8e Journée de la recherche de la Division de gériatrie de McGill
8th Annual McGill Geriatric Medicine Research Day

Holiday Inn
Montréal-Midtown
420 Sherbrooke Street West

Vendredi 6 juin 2003 - Friday, June 6, 2003

TABLE DES MATIÈRES – TABLE OF CONTENTS

PROGRAMME – PROGRAM

8th Annual Research Day

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McGill Division of Geriatric Medicine

Friday, June 6, 2003

Holiday Inn
Montréal-Midtown, 420 Sherbrooke Street West
☎ 514-842-6111

PROGRAM

08:00 - 08:30	Continental Breakfast (Foyer Ambassadeur)
08:30 - 08:45	**Welcome** (Ambassadeur A) Dr. Howard Bergman
08:45 - 9:45	**Round table discussion** (Ambassadeur A) *The Canadian Longitudinal Study on Aging (CLSA)* *A research opportunity for the future* Dr. Howard Bergman (Chair) Dr. Susan Kirkland (Co-PI, Protocol Development for the CLSA) Dalhousie University Dr. Christina Wolfson (Co-PI, Protocol Development for the CLSA) McGill University
9:45 - 10:30	Poster session / coffee & tea (Ambassadeur B/Foyer Ambassadeur)
10:45 - 12:30	Paper session (Ambassadeur A)
12:30 - 13:30	Lunch (Gouverneur 1)
13:30 - 15:30	Paper session (Ambassadeur A)
15:130- 15:45	Coffee and refreshments (Foyer Ambassadeur)
15:45 - 16:15	Closure / Prizes (Ambassadeur A)

COMMUNICATIONS ORALES – ORAL PRESENTATIONS

Ambassadeur A		
10:30	Neuroleptic malignant syndrome: a case-study and review of the literature	Daren Nicholson
10:45	Evaluation of the Utilization of a Methicillin-Resistant Staphylococcus Aureus decolonization protocol in patient aged 75 and older at the McGill University Heath Centre	Caroline Beauchamp
11:00	$p75^{NTR}$ protects against extracellular amyloid toxicity in human neurons	Yan Zhang
11:15	Function of qki, the quaking viable mouse gene product, in myelination and brain development	Daniel Laroque
11:30	Prevalence and correlates of self-rated health in a community-dwelling cohort of seniors 75 years of age and over	Vittorio Addona
11:45	Donepezil improves lexical-semantic and attentional functions in Alzheimer's disease.	Daniel Saumier
12:00	Investigating the Role of Telomerase in Chemotherapeutic Resistance	Ryan Ward
12:15	Pathogenic Tau Protein Mutations and Neurodegenerative Diseases	Dong Han
Ambassadeur A		
1:30	Focus Group Analysis "How does Medical School influence medical students' attitudes toward the elderly? In search of strategies to encourage interest in a career in Geriatrics"	Rene Leiva
1:45	Frailty amplifies the effects of aging on protein metabolism; role of protein intake	Stéphanie Chevalier
2:00	Interaction of Glycogen Synthase Kinase-3β with Tau Protein	Zongfei Yuan
2:15	A proteomic approach to biomarker discovery in Alzheimer's disease	Hanling Yu
2:30	La modélisation de l'utilisation de services hospitaliers d'urgence au sein de SIPA	François Truchon
2:45	Limitations and lessons leaned for assessing agreement between self-reported physician utilization and data obtained from the RAMQ medical services database	John Podoba
3:00	Cross-talk between cyclin-dependent protein kinaze 5 and glycogen synthase-3ß within a microtubule-associated tau phosphorylation complex	Tong Li
3:15	An ^{15}O PET study of word meaning. in AD	Christine Whatmough

NEUROLEPTIC MALIGNANT SYNDROME: A CASE-STUDY AND REVIEW OF THE LITERATURE

Daren Nicholson, Med-3, Faculty of Medicine, McGill University;Wendy Chiu, MD.CM, FRCPC, Assistant professor/physician, Division of Geriatric Medicine, McGill University Health Centre

Neuroleptic malignant syndrome (NMS) is a rare adverse reaction to neuroleptics. Although the incidence of NMS in the elderly population has never been studied, several cases of NMS in elderly patients have been reported. There are several reasons why geriatricians should be aware of the syndrome. First, on a theoretical basis, elderly patients may be more susceptible to NMS since dopamine activity decreases with age (the proposed mechanism of NMS is a widespread block of dopaminergic activity in the brain). Second, some studies identify dementia and cerebral vascular accidents, two common conditions in the elderly, as risk factors for NMS. Third, clinicians are increasingly using neuroleptics to treat psychosis, dementia and delirium management in the elderly. Further research regarding NMS in the elderly is warranted.

