous les virus respiratoires par RT-PCR (14 virus) sur des prélèvements respiratoires collectés au niveau du nasopharynx (NP) ou de lavages broncho-alvéolaires (LBA) a été effectuées su chaque cas participant à l'étude. Ce screening a été effectué dans les 3 situations cliniques suivantes : 1) trois fois par année sur convocation lors de périodes dite de screening préprogrammées couvrant toutes les saisons ; 2) lors de contrôles dits de post-transplantation, également préprogrammés ; 3) lors d'évènement motivant une consultation médicale en raison de l'exacerbation ou l'apparition de symptômes respiratoires inhabituels. Dans ce dernier sous-groupe, un certain nombre de patient subissent également un lavage broncho-alvéolaire quand ceci est indiqué. Le recrutement des patients s'étant achevé en mars 2011, le présent abstract décrit les résultats préliminaires, une partie des résultats virologiques n'est pas encore disponible (plus de 12\'000 PCR effectuées).
Résultats: 116 patients remplissaient les critères de sélection, 112 ont signé un consentement informé ; 34% ont été inclus avec une transplantation de moins de 3 mois, et 12 sont décédés durant la période de l'étude. Au total, 922 évènements ont été analysés, soit 577 durant les périodes de screening, 125 dans le cadre de bilan post-transplantations, 220 en raison de symptômes respiratoires motivant une consultation médicale (107 d'entre eux avec LBA). Sur la base des analyses disponibles à ce jour, nous pouvons observer que durant les périodes de screening préprogrammées, entre 8 et 38% des patients rapportent des symptômes respiratoires inhabituels qui sont dans l'immense majorité, des rhinosinusites, des pharyngites ou des bronchites. Le taux de positivité viral au niveau du nasopharynx est de 11% lors des screening asymptomatiques, de 29% en présence de symptômes et s'élève à 49% lors d'exacerbations motivant une consultation médicale. Au niveau des LBA, un virus est détecté dans moins de 8% des cas lorsqu'il s'agit d'un screening post-transplantation pré-programmé et 22% des cas, lors d'évènements respiratoires conduisant à une bronchoscopie. Le rhinovirus est le virus le plus fréquent. Des analyses visant à élucider une association entre une infection virale ou bactérienne, le rejet et le développement d'une bronchiolite oblitérante sont programmées.
Conclusion: Cette étude de cohorte permet de caractériser les évènements cliniques respiratoires suivant une transplantation pulmonaire. Grâce à un screening systématique lors de périodes préprogrammées, nous avons mis en évidence qu'en l'absence de tous symptômes, le taux de détection virale est de l'ordre de 10%. En fonction de la saison les symptômes respiratoires supérieurs sont fréquents et associés à un taux de détection de l'ordre de 30%. En présence de symptômes motivant une consultation médicale, ce taux s'élève rapidement à près de 50% des cas. Ces observations démontrent une association entre la présence d'une infection virale respiratoire détectée par PCR et la genèse de symptômes.

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EFFETS DE LA DUREE D'ENTREPOSAGE DES CULOTS GLOBULAIRES SUR L'EVOLUTION CLINIQUE DES ENFANTS AUX SOINS INTENSIFS

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Introduction: La transfusion est un traitement très fréquent aux soins intensifs. Plusieurs études adultes ont montré que le temps d'entreposage des culots érythrocytaires a un effet sur la morbidité et la mortalité, mais ces résultats sont controversés. Nous avons évalué l'impact du temps d'entreposage sur l'évolution clinique des enfants aux soins intensifs.
Méthode: Les données ont été recueillies chez tous les patients consécutifs, âgés de < 18 ans, admis aux soins intensifs pour > 48 heures. Le critère de jugement primaire est l'apparition ou la progression d'une défaillance multi-viscérale (multiple organ dysfunction syndrome: MODS). Les critères de jugement secondaires sont la mortalité à 28 jours et la durée de séjour aux SIP. Les risques relatifs sont ajustés par régression logistique.
Résultats: 930 enfants ont été inclus dans l'étude, et 447 enfants (49%) ont eu au moins une transfusion. La durée d'entreposage était connue pour 298 patients (67%), avec une médiane à 14 jours. Pour les patients ayant été transfusés avec du sang entreposé ≥ 14 jours, le risque relatif ajusté pour l'apparition ou la progression d'un MODS était 1.87 (95%CI 1.06;3.31, p=0.03). Il y avait aussi une différence ajustée dans la durée d'hospitalisation aux soins intensifs de 3.7 jours (p<0.001), mais pas d'impact sur la mortalité à 28 jours.
Conclusion: Chez les patients admis aux soins intensifs pédiatriques, une transfusion de sang entreposée plus de 14 jours semble être associée à une incidence augmentée de défaillances multi-viscérales

P28

MARCHE ET COGNITION DANS LA SCLEROSE EN PLAQUES

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Introduction: Les déficits de la marche et les troubles cognitifs sont fréquents dans la sclérose en plaques, mais ne sont souvent pas ou tardivement détectés, notamment en raison du temps, de la complexité et du coût des examens requis. Le « Timed Up and G! o test» (TUG) est un test clinique rapide largement utilisé pour l'évaluation fonctionnelle de la marche. Nous avons récemment montré qu'une version adaptée du TUG, le TUG imaginé (iTUG), était corrélée avec le fonctionnement cognitif. L'objectif de cette étude était de mesurer le TUG, le iTUG et l'association de ces deux tests (temps delta) chez des patients avec sclérose en plaques (SEP) et des contrôles appareillés, et d'examiner si ces performances sont liées aux paramètres moteurs et cognitifs.
Méthode: La moyenne ± la déviation standard du TUG, de l'iTUG, et du temps delta, ainsi que les performances aux évaluations de la marche et neuropsychologique, ont été mesurées chez vingt patients SEP et vingt sujets contrôles appareillés.
Résultats: Les patients avec SEP ont effectué plus lentement le TUG que les contrôles (p = 0.01), alors que le iTUG n'est pas différent. Le temps du TUG est corrélé avec les paramètres de! marche, les fonctions cognitives et le comportement, alors que le temps delta est seulement corrélé avec les fonctions cognitives.
Conclusion: Cette étude montre qu'une version adaptée du TUG pourrait être un outil clinique utile chez les patients SEP pour fournir des informations sur les déficits de la marche et cognitifs

P29

SPATIO-TEMPORAL DYNAMICS OF OLFACTORY PROCESSING IN THE HUMAN BRAIN: AN EVENT-RELATED SOURCE IMAGING STUDY

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Introduction: Although brain structures involved in central nervous olfactory processing in humans have been well identified with functional neuroimaging, little is known about the temporal sequence of their activation.
Méthode: We recorded olfactory event-related potentials (ERP) to H(2)S stimuli presented to the left and right nostril in 12 healthy subjects. Topographic and source analysis identified four distinct processing steps between 200 and 1000 ms.
Résultats: Activation started ipsilateral to the stimulated nostril in the mesial and lateral temporal cortex (amygdala, parahippocampal gyrus, superior temporal gyrus, insula). Subsequently, the corresponding structures on the contralateral side became involved, followed by frontal structures at the end of the activation period.
Conclusion: Thus, based on EEG-related data, current results suggest that olfactory information in humans is processed first ipsilaterally to the stimulated nostril and then activates the major relays in olfactory information processing in both hemispheres. Most importantly, the currently described techniques allow the investigation of the spatial processing of olfactory information at a high temporal resolution.

P30

PROTEOMICS APPLICATIONS FOR CLINICAL CHEMISTRY AND CLINICAL PATHOLOGY

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Introduction: Proteomics stimulated the development of very powerful methods for protein analysis and it offers new opportunities for identification and quantification of disease biomarkers. In this study, we applied proteomic methods for the identification of cancer-associated proteins in bile and pancreatic cyst fluids.
Méthode: Bile and cyst fluid samples from patients with malignant or benign diseases causing biliary stenosis or pancreatic cysts were subjected to qualitative and quantitative proteomic analyses using high-performance mass spectrometry (MS). MS data for the proteins of interest were correlated to immunoblot and immunohistochemistry analysis.
Résultats: Proteomic analysis of bile and pancreatic cyst fluids allowed the identification of a large number of proteins achieving a better knowledge of the proteome of these biological fluids. Subsequent literature search highlighted a number of proteins previously described as being related to malignant diseases. Differential expression of specific cancer-associated proteins in bile and cyst fluid samples from malignant etiologies was verified using immunoblot. We also performed immunohistochemistry experiments to correlate protein expression in pancreatic cyst fluids and tissues.
Conclusion: This work demonstrated that proteomic analysis of bile and pancreatic cyst fluids can provide reliable candidates for developing new biomarkers for the management of malignant pancreatic cysts and biliary strictures. Our objective is now to develop MS-based methods for the quantification of specific proteins in biological fluids and tissues that could be used in clinical studies for the validation of biomarkers and, ultimately, be transferred for application in routine laboratory medicine.