EVALUATION OF THE UTILIZATION OF A METHICILLIN-RESISTANT *STAPHYLOCOCCUS AUREUS* DECOLONIZATION PROTOCOL IN 75 YEARS AND OLDER PATIENTS AT THE MCGILL UNIVERSITY HEALTH CENTRE

Caroline Beauchamp[1,2]**,** B.Pharm, MSc, Jacynthe Roy-Petit[1,2], B.Pharm, MSc, Hélène Paradis[2], B.Pharm, MSc, Wendy Chiu[3], MD, Gary Inglis[3], MD, Louise Mallet[1,2,3], PharmD,
[1]Faculté de Pharmacie, Université de Montréal
[2]Department of Pharmacy, McGill University Health Centre
[3]Department of Geriatrics, McGill University Health Centre

Objectives: To evaluate the efficacy and the safety of a methicillin-resistant *Staphylococcus aureus* (MRSA) decolonization protocol in patients aged 75 years and older at the McGill University Health Centre.
Methods : Retrospective chart review of decolonization treatments prescribed between September 2000 and December 2001 patients aged 75 years and older patients at the Royal-Victoria Hospital and the Montreal General Hospital.
Results: The decolonization protocol was respected in 49.5 % of patients treated for MRSA colonization. The two main causes of non-respect were duration of treatment shorter or longer than 10 days and use of rifampin and trimethoprim-sulfamethoxazole despite a drug interaction. Efficacy was confirmed in 24.2 % of all treatments (n=182). When all follow up cultures were available (n=91), 48.2 % of treatments were effective. Systemic and topical treatment tends to be more effective than topical treatment alone. However, some adverse reactions (nausea or vomiting, esophagitis, renal failure) were more common with the systemic and topical treatment. A clinical consequence to a drug interaction was seen in 3 patients.
Conclusion: Since the study was retrospective, many follow up cultures were missing. Thereby, the efficacy of the MUHC decolonization protocol could not be established. Follow up cultures should be systematically done to assess the efficacy of the decolonization treatment.

P75^{NTR} PROTECTS AGAINST EXTRACELLULAR AMYLOID TOXICITY IN HUMAN NEURONS

Yan Zhang*[¶], Yanguo Hong[¶], Younes Bounhar*[¶], Megan Blacker[¶], Xavier Roucou[¶], Omar Tounekti[¶], Emily Vereker[¶], William Bowers[§], Howard Federoff[§], Cynthia Goodyer, Andréa LeBlanc*[¶]
*Department of Neurology and Neurosurgery, §Department of Pediatrics, McGill University
[¶]Lady Davis Institute for Medical Research, Jewish General Hospital
[§]Department of Neurology and Center for Aging and Developmental Biology, University of Rochester

Amyloid β (Aβ) peptides added in the extracellular cell culture medium are toxic to various rodent cell lines but not to human neurons in primary cultures. To address why human neurons are less vulnerable to extracellular Aβ insult, neurotrophin receptor p75^{NTR} was studied since it exaggerates extracellular Aβ toxicity in rodent cell lines. In contrast to rodent cells, p75^{NTR} lowers the extracellular Aβ toxicity in human neurons determined by p75^{NTR} anti-sense constructs and its neutralizing antibody. These results open a new avenue that p75^{NTR} might be neuroprotective in human neuronal system and p75^{NTR} upregulation might be one of the mechanisms that lead to high tolerance of human neurons to extracellular Aβ toxicity.

FUNCTION OF QKI, THE QUAKING VIABLE MOUSE GENE PRODUCT, IN MYELINATION AND BRAIN DEVELOPMENT

Daniel Larocque[1], Julie Pilotte[1], Hugo Dilhuydy[3], Guillermina Almazan[2] and Stéphane Richard[1]
[1]. Bloomfield Center for Research on Aging, Lady Davis Institute for Medical Research, Sir Mortimer B. Davis Jewish General Hospital, McGill University, Montréal, Canada
[2]. Department of Pharmacology and Therapeutics, McGill University, Montréal, Canada.
[3]. Laboratoire de microscopie, Centre de recherche, Institut universitaire de gériatrie de Montréal

Oligodendrocytes are highly specialized cells that produce central nervous system (CNS) myelin. Myelin proteins have to be transported to the cell periphery and this process is poorly understood. The quaking viable mice (qkV) oligodendrocytes fail to properly compact the myelin in their CNS, thus representing an animal model of dysmyelination.

Ten days after birth these mice develop a rapid tremor phenotype that is especially pronounced in the hind limbs. Although the defect in the qkV mice involves a deletion mutation affecting the expression of the alternatively spliced qk gene products, their respective roles in myelination and brain development are unknown.

We show that the QKI RNA binding proteins (QKI-5, QKI-6, QKI-7) regulate the nuclear export of MBP mRNAs by binding a short RNA element in their 3'-UTR. The expression of QKI-5 in oligodendrocyte cultures disrupts the QKI nucleocytoplasmic equilibrium resulting in nuclear and perikaryal retention of the MBP mRNAs and lack of export to cytoplasmic processes, as occurs in qkV mice. By using adenovirus vectors injected in the corpus callosum region of the brain, we found that QKI-5 down regulates the expression of the MBP isoforms *In Vivo*. The MBP mRNA export defect leads to a reduction in the levels of MBP proteins and their improper cellular targeting to the periphery. Our findings suggest that qkV mice are defective in the nuclear export of mRNAs encoding key myelin proteins. In other studies using mouse brain, we found that the different QKI proteins had distinct developmental profiles. To determine the role of QKI proteins in brain development and aging, we achieved focal misexpression of QKI genes early during mouse embryo forebrain development. Cell lineage analysis have also shown that QKI proteins are important for glial cell development. These observations could have implications in the repair of myelin in neuropathology diseases such as multiple sclerosis.

Reference: Neuron Vol 36, 815-829, December 2002.
This work is supported by the Multiple Sclerosis Society of Canada.

PREVALENCE AND CORRELATES OF SELF-RATED HEALTH IN A COMMUNITY-DWELLING COHORT OF SENIORS 75 YEARS OF AGE AND OVER

Vittorio Addona, MSc, Christina Wolfson, PhD, David Wolfson, PhD

Department of Mathematics and Statistics, McGill University

Self-rated health (SRH) is a measure of perceived health which has garnered much attention in the medical literature. The underlying concept is that an individual's self-report of health is a marker of their overall medical outlook which cannot be fully identified by medical assessments and known conditions. SRH has been shown to be associated with usage of community services, functional decline, pain, and mortality. The results of a sub-analysis from a larger study addressing the prevalence of unmet needs for community services in the community dwelling elderly will be presented. Unmet need status is a dichotomous variable determined by an algorithm which specifies whether an individual has an unmet need for help with ADL's or IADL's (Allen and Mor 1997). The objectives of this sub-analysis are: (i) to estimate the prevalence of various categories of SRH and (ii) to determine the correlates of SRH. A logistic regression was fit to SRH, with the "poor" SRH category being modeled by 18 independent variables. The variables which were significantly associated with SRH are: unmet need status, education, nutrition, control/mastery, co-morbidity, and # of cohabitants. These results primarily agree with the literature. Nevertheless, the relationship between SRH and control/mastery and nutrition are intriguing. An individual's nutrition can be altered, while control/mastery has not yet been adequately studied in relation to SRH.

DONEPEZIL IMPROVES LEXICAL-SEMANTIC AND ATTENTIONAL FUNCTIONS IN ALZHEIMER'S DISEASE

Daniel Saumier, Howard Chertkow(supervisor), Susan Murtha, Howard Bergman, & Victor Whitehead

Department of Neurology and Neurosurgery, McGill University.

The current study sought to evaluate changes in domain-specific cognitive performance following Donepezil treatment in individuals with mild to moderate Alzheimer's disease (AD). Donepezil 10 mg was administered in an open-label treatment study for 6 months to 30 individuals with mild probable AD. Global treatment response was assessed using an algorithm combining changes in the ADAS-cog (Alzheimer's Disease Assessment Scale, cognitive subscale), MMSE (Folstein Mini-mental State Exam) and CIBIC (Clinician interview-based Impression of Change), with "response" defined as improvement or stabilization on the combination algorithm over the six month period. Wide-ranging standardized neuropsychological and experimental cognitive tests were also administered before and after six months of treatment. The tests examined attention, working memory, learning and memory, visuo-spatial constructive skills, and lexical-semantic knowledge. The results indicate that eighteen subjects were rated as having responded, while 12 were rated as non-responders. Significant differences between Responders and Non-responders were found in the domains of visuo-spatial motor skills and lexical-semantics. No significant group differences were noted on the other cognitive domains. However, when Donepezil treatment effects were evaluated for the entire AD sample, independent of global response outcome, improved or stable cognitive scores were also obtained on measures of attention and working memory.
Conclusion: There is a benefit of Donepezil on attention and working memory performance that is independent of global clinical response outcome. Donepezil Responders are further characterized by significant improvement on tasks of lexical-semantics, and improvement overall on visuospatial processing.