P31

COMPARISON OF DRUG RETENTION BETWEEN NEW BIOLOGICAL AGENTS AND CLASSIC ANTI-TNF AGENTS IN TNF INADEQUATE RESPONDER RHEUMATOID ARTHRITIS PATIENTS

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Introduction: After failure of a first anti-TNF agent, clinicians may chose to prescribe an alternative anti-TNF or switch to newer biologic agent .Overall drug retention is a useful composite measure of effectiveness, tolerance and patient satisfaction. To compare drug retention rates of the newer biologics (non-anti-TNF group: Rituximab, Tocilizumab, Abatacept) with those of alternative anti-TNF (Etanercept, Adalimumab, Infliximab) prescribed in second or third intention.
Méthode: Longitudinal population-based Swiss RA cohort including all patients treated with an alternative biological, after a first inadequate response to an anti-TNF agent. Drug survival was analyzed using a Cox proportional hazards model, adjusting for potential confounders.
Résultats: We identified 1467 biologic treatment courses in anti-TNF inadequate responders, 835 with an alternative anti-TNF and 632 with biologic agent of a different mode of action. A second biological was administrated 1031 times, a third - 328, a fourth - 88, and a fifth - 20 times, contributing a total of 4064 patient-years on biological agents. Overall, drug retention was lower in the anti-TNF group (crude HR for anti-TNF: 1.44 [95% CI: 1.25-1.66], adjusted HR for anti-TNF: 1.32 [95% CI: 1.11-1.59]). The median survival time was 25 (IQR: 9.4 - 54.1) months for alternative anti-TNFs and 32 (IQR: 12.4 – NA) months on non-anti-TNF biologics.
Conclusion: In patients having experienced at least one inadequate response to a previous anti-TNF agent, we report significantly higher drug retention for biologics of a different mode of action compared to alternative anti-TNF agents

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SPINAL AND SUPRASPINAL ANTINOCICEPTIVE AND ANALGESIC EFFECTS OF MILNACIPRAN IN FIBROMYALGIA

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Introduction: Fibromyalgia is linked to dysfunctions of nociception. Milnacipran, a SNRI, was shown to be effective in reducing pain in fibromyalgia and to increase activity in brain areas associated with descending inhibitory pain pathways.
Méthode: Randomized, placebo-controlled double-blind study evaluating antinociceptive effects of milnacipran following 7-week exposure (100,150,200 mg/day) in female fibromyalgia patients. Evaluation included Nociceptive Flexion Reflex (NFR) as primary endpoint, Quantitative Sensory Testing (QST), Cold Pressor Test (CPT), and self-reported questionnaires such as Weekly-Recall Pain VAS (VAS), fibromyalgia impact (FIQ), health-related quality of life (SF-36 and PGWB), depression (BDI), anxiety (STAI), patient's global impression of change (PGIC). Covariance analysis was used on primary and secondary criteria.
Résultats: 77 [39 Placebo, 38 Milnacipran all doses], out of 80 randomized patients, were available for analysis. On the NFR, there were no differences between the two groups. However, consistent with previous studies, the Milnacipran treated group reported a 16.5 mm reduction in pain score (VAS) vs. 4.1 mm in the placebo group ($p<0.05$). The adjusted change difference in pain reduction (VAS) between placebo and the tertile with the highest plasma levels of Milnacipran was 34.2 mm ($p<0.05$). BDI and STAI scores remained unchanged in Milnacipran. Self-reported questionnaires consistently reflected positive effects of Milnacipran on quality of life (SF-36) and psychological well-being (PGWB). Odds Ratio (OR) 5.1 for PGIC responders (i.e. very much improved, much improved) was greatly in favour of Milnacipran ($p<0.05$).
Conclusion: Milnacipran has a predominantly supraspinal analgesic effect as evidenced by the absence of nociceptive spinal reflex changes. Higher plasma concentration was associated with higher pain reduction. Reported analgesia was independent of patients' emotional status.

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CLINICAL FEATURES AND OUTCOME OF 2009-INFLUENZA A (H1N1) AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Introduction: The impact of the 2009 H1N1-Influenza A pandemic in allogeneic hematopoietic stem cell transplant recipients (allo-HSCT) is not well defined. The aim of this study was to better characterize the features and outcomes of this infection among adult allo-HSCTs.
Méthode: Between May 2009 and May 2010, all allo-HSCTs who presented with respiratory symptoms were screened for the presence of the H1N1 virus. Oseltamivir resistance was assessed and chart reviews were performed for all cases.
Résultats: In all, 51 of 248 (20%) allo-HSCTs followed at our outpatient clinic were screened. We identified 10 patients with H1N1 infection, representing an overall incidence of 4% (95% CI, 2-7%). Close contact with children was the most commonly suspected mode of transmission. Upper and lower respiratory tract infections were present in eight and five patients, respectively.
Conclusion: In conclusion, although most allo-HSCTs had mild symptoms from H1N1 infection, severe immunosuppression and emergence of oseltamivir resistance were likely responsible for a substantial morbidity, further supporting the need for vaccination and monitoring of close contacts, especially children.

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ANTI-APOA-1 AUTO-ANTIBODIES ARE ACTIVE MEDIATORS OF ATHEROSCLEROTIC PLAQUE VULNERABILITY

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Introduction: Anti-ApolipoproteinA-1 auto-antibodies (anti-ApoA-1 IgG) represent an emerging prognostic cardiovascular marker in patients with myocardial infarction or autoimmune diseases associated with high cardiovascular risk. The potential relationship between anti-ApoA-1 IgG and plaque vulnerability remains elusive. Thus, we aimed to investigate the role of anti-ApoA-1 IgG i! n plaque vulnerability.
Méthode: Potential relationship between anti-ApoA-1 IgG and features of cardiovascular vulnerability was explored both in vivo and in vitro. In vivo, we investigated anti-ApoA-1 IgG in patients with severe carotid stenosis (n=102) and in ApoE-/- mice infused with polyclonal anti-ApoA-1 IgG. In vitro, anti-ApoA-1 IgG effects were assessed on human primary macrophages, monocytes and neutrophils.
Résultats: Intraplaque collagen was decreased, while neutrophil and MMP-9 content was increased in anti-ApoA-1 IgG positive patients and anti-ApoA-1 IgG-treated mice as compared to corresponding controls. In mouse aortic roots (but not in abdominal aortas), treatment with anti-ApoA-1 IgG was associated with increased lesion size as compared to controls. In humans, serum anti-ApoA-1 IgG levels positively correlated with intraplaque macrophage, neutrophil and MMP-9 content, and inversely with collagen. In vitro, anti-ApoA-1 IgG increased macrophage release of CCL2, CXCL8 and M MP-9, as well as neutrophil migration towards TNF-alpha or CXCL8.
Conclusion: These results suggest that anti-ApoA-1 IgG might be associated with increased atherosclerotic plaque vulnerability in humans and mice.

P35 – non affiché

ANTI-CD154 MAB AND RAPAMYCIN INDUCE T REGULATORY CELL MEDIATED TOLERANCE IN RAT-TO-MOUSE ISLET TRANSPLANTATION

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Introduction: Anti-CD154 (MR1) monoclonal antibody (mAb) and rapamycin (RAPA) treatment both improve survival of rat-to-mouse islet xenograft. The present study investigated the effect of combined RAPA/MR1 treatment on rat-to-mouse islet xenograft survival and analyzed the role of CD4+CD25+Foxp3+ T regulatory cells (Treg) in the induction and maintenance of the ensuing tolerance.
Méthode: C57BL/6 mice were treated with MR1/RAPA and received additional monoclonal anti-IL2 mAb or anti CD25 mAb either early (0–28 d) or late (100–128 d) post-transplantation. Treg were characterised in the blood, spleen, draining lymph nodes and within the graft of tolerant and rejecting mice by flow cytometry and immunohistochemistry.
Résultats: Fourteen days of RAPA/MR1 combination therapy allowed indefinite islet graft survival in >80% of the mice. Additional administration of anti-IL-2 mAb or depleting anti-CD25 mAb at the time of transplantation resulted in rejection (100% and 89% respectively), whereas administration at 100 days post transplantation lead to lower rejection rates (25% and 40% respectively). Tolerant mice showed an increase of Treg within the graft and in draining lymph nodes early post transplantation, whereas 100 days post transplantation no significant increase of Treg was observed. Rejecting mice showed a transient increase of Treg in the xenograft and secondary lymphoid organs, which disappeared within 7 days after rejection.
Conclusion: These results suggest a critical role for Treg in the induction phase of tolerance early after islet xenotransplantation. These encouraging data support the need of developing further Treg therapy for overcoming the species barrier in xenotransplantation

P36

NEURAL CORRELATE OF ANTEROGRADE AMNESIA IN WERNICKE–KORSAKOFF SYNDROME

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Introduction: The neural correlate of anterograde amnesia in Wernicke–Korsakoff syndrome is still debated. While the capacity to learn new information has been associated with integrity of the medial temporal lobe, previous studies indicat! ed that the Wernicke–Korsakoff syndrome is associated with diencephalic lesions, mainly in the mammillary bodies and anterior or dorsomedial thalamic nuclei. The aim of the present study was to test the hypothesis that amnesia in Wernicke–Korsakoff syndrome is associated with a disrupted neural circuit between diencephalic and hippocampal structures.
Méthode: High-density evoked potentials were recorded in 4 severely amnesic patients with chronic Wernicke–Korsakoff syndrome and in 10 age matched controls. Subjects performed a continuous recognition task of pictures in which each item was repeated either immediately or after intervening items. Immediate picture repetition has been shown to induce early activation of the left medial temporal lobe (MTL; James et al, Hippocampus 2009; 19: 371-8; Nahum et al, Hippocampus 2010, in press). In addition, Diffusion Tensor Imaging (DTI) was performed with a 3 tesla unit.
Résultats: Recognition of delayed repetition was severely impaired in a! ll patie nts. Electrophysiologically, patients showed absence of the early, left MTL dependent positive potential (P2) between 250 and 350 ms following immediate picture repetitions. DTI indicated disruption of the anterior inferior fornix, which connects diencephalic and hippocampal structures.
Conclusion: The findings support an interpretation of anterograde amnesia in Wernicke–Korsakoff syndrome as a consequence of a disconnexion between diencephalic and hippocampal structures with deficient contribution of the medial temporal lobe to rapid consolidation.

P37

ADEQUACY OF VENOUS THROMBOPROPHYLAXIS IN ACUTELY ILL MEDICAL PATIENTS (IMPART): MULTISITE COMPARISON OF DIFFERENT CLINICAL DECISION SUPPORT SYSTEMS

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Introduction: The adequacy of thromboprophylaxis prescriptions in acutely ill hospitalized medical patients needs improvement. The objective of the study was to prospectively assess the efficacy on thromboprophylaxis adequacy of various clinical decision support systems (CDSS) designed to increase the use of explicit criteria for thromboprophylaxis prescription in nine Swiss medical services.
Méthode: We randomly assigned medical services to a pocket digital assistant program (PDA), pocket cards (PC) and no CDSS (controls). In centers using an electronic chart, an e-alert system (eAlerts) was developed. After 4 months, we compared post-CDSS with baseline thromboprophylaxis adequacy for the various CDSS and control groups.
Résultats: Overall, 1085 patients were included (395 controls, 196 PC, 168 PDA, 326 eAlerts), 651 pre- and 434 post- CDSS implementation: 472 (43.5%) presented a risk of VTE justifying thromboprophylaxis (31.8% pre, 61.1% post) and 556 (51.2%) received thromboprophylaxis (54.2% pre, 46.8% post). The overall adequacy (% patients with adequate prescription) of pre- and post-CDSS implementation was 56.2 and 50.7 for controls (P = 0.29), 67.3 and 45.3 for PC (P = 0.002), 66.0 and 64.9 for PDA (P = 0.99), 50.5 and 56.2 for eAlerts (P = 0.37), respectively. EAlerts limited overprescription (56% pre, 31% post, P = 0.01).
Conclusion: While pocket cards and handhelds did not improve thromboprophylaxis adequacy, eAlerts had a modest effect, particularly on the reduction of overprescription. This effect only partially contributes to the improvement of patient safety and more work is needed towards institution-tailored tools.

P38

NOX-4 IS EXPRESSED IN THICKENED PULMONARY ARTERIES IN IDIOPATHIC PULMONARY FIBROSIS

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Introduction: Idiopathic pulmonary fibrosis (IPF) is a fatal disease, and there is a need for an improved understanding of its pathophysiology and for new therapeutic concepts. Recent work by Hecker et al. suggests that the generation of reactive oxygen species by the NADPH oxidase NOX-4 is involved in the pathophysiology of IPF. More specifically, the work suggests that NOX-4–dependent generation of reactive oxygen species is required for transforming growth factor-β1 (TGF-β1)-induced myofibroblast differentiation, extracellular matrix production and contractility. The authors provide the first elements to support the concept that NOX-4 might be a target for the treatment of pulmonary fibrosis. The paper includes, however, a misidentification of anatomical structures, which is of importance for the scientific message of the work and needs clarification. They demonstrated "expression of NOX-4 in myofibroblastic foci in lungs of a representative human subject with IPF." However, the figure shows a branching lung artery, not a fibrotic focus and visual analysis of sections labeled with antibody to α-SMA suggests a thickening of the wall of the lung artery. Indeed, there is now emerging evidence that, in humans, IPF leads to secondary pulmonary hypertension and subsequent vascular lesions. However, to our knowledge, no quantitative morphometric analysis of pulmonary arteries in subjects with IPF has been performed.
Méthode: To illustrate this point, formol-fixed pulmonary sections of lungs from subjects with IPF and control lungs were stained with an antibody to α-SMA (mouse IgG2a) and thickness of lung arteries in idiopathic pulmonary fibrosis was evaluated by measuring the vessel wall diameters and surfaces with the Mirax Midi program (Zeiss).
Résultats: We confirmed that cells stained for α-smooth muscle actin (α-SMA) and NOX-4 shown in the article of Hecker are not myofibroblasts, but vascular smooth muscle cells, which obviously express α-SMA. We have therefore quantified pulmonary artery thickness in ten control and ten IPF lung samples. The controls were lung samples from subjects who died from causes other than pulmonary disease, matched for age and sex. We used two approaches: determination of the percentage of the total vessel diameter occupied by media and intima and determination of the percentage of total vessel surface occupied by intima or media. These analyses showed a highly significant increase in the thickness of the vessel wall (P < 0.001).
Conclusion: Finally, we demonstrated a strong NOX-4 staining of the thickened wall of pulmonary arteries of IPF subjects and the thickened lung arteries can be confidently considered as a disease-typical histological feature of IPF. This is notable and raises the question of whether NOX-4 might also be involved in the pathophysiology of lung artery hypertrophy in human IPF, in line with what has been suggested for hypoxia-induced and idiopathic pulmonary hypertension.

P39

LES FEMMES AYANT SOUFFERT DE PRE-ECLAMPSIE PRESENTENT UNE SENSIBILITE AU SODIUM ET DES ATTEINTES CARDIOVASCULAIRES AVANT LEUR MENOPAUSE

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Introduction: La pré-éclampsie est définie par une hypertension artérielle et une protéinurie survenant après 20 semaines de grossesse. La sensibilité au sodium, c\'est-à-dire l\'élévation de la pression artérielle en cas d\'apport de sodium augmenté est un facteur de risque cardiovasculaire.
Méthode: Vingt femmes ayant souffert d\'une pré-éclampsie avant la 34e semaine de grossesse,dans les 5 à 10 dernières années, et 18 femmes matchées pour l\'âge et la race (étude cas-témoin) ont été allouées à un régime pauvre en sodium, puis riche en sodium (ajout de 6g de NaCl à leur diète habituelle. Au terme des 2 phases de régime, une mesure de la pression artérielle de 24 heures, et une collecte urinaire de 24 heures ont été réalisées.
Résultats: Les femmes pré-éclamptiques étaient âgées de 39 ans (24-49), et les contrôles de 40 ans (29-49). Trois/20 femmes ont déjà présenté une attaque cérébrale et 2 infarctus du myocarde. Sous régime hypersodé, les femmes pré-éclamptiques ont une augmentation significative de leur pression artérielle, un émoussement de la baisse nocturne, et une variabilité tensionnelle significativement augmentée comparé aux contrôles.
Conclusion: Les femmes ayant été atteintes d\'une pré-éclampsie sévère ont déjà une sensibilité au sodium et des atteintes cardiovasculaires avant leur ménopause. Ces patientes devraient faire l'objet d'une prise en charge et d\'une prévention ciblées déjà dans le post partum.

P40

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: 14 1ers patients avec cancers pulmonaires ont eu un CT4D, soit l'équivalent de 10 scanners pour 10 phases respiratoires. RPO a été développé pour traiter ces données informatiques sur la base de critères morphologiques de comparaison des phases, et permettre ainsi au médecin de choisir la meilleure phase d'irradiation parmi les 10. Une étude dosimétrique a compare les résultats d'un traitement virtuel en phase optimale.
Résultats: Dans 1/14 patients (7%), pas de mouvements détectés suggérant l'absence de bénéfice d'une RAR. Pour 13/14 patients (93%), 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: Facile à utiliser en pratique courante, RPO est un outil permettant de sélectionner les patients qui pourront bénéficier d'une RAR. 1er outil à identifier le moment respiratoire idéal, il ouvre la perspective d'une radiothérapie moins toxique et plus efficace sur la 1ère cause de mortalité par cancer.