INVESTIGATING THE ROLE OF TELOMERASE IN CHEMOTHERAPEUTIC RESISTANCE

Ryan J. Ward[1,2], Tara Moriarty[1,3], & Chantal Autexier[1,2,3]
[1]Bloomfield Centre for Research in Aging, Lady Davis Institute for Medical Research,
Sir Mortimer B. Davis Jewish General Hospital, Montreal, QC.
[2]Division of Experimental Medicine, Faculty of Medicine, McGill University, Montreal, QC.
[3]Department of Anatomy and Cell Biology, Faculty of Medicine, McGill University, Montreal, QC.

Acute myeloid leukemia (AML) is predominantly a disease of the elderly, with more than 50% of all cases in patients older than 60. Unfortunately, AML in the elderly is associated with poor prognosis, decreased therapeutic tolerability, and chemotherapeutic drug resistance. Inhibiting drug efflux mechanisms or increasing cytotoxic sensitivities are strategies to overcome resistance; however these practices have not affected patient survival.

Telomerase is the reverse-transcriptase enzyme involved in maintaining telomeres. Recent observations support the hypothesis that telomerase protects against anti-cancer treatments. We are studying the role telomerase plays in generating or maintaining chemotherapeutic resistance, hypothesizing that telomerase inhibition will re-sensitize cells to drug treatment.

We have treated sensitive and resistant human leukemia cells with clinically relevant doses of the DNA-damaging drug etoposide. We observed an upregulation of telomerase activity at early time points and a down-regulation of activity at later time points after treatment of etoposide-sensitive cells. Conversely, we observed stable telomerase activity throughout etoposide treatment in resistant cells despite increased drug concentrations and equivalent levels of cell death. Further, we observed differences in mean telomere length and basal telomerase activity levels in the two cell types. Currently we are investigating the effect of telomerase inhibition and etoposide treatment on reversing drug resistance. Results from these experiments may support the use of telomerase inhibitors for the treatment of drug-sensitive and drug-resistant adult myeloid leukemias.

PATHOGENIC TAU PROTEIN MUTATIONS AND NEURODEGENERATIVE DISEASES

Dong Han, and Hemant K. Paudel, Tong Li
The Bloomfield Centre for Research in Aging, Lady Davis Institute for Medical Research, Sir Mortimer B. Davis-Jewish General Hospital, McGill University

Tau proteins are microtubule-associated proteins. They are mainly expressed in neurons where they bind to and stabilize microtubules in addition to promoting microtubule assembly. Filamentous deposits made of tau proteins are a defining characteristic of a number of neurodegenerative diseases, including Alzheimer's disease. Furthermore, multiple *tau* gene mutations have been identified in familial frontotemporal dementia and parkinsonism linked to chromosome 17 (FTDP-17). In all tauopathies, tau is abnormally hyperphosphorylated. Thus tau dysfunction due to hyperphosphorylation is sufficient to cause neurodegeneration and dementia. In an effort to purify proteins that interact with tau, our laboratory has identified an ~500-kDa multiprotein complex (tau phosphorylation complex) in the brain. This complex contains tau, glycogen synthase kinase-3β (GSK-3β), cyclin-dependent kinase 5 and 14-3-3. The function of tau phosphorylation complex is not entirely clear but current data suggest a regulatory role in tau phosphorylation. In order to determine how tau becomes hyperphosphorylated in various tauopathies, we are investigating the effect of pathogenic tau mutations on the interaction of tau with other tau phosphorylation complex components. We have selected G272V, P301L and R406W tau mutants for our study. We find that these mutants are differently phosphorylated than the wild type tau by GSK-3β. Our data suggest that pathogenic tau mutations alter the interaction of tau with other tau phosphorylation complex components.