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OCCULT FRACTURES OF THE SCAPHOID: THE ROLE OF ULTRASONOGRAPHY IN THE EMERGENCY DEPARTMENT

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Introduction: to evaluate ultrasonography (US) performed by an emergency radiologist in patients with clinical suspicion of scaphoid fracture and normal radiographs
Méthode: sixty-two consecutive adult patients admitted in our emergency department with clinical suspicion of scaphoid fracture and normal radiographs underwent US examination of the scaphoid prior to wrist computed tomography (CT), within 3 days following wrist trauma. US examination was performed by a board certified emergency radiologist, non-specialized in musculoskeletal imaging, using the linear probe (5-13 MHz) of the standard sonographic equipment of the emergency department. The radiologist did evaluate the presence of a cortical interruption of the scaphoid along with a radio-carpal or scapho-trapezium-trapezoid effusion. A CT of the wrist (reference standard) was performed in every patient, immediately after ultrasonography. Fractures were classified into 2 groups, according to their potential for complication: group 1 (high potential, proximal or waist), group 2 (low-potential, distal or tubercle).
Résultats: a scaphoid fracture was demonstrated by CT in 13 (21%) patients: 8 (62%) of them belonged to group 1 (3 in the proximal pole, 5 in the waist), 5 (38%) to group 2 (3 in the distal part, 2 in the tubercle). US was 92% sensitive (12/13) to detect a scaphoid fracture. It was 100% sensitive (8/8) to detect a fracture with a high potential of complication (group 1).
Conclusion: our data show that, in emergency settings, US can be used for the triage to CT in patients with clinical suspicion of scaphoid fracture and normal radiographs.

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L'HYPOXEMIE VEINEUSE EST ELLE UN DETERMINANT DE L'EXPRESSION DES CANAUX KATP CHEZ L'ENFANT SOUFFRANT DE MALFORMATIONS CARDIAQUES ?

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Introduction: Les malformations cardiaques chez l'enfant suscitent une grande préoccupation mondiale. Dans les pays en voie de développement, elles sont souvent tardivement dépistées et prises en charge. Il convient donc de poursuivre la compréhension des mécanismes physiologiques et cellulaires induits; afin de soulager certains patients via des traitements pharmacologiques pré-chirurgicaux. Des études sur les animaux ont pu montrer que parmi les nombreuses voies de signalisation protégeant le myocarde, certaines impliquent des canaux potassiques ATP-dépendants (KATP).
Méthode: L'étude présente a été réalisée sur 25 enfants souffrant de malformations cardiaques congénitales ou acquises. Les canaux KATP ont été mesurés dans des échantillons de tissus d'oreillettes droites et étudiés statistiquement avec 31 paramètres (physiologiques, pathologiques et personnels).
Résultats: L'analyse de plus de 400 relations entre le! s paramètres, l'expression des canaux KATP, mais aussi de leurs éventuels facteurs de transcription, montre distinctement une corrélation positive entre l'hypoxémie veineuse et l'expression des canaux KATP. Par ailleurs, cette surexpression est à l'origine d'une chaine d'activation qui, comme nous l'avons démontré, implique une voie HIF-1α/FOXO.
Conclusion: Cette étude ouvre de nouvelles perspectives cliniques et pharmacologiques. La pression veineuse semble être un marqueur non négligeable dans le suivi d'évolution des malformations cardiaques chez l'enfant. Par ailleurs, il est censément possible d'envisager l'utilisation de drogues activant cette nouvelle voie HIF-1α/FOXO/KATP dans le cadre d'une thérapie visant à soulager des enfants souffrant d'hypoxémie.

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SITE-SPECIFIC MUTATION OF STAPHYLOCOCCUS AUREUS VRAS REVEALS A CRUCIAL ROLE FOR THE VRAR-VRAS SENSOR IN THE EMERGENCE OF GLYCOPEPTIDE RESISTANCE

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Introduction: The prevalence of MRSA in hospitals severely limits therapeutic options. Glycopeptide antibiotics are first line drugs for treatment of MRSA infections. The emergence of resistance to glycopeptides is major challenge to the treatment of MRSA infections since few clinically proven and effective alternative therapies exist. To overcome resistance we need to get a closer understanding of the mechanisms that may help blocking emergence of resistant bacteria.
Méthode: We have identified the critical aminoacid residue of membrane sensor VraS required to phosphorylate VraR, a master gene regulator of glycopeptide resistance. The mutated vraS residue was engineered in S. aureus chromosome. The in vivo effect of this mutation on glycopeptide resistance was studied by comparing the emergence frequency of wild-type and mutant strains on glycopeptide containing agar plates.
Résultats: -We have identified VraS H156 as the site of autophosphorylation and shown phosphotransfer in vitro using purified VraR. -The vraS-H156A mutation reduces significantly methicillin, teicoplanin and vancomycin MICs. -Genetic studies showed that the vraS-H156A mutation fail to generate first step teicoplanin and vancomycin mutants.
Conclusion: Collectively, our results reveal important details of the VraRS signaling system and predict that pharmacologic blockade of the VraS sensor kinase should help to block emergence of glycopeptide resistance in S. aureus.

P44

DUREE DE L'ANTIBIOTHERAPIE POSTOPERATOIRE POUR OSTEOMYELITE CHRONIQUE DE L'ADULTE SANS IMPLANT - NOTRE EXPERIENCE

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Introduction: La durée d'antibiothérapie postopératoire après traitement chirurgical d'ostéomyélite chronique de l'adulte sans implant n'est pas connue. Les recommandations disponibles sont basées sur des avis d'experts. Nous avons évalué la relation entre le taux de rémission d'ostéomyélite chronique sans implant et la durée d\'antibiothérapie postopératoire.
Méthode: Étude rétrospective monocentrique aux HUG des cas d'ostéomyélite chronique sans implant avec au moins 2 ans de follow-up. Analyse statistique par régression logique multivariée, en excluant les cas d'ostéomyélite pédiatrique ou liés à un implant.
Résultats: Un total de 49 ostéomyélites chez 49 patients ont été identifiés. Chaque patient a bénéficié d'en moyenne 2 interventions chirurgicales (intervalle 1 - 10). La durée moyenne d'antibiothérapie postopératoire est de 8 semaines (intervalle 4 - 14). Après minimum 2 ans de suivi, 80% des patients sont en rémission. Statistiquement, 1 semaine d'antibiotiques iv procure le même taux de rémission que 2-3 semaines ou >3 semaines. Moins de 6 semaines d\'antibiothérapie au total offre le même taux de rémission que plus de 6 semaines.
Conclusion: Concernant l'ostéomyélite chronique de l'adulte sans implant, une antibiothérapie post-débridement chirurgical de plus de 6 semaines, ou un traitement iv de plus d'une semaine, n'offrent pas d'avantage en terme de rémission.

P45

EFFECT OF PRISM ADAPTATION IN CORTICAL ACTIVITY IN NEGLECT PATIENT

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Introduction: Hemispatial neglect is often resistant to rehabilitation. Recent studies suggested that this disorder may be improved by prism-adaptation, with remarkable generalization and persistence of such effects, but the underlying neural mechanisms remain unclear. Functional neuroimaging in healthy volunteers indicates that prism-adaptation relies on a distributed network including posterior parietal, temporal, and cerebellar regions, which is partly damaged in neglect patients.
Méthode: We used fMRI to investigate the effect of (right-deviating) prism-adaptation on seven patients with left neglect while they perform various cognitive tasks on the same visual stimuli (bisection, search, and memory), before and after a brief prism-adaptation session.
Résultats: Behavioural data showed significant improvement (p before adaptation showed selective increases in activation (p = 0.001) of the right posterior parietal cortex and left superior parietal cortex, as well as bilateral occipital cortex. For the search task, the right temporo-parietal junction was significantly more activated, together with bilateral posterior parietal cortex and bilateral occipital cortex. No significant changes in behavioural performance or cortical activity were found in any region.
Conclusion: Our results provide new evidence that the beneficial effects of prism adaptation on neglect are linked to a specific modulation of brain regions crucially involved in spatial attention

P46

COMPARISON OF THE INTER-OBSERVATORY REPRODUCIBILITY OF TWO DIFFERENT METHODS OF DIETARY ASSESSMENT IN A GERIATRIC WARD

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Introduction: Protein-energy malnutrition is highly prevalent in aged populations. Associated clinical, economical and social burden is important. A valid screening method is essential for an adequate therapeutic management. Digital photography is an easy and rapid tool for food intake assessment. In this study, we compared the inter-observatory reproducibility of two methods measuring food intake: semi-quantitative estimations and a method based on digital photography. In contrast to previous studies, the methods were applied in a “ready to use” way, since there was no previous training of the observers.
Méthode: Six (6) meals consumed by geriatric inpatients were each assessed by four observers for each method. Analysis of variances (ANOVA) was performed to compare their inter-observatory reproducibility.
Résultats: The digital photography method showed a higher variability of calorie intake estimations. The difference between the inter-observatory reproducibility of the compared methods was statistically significant (p=0.025).
Conclusion: Calorie intake measures of geriatric patients are more concordant with semiquantitative-estimations. Digital photography for food intake estimation, without previous specific training of dieticians, cannot be recommended for the moment in geriatric wards as it shows no advantages in terms of inter-observatory reproducibility.

P47a

CELL ENCAPSULATION TECHNOLOGY AS A NOVEL STRATEGY FOR HUMAN ANTI-TUMOR IMMUNOTHERAPY

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Introduction: GM-CSF as an adjuvant in autologous cell-based anti-tumor immunotherapy has recently been approved for clinical application. To avoid the need for individualized processing of autologous cells, we developed a novel strategy based on the encapsulation of GM-CSF-secreting human allogeneic cells.
Méthode: The human K562 cell line was genetically engineered for GM-CSF secretion. Cells were then enclosed into hollow fiber biocompatible membranes in order to protect them from immune rejection. Those capsules were irradiated and frozen for banking purpose. When thawed, the GM-CSF secreted from the capsules was assessed. Finally capsules were implanted in mice for evaluation of the biological activity of GM-CSF.
Résultats: GM-CSF-producing K562 cells showed high, stable and reproducible cytokine secretion when enclosed into macrocapsules. For clinical development, the cryopreservation of these devices is critical. Thawing of capsules frozen at different time points displayed differences in GM-CSF release shortly after thawing. However, similar secretion values to those of non-frozen control capsules were obtained 8 days after thawing at a rate of more than 1000 ng GM-CSF/capsule/24h. For future human application, longer and reinforced capsules were designed. After irradiation and cryopreservation, these capsules produced more than 300 ng GM-CSF/capsule/24h one week after thawing. The in vivo implantation of encapsulated K562 cells was evaluated in mice and showed preserved cell survival. Finally, as a proof of principle of biological activity, capsules containing B16-GM-CSF allogeneic cells implanted in mice induced a prompt inflammatory reaction.
Conclusion: The ability to reliably achieve high adjuvant release using a standardized procedure may lead to a new clinical application of GM-CSF in cell-based cancer immunization.

P47b

CLINICORADIOLOGICAL SCORE FOR PREDICTING THE RISK OF STRANGULATED SMALL BOWEL OBSTRUCTION

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Introduction: Intestinal ischaemia as a result of small bowel obstruction (SBO) requires prompt recognition and early intervention. A clinicoradiological score was sought to predict the risk of ischaemia in patients with SBO
Méthode: A prospectively determined protocol for the assessment of patients presenting with SBO was used. A logistic regression model was applied to identify determinant variables and construct a clinical score that would predict ischaemia requiring resection.
Résultats: Of 233 successive patients with SBO, 138 required laparotomy of whom 45 underwent intestinal resection. In multivariable analysis, six variables correlated with small bowel resection and were given one point each towards the clinical score: history of pain lasting more than 4 days, guarding, C-reactive protein level at least 75 mg/l, leucocyte count over 10 G/l, free intraperitoneal fluid volume exceeding 500 ml on computed tomography (CT) and reduction of CT small bowel wall contrast enhancement. The risk of intestinal ischaemia was 6 per cent in patients with a score of 1 or less, whereas 21 of 29 patients with a score of three or more 3 underwent small bowel resection. A positive score of 3 or more had a sensitivity of 67.7 per cent and specificity 90.8 per cent; the area under the receiver operating characteristics curve was 0.87 (95 per cent confidence interval 0.79 to 0.95).
Conclusion: By combining clinical, laboratory and radiological parameters, the clinical score allowed early identification of strangulated SBO.

P48

LE TNFα: CIBLE POTENTIELLE POUR LE TRAITEMENT DE L'HYPERFLAMMATION DE LA MALADIE GRANULOMATEUSE CHRONIQUE?

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Introduction: La maladie granulomateuse chronique (CGD) est caractérisée par une immunodéficience associée à une hyperinflammation stérile contribuant de manière significative à la morbidité. Les corticoïdes sont une des rares options thérapeutiques, même s'ils restent non-spécifiques et peu compatibles avec une immunodéficience. Il existe une production importante de TNFα par les cellules phagocytaires des patients CGD pouvant participer à l'hyperinflammation observée. Nous avons investigué si la suppression du TNFα permettait une diminution de l'inflammation dans un modèle murin CGD.
Méthode: La suppression de TNFα a été obtenue soit par délétion génétique grâce à des souris CGD-déficientes en TNFα soit par suppression pharmacologique par injection d'anti-TNFα (Etanercept). L'inflammation a été induite par injection intradermique de β-glycan. La sévérité de l'inflammation a été évaluée par un score inflammatoire histologique allant de 0 à 4; ainsi que par la mesure de l'épaisseur de l'oreille injectée.
Résultats: La mesure de l'épaisseur d'oreille ainsi que le score histologique ont permis de démontrer que le β-glycan induit une inflammation modérée chez les souris contrôles et déficientes en TNFα.Chez les souris CGD, une inflammation prolongée et sévère est observée. Par contre, ni l'inhibition pharmacologique, ni la délétion génétique du TNFα n'ont permis une diminution de l'inflammation chez les souris CGD.
Conclusion: Ni la délétion génétique du TNFα, ni le traitement par un anti-TNFα n'ont eu un rôle préventif sur l'inflammation cutanée chez les souris CGD. Il semble donc que le TNFα ne représente pas une cible essentielle pour le traitement de l'inflammation des patients atteints de CGD.

P49

3D RELATIONS BETWEEN RIGHT COLON ARTERIES AND THE SUPERIOR MESENTERIC VEIN: A PRELIMINARY STUDY WITH MULTIDETECTOR COMPUTED TOMOGRAPHY

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Introduction: 3-D relations between the ileocolic (ICA), right colic artery (RCA) with the superior mesenteric vein (SMV) have been described in cadavers. However, no data exists on preoperative evaluation of these relations. The aim was to define the length of crossing and 3-D position of the ICA and RCA to the SMV in patients undergoing multidetector computerized tomography (MDCT) angiography.
Méthode: MDCT angiographies were analyzed with the aid of Osirix v.3.0.2. image processing application. All the datasets included arterial and venous phase, undergoing multimodal visualization: 2D multiplanar reconstruction with maximum intensity projection and 3D Volume rendering. The anatomical relations were analyzed in various planes (orthogonal and oblique), depending upon their particular course. When a clear spatial reference was achieved, the distance of the colic artery from their origin on the aorta to the right border of the SMV was measured, and its position noted.
Résultats: 50 MDCTs were analyzed (29 male). RCA occurred in 27 patients (54.0%), 25 (92.6%) passed anterior to the SMV. Length of crossing was 22.7 ± 8.1 (8.3 – 41.3) mm. The ICA occurred in 48 (96%) passing under the SMV in 38 (79.2%). Length of crossing 15.4 ± 5.8 (14.0 – 26.6) mm.
Conclusion: RCA occurs in 54% patients, passes over the SMV in 92.6% specimens and leaves a 22.7 mm stump. ICA passes under the SMV in most cases, leaving a 15.4 mm stump. These data could be of crucial importance to the surgeon facing laparoscopic right colectomy for cancer.

P50

RECHERCHE DE BIOMARQUEURS PHOSPHOLIPIDIQUES DE L'ATHEROSCLEROSE PAR SPECTROMETRIE DE MASSE A PARTIR DE MICRO-PRELEVEMENTS

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Introduction: Les phospholipides jouent un rôle important dans la biochimie des cellules vivantes en assurant l'architecture de la structure membranaire et en régulant des processus physiologiques comme l'homéostasie, le métabolisme ou encore certaines voies de signalisation. Ce rôle primordial est mis en évidence par les nombreuses maladies où les phospholipides sont impliqués telles que l'athérosclérose, le cancer ou la maladie d'Alzheimer. L'athérosclérose est une des causes de mortalité principales dans les pays occidentaux. Ce travail présente une stratégie visant à évaluer les différences du contenu phospholipidiques dans le plasma de souris athérosclérotiques (ApoE-/-) et des souris saines à partir de micro-volumes (2µL) spottés sur des papiers buvards.
Méthode: Les spots de plasma séchés (DPS) sont directement désorbés vers le spectromètre de masse en utilisant un automate développé dans notre laboratoire et permettant l'analyse des DPS sans aucune préparation des échantillons et permettant de rechercher jusqu'à 2700 espèces potentielles. Les variations phospholipidiques entre 15 souris malades et 15 souris saines ont été évaluées à l'aide de test de T, de réduction et de combinaison de matrices, ainsi que d'analyse en composantes principales (PCA) comme approches chemométriques.
Résultats: L'analyse PCA a permis de mettre en évidence un rôle important des phophatidylsérines et des sphingomyélines en association à l'athérosclérose et d'établir des biomarqueurs potentiels sur- ou sous- exprimés durant la maladie.
Conclusion: Cette approche globale a démontré des résultats prometteurs ainsi que des perspectives intéressantes pour la recherche de biomarqueurs phospholipidiques associés aux maladies.

P51

THE IMPACT OF WAITING LIST ALPHA-FETOPROTEIN CHANGES ON THE OUTCOME OF LIVER TRANSPLANT FOR HEPATOCELLULAR CARCINOMA

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Introduction: Liver transplantation is a recognized treatment for selected patients with hepatocellular carcinoma (HCC), but transplant criteria still need to be refined, especially in the case of more advanced or downstaged tumors.
Méthode: The present study investigated alpha-fetoprotein (AFP) as a predictor of outcome in 6817 patients listed with a diagnosis of HCC in the Scientific Registry of Transplant Recipients.
Résultats: Local pre-transplant HCC treatment was used in 41% of patients on the waiting list. Patients with AFP levels >400 ng/ml at the time of listing who were downstaged to AFP ≤400 ng/ml had better intent-to-treat survival than patients failing to reduce AFP to ≤400 (81% vs. 48% at 3 years, p≤0.001) and similar survival to patients with stable AFP ≤400 ng/ml (74%, p=0.14). Patients with AFP levels decreased ≤400 ng/ml and patients with levels persistently ≤400 ng/ml also had similar drop-out rates from the list (10% in both groups) and posttransplant survival rates (89% vs. 78% at 3 years, p=0.11). Such an AFP downstaging was associated with good survivals whatever the level of the original AFP (even if originally >1000 ng/ml). Only the last pre-transplant AFP independently predicted survival (p≤0.001), unlike AFP at listing or AFP changes.
Conclusion: Overall, downstaging HCC patients with high AFP is feasible and leads to similar intent-to-treat and post-transplant survivals to those of patients with AFP persistently low. Only last AFP appears relevant for patient selection before transplantation and should be used in combination with morphological variables.

P52

ENHANCED IL-17A AND IL-22 PRODUCTION BY PERIPHERAL BLOOD MONONUCLEAR CELLS DISTINGUISH SYSTEMIC SCLEROSIS FROM HEALTHY INDIVIDUALS

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Introduction: In systemic sclerosis (SSc) inappropriate T cell responses are thought to participate to events ultimately leading to fibrosis. The objectives of the study were to investigate the pattern of cytokines produced and chemokine-receptors expressed by peripheral blood T helper (Th) cells in SSc and healthy donors (HD), to assess the ability of these Th subsets to modulate human dermal fibroblasts (HDF) metabolism and identify clinical associations.

Méthode: Cytokine and chemokine receptor usage were assessed by multiparametric flowcytometry ex vivo and after 7 days of culture in CD4+ T cells from 33 SSc and 29 HD. The production of monocyte chemoattractant protein (MCP)-1, matrix metalloproteinase (MMP)-1 and type-I collagen was assessed in HDF activated by Th cell clone supernatants

Résultats: The number of Th22, Th17 but not Th1 cells was increased in SSc individuals compared to HD both ex vivo and at day 7. Moreover, the expression of the skin- and lung-homing chemokine receptor CCR6 correlated with the frequency of Th22 and! Th17 ce lls in SSc but not in HD. While lung fibrosis in SSc was strongly associated with higher numbers of Th22 and, to a less extent, Th17 cells, the supernatants of Th22 and Th17 clones enhanced MMP-1 and MCP-1 and decreased collagen production by HDF.

Conclusion: Th22 and Th17 cells with skin- and lung-homing capabilities are characteristically increased in SSc, particularly with lung fibrosis, and favor a pro-inflammatory phenotype in HDF. These findings support the hypothesis that Th22 and Th17 cells may be involved in SSc and help in identifying novel therapeutic targets.

P53

SIT-TO-STAND ALTERATIONS IN ADVANCED KNEE OSTEOARTHRITIS

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Introduction: Functional alterations in patients with knee osteoarthritis (OA) are well recognized. It has also been documented that abnormal movement patterns developed with knee OA can persist for a long time after a total knee arthroplasty (TKA), although pain and function are usually improved. Therefore, identification of altered movement patterns prior to TKA is essential for patients' follow-up. Thus, this study aims to investigate the full body strategies during a sit-to-stand (STS) task in patients with knee OA and, the association between STS alterations and clinical measurements.

Méthode: Twenty-five patients with advanced knee OA were recruited to participate in this study. Twenty healthy elderly were recruited as the control group. A 3D motion analysis system was used to capture the full body motion during the STS task. Two force plates were used to capture the forces under each leg. The pain and functional capacity were obtained from the WOMAC.

Résultats: The results showed that patients with knee OA put 10% additional weight on the non-affected side, when compared with the symmetrical strategy of the control group. Patients with knee OA showed a significant lower knee internal flexion moment, a higher maximal trunk flexion, and a higher lateral trunk lean, when compared with the control group. The main correlations were found between pain and the averaged time to complete the STS.

Conclusion: With the quantification of full body mechanisms during the STS task, our study brings new insights leading to a better understanding of the functional alterations in patients with advanced knee OA. The identification of relevant parameters reflecting patients' function prior to TKA might be helpful in the rehabilitation process of patients following TKA, and thus improve patients' satisfaction.

P54a

SHORT PARENTERAL ANTIBIOTIC TREATMENT FOR NATIVE SEPTIC ARTHRITIS

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Introduction: The ideal duration of antibiotic treatment in the therapy of septic native joint arthritis is unknown. We assess risk factors for recurrence with emphasis on surgical and medical treatment parameters.
Méthode: Single-centre case-control study in the Orthopaedic Service of Geneva University Hospitals.
Résultats: A total of 169 episodes in 157 patients (median age 63 years, 65 females) were retrieved. The infected joints were: knee (n=51), hip (n=21), shoulder (n=32), ankle (n=9), sterno-clavicular (n=2), elbow (n=2), sacroiliac (n=1), and interdigital (n=43). In 21 episodes (21/169, 12%), arthritis recurred after the end of antibiotic treatment. In multivariate analysis, lack of surgical intervention (odds ratio 11.3, 95% confidence interval 2.7-46.2), Gram-negative infection (OR 5.9, 1.4-25.3), and immunosuppression (OR 5.3, 1.3-22) were significantly associated with recurrence, while open arthrotomy vs. arthroscopic drainage (OR 0.5, 0.2-1.8), total duration of antibiotic therapy (OR 1.0, 1.0-1.0), or duration of intravenous antibiotic therapy (OR 1.0, 1.0-1.0) were not. Seven days of intravenous therapy had the same effect than 8 to 15 days (OR 0.4, 0.1-1.7) or 4 weeks (OR 0.4, 0.1-1.6).
Conclusion: Among modifiable parameters, at least one surgical intervention is of utmost importance in the treatment of septic native joint arthritis. The modalities of concomitant antibiotic therapy are secondary. Selected antibiotics might be administered orally after few days of parenteral regimen for a total duration of two-three weeks.

P54b

FEVER IN THE FIRST POSTOPERATIVE WEEK DOES NOT HELP TO DIAGNOSE INFECTION IN CLEAN ORTHOPEDIC SURGERY

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Introduction: Postoperative fever is often misinterpreted as a sign of infection, especially when occurring after the third postoperative day. We assess the epidemiology of postoperative fever in adult orthopaedic patients and its association with infection.
Méthode: One-year prospective observational study in the Orthopedic Service of Geneva University Hospitals
Résultats: Among 1,073 patients participating in the study, 198 (19%) had a postoperative fever (>38°C). Thirteen patients (1.2%) had a surgical si te infection and 78 patients (7.3%) had other remote bacterial infections during their hospital stay (pneumonia, urinary tract infection, catheter-related infections, etc). Including for asymptomatic bacteriuria, a total of 174 patients were under antibiotic therapy for a median duration of 6 days. In multivariate analysis, no clinical parameter was associated with fever, including hematoma (odds ratio 0.9, 95%CI 0.6-1.3), infection (1.6, 0.7-3.7), or antibiotic use (1.6, 0.9-3.0). The maximum temperature on each of the first seven days postoperative did not differ between infected and uninfected patients (Wilcoxon-ranksum-tests; p>0.10).
Conclusion: Fever, even up to postoperative day 7, is not helpful to distinguish infection from general inflammation in clean orthopaedic surgery. Antibiotic use for any reason does not prevent or influence postoperative fever.

P54c

OPEN FRACTURES: EPIDEMIOLOGY, INFECTIONS AND ASSOCIATED ANTIBIOTIC PROPHYLAXIS

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Introduction: We intend to assess epidemiology and risk factors for open fracture infections with an emphasis on the duration of pre-emptive antibiotic therapy.
Méthode: Retrospective study at the Orthopaedic Service of University Hospitals of Geneva, 1996-2010. Exclusion of nosocomial infections (due to methicillin-resistant S. aureus and occurring 60 d after trauma).
Résultats: A total of 1492 open fractures (Gustilo and Anderson grade I, 663; grade II, 370; grade III, 310; unclassifiable, 149) were retrieved. Median duration of pre-emptive antibiotic therapy was 3 days (interquartile range (IQR), 1-3 days); median delay between trauma and surgery was 0 days, and the median number of surgical intervention was 2. We revealed 54 (3.6%) infections after a median delay of 10 days after trauma (IQR, 5-20 d). Intrinsically resistant pathogens to the empirical antibiotic used (Enterococci, Enterobacter, Pseudomonas spp) were documented in 35 of 49 cases (71%). In regression analyses, male gender, psychiatric co-morbidities, grade II fractures, and vascular injury & compartment syndrome (grade III fractures) were signif! icantly associated with infection, while the number of surgical interv entions, intra-medullary reaming, type of osteosynthesis, immune suppression, delay until first surgery and duration of antibiotic therapy were not. Overall, compared to one day of antibiotic treatment, 2-3 days (OR 0.6, 0.2-2.0), 4-5 days (1.2, 0.3-4.9) or >5 days (1.4, 0.4-4.4) did not prevent infection. These results were similar when multivariate analysis was stratified to grade III fractures (OR 0.3, 0.1-3.4; 0.6, 0.2-2.1, and 1.7, 0.5-6.2, respectively).
Conclusion: Infection in open fractures is strongly related to the extent of tissue damage, but not to the duration of pre-emptive antibiotic therapy. If confirmed in prospective trials, even in grade III fractures, pre-emptive antibiotic might be reduced to less than 3 days.

P55a

DYNAMIC MR ANGIOGRAPHY (MRA) OF SPINAL VASCULAR DISEASES AT 3T.

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Introduction: Spinal magnetic resonance angiography (MRA) is difficult to perform because of the size of the spinal cord vessels. High-field MR improves resolution and imaging speed.
Méthode: We have examined 17 patients,8 female and 9 male, aged 26–82 years, median age 52 years on a 3-Tesla MR system (Trio, Siemens,Forchheim, Germany. The protocol used was sagittal and axial T2WI,sagittal T1WI, DTI, 3D MRA sequences and fat-saturated T1WI in the sagittal and axial planes after gadolinium.
Résultats: In all patients the main spinal vessels were seen and abnormal vascular lesions were visualized. In two out of three patients examined for localization of the AKA, the visualization was easily done, whereas in the third patient differentiation between artery and vein was more difficult, but possible by performing MIP and MPR. In four cases of dural fistula the exact localization was possible. In three cases with AVM, the level of malformation and the intra- and perimedullary localization was done as well as the arteries implicated. The little shunts inside the nidus could not be individualized. Cavernomas are not seen on MRA and on conventional angiography; therefore, the realization of angiographic sequences is not necessary. In tumours such as hemangiomas or hemangioblastomas, hypervascularization was detected in addition to morphology and location of the masses. In ischaemia, the parenchymal anomalies were visible early on diffusion imaging but unfortunately the implicated vessel was not detectable by MRA.
Conclusion: Currently, MRA can provide the exact localization of a vascular malformation and Adamkievicz artery, and thus help detect and characterize spinal vascular lesions before conventional angiography for the diagnosis, thus avoiding an unnecessary intervention and decreasing the risk of embolism or dissections. Standard angiography should be used only fortherapeutic purposes.

P55b

THE CORPUS CALLOSUM: WHITE MATTER OR TERRA INCOGNITA

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Introduction: The corpus callosum is the largest white matter structure in the brain,consisting of 200–250 million contralateral axonal projections and the major commissural pathway connecting the hemispheres of the human brain.
Méthode: MRI is the modality of choice for the study of the CC. MRI protocole used was composed of sagittal T1 or T2 (fluid-attenuated inversion recovery (FLAIR)) weighted imaging, Difussion tensor imaging (DTI). Contrast medium when tumoral or inflammatory pathologies were suspected.
Résultats: MRI is the modality of choice for the study of the CC. MRI protocole used was composed of sagittal T1 or T2 (fluid-attenuated inversion recovery (FLAIR)) weighted imaging, Difussion tensor imaging (DTI). Contrast medium when tumoral or inflammatory pathologies were suspected.
Conclusion: Despite its essential role in interhemispheric communication,there are only a few studies concerning the CC. As a result, up until now, the CC remains a relatively unexplored region of the brain, somewhat of a‘‘terra incognita’’ for the clinician and the radiologist. Familiarity with its anatomy and pathology is important to the radiologist in order to recognise its disease at an early stage and help the clinician establish the optimal therapeutic approach.

P56

DETECTION DE LA RESISTANCE AUX GLYCOPEPTIDES CHEZ DES SOUCHES MRSA DE PATIENTS HUG BACTERIEMIQUES.

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Introduction: La détection de souches MRSA exprimant une sensibilité réduite aux glycopeptides (vancomycine, teicoplanine), dénommées GISA pour « glycopeptide-intermediate Staphylococcus aureus », reste problématique pour la décision d’antibiothérapie. La méthode de référence proposée par les Comités Européen (EUCAST) ou Américain (CLSI) de Mesures de Sensibilité aux Antibiotiques est la détermination des concentrations minimales inhibitrices (CMI) de vancomycine ou teicoplanine en microdilution sur plaques de microtitration. La sensibilité de la méthode de microdilution est considérée comme sub-optimale pour détecter les GISA.
Méthode: Nous avons évalué la performance du test de microdilution pour détecter les GISA, en comparant les CMIs de vancomycine et teicoplanine mesurées par microtitration avec celles obtenues par macrodilution ou en milieu gélosé. 56 souches MRSA, isolées de patients bactériémiques des HUG entre les années 1995 et 2003, ont été testées.
Résultats: Pour >80% des MRSA, les CMIs de vancomycine et teicoplanine étaient systématiquement plus élevées (2-4 mg/L) par test de macrodilution ou en milieu gélosé que celles (1 mg/L) mesurées par microdilution. Seulement 3 souches ont montré des CMIs de vancomycine et teicoplanine de 4 mg/L (seuil de détection des GISA) par microdilution, alors que la macrodilution a détecté 13 et respectivement 36 souches avec des CMIs de 4 mg/L pour la vancomycine et la teicoplanine. L’extension du temps d’incubation à 48 h a optimisé la détectio n des GISA, en permettant la croissance de sous-populations glycopeptide-résistantes caractérisées par une croissance ralentie.
Conclusion: La sensibilité du test de microdilution recommandé par EUCAST et CLSI est insuffisante pour une détection efficace des souches GISA.

P57

MODELLING THE IMPACT OF ANTIBIOTIC USE ON ANTIBIOTIC-RESISTANT ESCHERICHIA COLI USING POPULATION-BASED DATA FROM A LARGE HOSPITAL AND ITS SURROUNDING COMMUNITY

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Introduction: To determine the temporal relationship between antibiotic use and incidence of antibiotic-resistant Escherichia coli in both the inpatient and outpatient setting of a large urban area.
Méthode: A retrospective observational time-series analysis was performed to evaluate the incidence of clinical isolates of E. coli resistant to ciprofloxacin, trimethoprim/sulfamethoxazole and cefepime from January 2000 through December 2007, combined with a transfer function model of aggregated data on antibiotic use in both settings obtained from the hospital's pharmacy and outpatient billing offices.
Résultats: Ciprofloxacin resistance statistically increased from 6.0% (2000) to 15.4% (2007) and cefepime resistance from 0.9% (2002) to 3.2% (2007). Total antibiotic use increased in both settings, while fluoroquinolone use increased significantly only among outpatients. A temporal effect between fluoroquinolone resistance in community E. coli isolates and outpatient use of ciprofloxacin (immediate effect and time lag 1 month) and moxifloxacin (4 months) was observed, explaining 51% of the variance over time. The incidence of cefepime resistance in E. coli was correlated with ciprofloxacin use in the inpatient (1 month) and outpatient (4 months) settings and with the use of ceftriaxone (0 month), piperacillin/tazobactam (3 months) and cefepime (3 months) in the hospital (R2 51%).
Conclusion: These result s support efforts to reduce prescribing of fluoroquinolones for control of resistant E. coli including extended-spectrum b-lactamase producers and show the added value to better understand the interaction between community and hospital antibiotic prescribing.

P58

DEPISTAGE CIBLE DE MEDICAMENTS DANS LE PLASMA HUMAIN UTILISANT UNE METHODE DE CHROMATOGRAPHIE LIQUIDE RAPIDE ASSOCIEE AVEC UN SPECTROMETRE DE MASSE TANDEM HYBRIDE

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Introduction: Une evaluation comparative du système LC-MS/MS par rapport au Remedi® (LC-DAD) a été réalisée avec des échantillons patients. Tous les résultats acquis en LC-MS/MS sont traités par la nouvelle plate-forme informatique SmileMS dédiée à l'identification de petites molécules (m/z < 1000). La librairie de Weinmann "élargie" est utilisée pour cette évaluation.
Méthode: Un total de 146 échantillons plasmatiques sélectionnés ont été comparés en utilisant les 2 méthodes.
Résultats: Au total, 336 identifications ont été observées. Celles-ci représentent 88 composés différents. Le nombre d'identifications obtenues avec la méthode LC-MS/MS est de 89% et de 60% avec la méthode LC-DAD. La LC-MS/MS offre une meilleure sensibilité et une meilleure sélectivité que le RemediÒ alors que ce dernier a actuellement l\'avantage de posséder une librairie plus fournie que la méthode LC-MS/MS utilisée.
Conclusion: La majorité des composés incriminés lors d\'intoxication sont identifiés par la méthode LC-MS/MS proposée malgré la restriction à une liste de composés préselectionnés. En général, l'utilisation des spectres MS/MS suffit à assurer l\'identification des composés. Seules certaines substances nécessitent d'inclure les temps de rétention comme discriminateur complémentaire. D'un point de vue analytique, la technologie MS permet d'améliorer la sélectivité et la sensibilité par rapport au Remedi®. D'un point de vue pratique, lié à son degré d'automatisation et à sa relative simplicité d'utilisation, cette nouvelle méthode offre une alternative au Remedi®.

P59

AGE ET RATIO GANGLIONNAIRE AXILLAIRE CHEZ LES PATIENTES MENOPAUSEES PRESENTANT UN CANCER DU SEIN (CS) DE STADE T1-T2 NODAL POSITIF

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Introduction: Nous examinons la relation qu'il y a entre l'âge de la patiente et le ratio ganglionnaire axillaire (LNR, proportion de ganglions envahis sur le nombre de ganglions examinés), et déterminons leur effet sur la mortalité globale et la mortalité spécifique par CS.
Méthode: Les femmes âgées de 50 ans ou plus, diagnostiquées en 1988-1997, traitées chirurgicalement pour carcinome mammaire unilatéral confirmé histologiquement, stade T1-T2 nodal positif, sont sélectionnées à partir du Surveillance, Epidemiology, and End Results (SEER). Le GAMLSS (Generalized Additive Models for Location Scale and Shape) est appliqué pour évaluer la relation âge-LNR. Fonctions d'incidence cumulative et analyse multivariée de risques compétitifs sur modèles sélectionnés par BIC (Bayesian Infromation Criterion) sont appliqués pour évaluer les effets âge et LNR sur la mortalité. LNR-bas était défini comme <=0.20, intermédiaire 0.21-0.65, élevé >0.65.
Résultats: Résultats: GAMLSS montrait une relation âge-LNR non-linéaire, augmentant de LNR moyen 0.26-0.28 à 50-70 ans, 0.30 à 80 ans, et 0.40 à 90 ans. En comparaison au risque sur 5 ans de décès par CS de 9.8% chez les femmes de 50-59 ans avec LNR-bas, le risque chez celles de 80+ ans était 12.6% avec LNR-bas, 18.1% avec LNR-intermédiaire, 29.8% avec LNR-élevé. Le risque de décès sur 5 ans toutes causes confondues augmentait de 40.8% avec LNR-bas, à 67.4% avec LNR-élevé. Le hasard ratio multivarié de mortalité globale chez les patientes de 80+ ans avec LNR-élevé était de 7.49 par rapport aux femmes de 50-59 ans avec LNR-bas.
Conclusion: LNR-élevé combiné avec âge avancé était associé à une augmentation de 3 fois le risque de décès par cancer du sein, et de 7 fois le risque de décès toutes causes confondues.

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THE HIGH PREVALENCE OF MALNUTRITION IN ELDERLY DIABETIC PATIENTS: IMPLICATIONS FOR ANTI-DIABETIC DRUG TREATMENTS

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Introduction: Type 2 diabetes usually occurs in the context of obesity and associated insulin resistance. Current treatment recommendations are based on lifestyle modifications and incremental drug therapy. However, this approach could lead to inappropriate priorities upon aging, when diabetes may be compounded by malnutrition and reduced insulin resistance.
Méthode: We prospectively evaluated glycemic and nutritional parameters in 146 consecutive diabetic patients (age 82.5+7.3 years, mean+SD) admitted to our geriatric service. We also implemented nutritional support therapy and a drug therapy adjustment protocol. Oral hypoglycemic agents (OHA) withdrawal was attempted in case of good glycemic control (HbA1c <7.5% or fasting blood glucose (FBG) <7.5 mmol/l).
Résultats: Mean BMI and HbA1c were 29.6+7.1 kg/m2 and 6.9+1.2% respectively. 51.4% were on 1-3 OHA, 30.8% on insulin and 9.6% on insulin/OHA therapy. Low MNA (Mini nutritional Assessment) scores and serum marker levels indicated a high prevalence of malnutrition and/or chronic disease, even in obese patients. MNA scores were positively associated with HbA1c values. Among patients treated by OHA, complete drug withdrawal was achieved in 65.8%, much more often than new treatments were added (p=0.002). Glycemic control did not worsen after approximately 30 days, despite in-hospital nutritional therapy. Successful OHA withdrawal was associated with lower MNA scores.
Conclusion: Malnutrition is highly prevalent in elderly diabetic inpatients, and paradoxically contributes to “good” glycemic control. Malnutrition should be screened for in these patients, and when present should prompt a revision in diet and drug therapy. In particular, the possibility of reducing unnecessary drug therapy should be considered.

P60b

THE INTERDEPENDENCE BETWEEN HYPERTENSION, OTHER METABOLIC SYNDROME COMPONENTS AND LOW-GRADE INFLAMMATION EVOLVES WITH AGING

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Introduction: The prognostic significance, interdependence and hierarchy of cardio-vascular risk factors may evolve with advancing age. Our study reports the interdependence of hypertension, other metabolic syndrome components and high sensitivity CRP according to age in hypertensive subjects.
Méthode: 5712 consecutive non-diabetic patients (50.1 % males, age range: 40-95 years) evaluated in outpatient hypertension clinics were included and divided into five age groups (40-49, 50-59, 60-69, 70-79, >80 years old). BP evaluated by both office and 24H ambulatory blood pressure monitoring (ABPM) measurements, metabolic and inflammation parameters were determined after a > two week drug washout period.
Résultats: The prevalence of the metabolic syndrome (ATP-III definition) remained stable across age groups. We observed a stable or increased association between waist circumference and insulin resistance and fasting plasma glucose. However, the association between waist circumference and ABPM systolic BP (ABPM-SBP; r2 from 9.9% to 1.0%, p80 years old, whereas its association with waist circumference markedly decreased.
Conclusion: Hypertension and dyslipidemia dissociate from central obesity with advancing age. They are increasingly determined by low-grade inflammation, independent of central obesity. These changing associations may underlie the weakening of both obesity and the metabolic syndrome as cardiovascular risk factors in older persons.

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TWICE-WEEKLY HYPOFRACTIONATED INTENSITY-MODULATED RADIOTHERAPY FOR LOCALIZED PROSTATE CANCER WITH LOW-RISK NODAL INVOLVEMENT: TOXICITY AND OUTCOME FROM A DOSE ESCALATION PILOT STUDY

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Introduction: To evaluate the toxicity and preliminary outcome of patients with localized prostate cancer treated with twice-weekly hypofractionated intensity-modulated radiotherapy (IMRT).
Méthode: Between 2003 and 2006, 82 prostate cancer patients with a nodal involvement risk ≤ 20% (Roach index) have been treated to the prostate ± seminal vesicles with 56 Gy (4 Gy/fraction twice-weekly) and an overall treatment time of 6.5 weeks. Acute and late genitourinary (GU) and gastrointestinal (GI) toxicities were scored according to the Radiation Therapy Oncology Group (RTOG) grading system. Median follow-up was 48 months (range, 9-67).
Résultats: All patients completed the treatment without interruptions. No patient presented with ≥ Grade 3 acute GU or GI toxicity. Only 4% presented with Grade 2 GU or GI persistent acute toxicity 6 weeks after treatment completion. The estimated 4-year probability of ≥ Grade 2 late GU and GI toxicity-free survival were 94.2% ± 2.9% and 96.1% ± 2.2%, respectively. One patient presented with Grade 3 GI and another one with Grade 4 GU late toxicity, transitory in both cases. The 4-year actuarial biochemical relapse-free survival according to the nadir plus 2ng/mL definition was 91.3% ± 5.9%, 76.4% ± 8.8 and 77.5% ± 8.9% for low-, intermediate-, and high-risk groups, respectively.
Conclusion: In patients with localized prostate cancer, acute and late toxicity was mini mal after dose-escalation administering twice-weekly 4 Gy to a total dose of 56 Gy, with IMRT. Further prospective trials are warranted to further assess the best fractionation schemes for these patients.