FOCUS GROUP ANALYSIS "HOW DOES MEDICAL SCHOOL INFLUENCE MEDICAL STUDENTS' ATTITUDES TOWARD THE ELDERLY? IN SEARCH OF STRATEGIES TO ENCOURAGE INTEREST IN A CAREER IN GERIATRICS"

Rene Leiva, MD,CCFP; Najmi Nazerali, MD, CCFP (Supervisor)
Department of Geriatrics

Objective: To look at what features of the medical school training attract (or deter) students to choose to work with elderly patients. As well, to inquire into medical students' thoughts on strategies for curriculum change to improve attitudes towards the care of the elderly.
Relevance: As the population of the elderly is continuing to increase in Canada, it has become clear that future physicians must have appropriately positive attitudes to ensure that care for the elderly is optimal. In addition, proper access to physicians trained in specialized care of older people is becoming more difficult since the number of new physicians with a specialty in geriatrics is decreasing to dangerous levels
Participants: A voluntary sample of eighteen 4th year medical students from the 1999 McGill graduating class.
Method: Qualitative method of focus group. Two focus groups were analysed for emerging patterns, themes, and categories using inductive analysis.
Main Findings: Participants concluded that attitudes towards the elderly might deteriorate as they progress through their years of training. They identified several probable factors for the loss of positive attitudes. In addition, they provided strategies for medical curriculum improvement such as modifying training to reflect the spectrum of elderly patients including exposure of senior healthy mentors to the students, exposure to enthusiastic geriatric teacher/role models; schedule 'time-off' to reflect upon students' experiences during clerkship; making the person the focus of the medical care of the elderly and rewarding 'caring/holistic approach' in evaluation process.

FRAILTY AMPLIFIES THE EFFECTS OF AGING ON PROTEIN METABOLISM; ROLE OF PROTEIN INTAKE

Stéphanie Chevalier, José A. Morais, Réjeanne Gougeon, Kiran Nayar
McGill Nutrition and Food Science Centre and Division of Geriatric Medicine,
(MUHC)-Royal Victoria Hospital.

We previously demonstrated that muscle contributes less to whole-body protein breakdown with healthy aging. We hypothesize that frailty further compromises protein metabolism and that a short-term protein supplementation will improve this. The **objective of the study** was to compare whole-body protein metabolism of frail to that of healthy elderly subjects and test the effects of a short-term protein supplementation. **Design and Methods:** Protein metabolism was studied with the oral, 60 h-[^{15}N]glycine and urinary excretion of N^{9}-methylhistidine methods in 8 frail and 13 healthy elderly women during an isoenergetic, isonitrogenous formula diet for 9 d, then with increased protein intake (from 0.87 ± 0.03 to 1.23 ± 0.02 g pro/kg≅d) in frail to match that of healthy subjects, for 12 d. **Results and Conclusions:** Frail women had higher rates of whole-body synthesis and breakdown per kg fat-free mass (FFM) and rates of muscle protein breakdown lower as total/d, but *higher* per unit of muscle mass than in healthy women. Since muscle mass was greatly reduced in frail women, this resulted in a lower contribution of muscle and higher contribution of non-muscle lean tissues to whole-body breakdown. The protein-enriched diet had no effect on these parameters but net protein balance (synthesis-breakdown) was increased, with a positive nitrogen balance at the end of the diet period. We conclude that frailty exacerbates the age-related alteration of protein metabolism. Reduced muscle mass associated with usual low protein intake and higher muscle protein catabolism are both involved in this process. Frail women maintained the capacity to retain nitrogen when given higher intakes, which could convey health benefits if sustained over a long enough period to result in lean tissue accretion.

INTERACTION OF GLYCOGEN SYNTHASE KINASE-3β WITH TAU PROTEIN

Zongfei Yuan, Alka Agarwal-Mawal and Hemant K. Paudel*
Bloomfield Centre for Research in Aging, Lady Davis Institute for Medical Research, SMBD-Jewish General Hospital and Department of Neurology and Neurosurgery, McGill University

In Alzheimer's Disease (AD), microtubule-associated protein tau is abnormally hyperphosphorylated. Abnormal hyperphosphorylation of tau causes microtubule disruption and neurodegeneration. Glycogen synthase kinase-3β (GSK-3β) phosphorylates tau in normal and AD brain. Mechanism by which GSK-3β causes abnormal tau phosphorylation in AD brain is not known. Recently our laboratory has shown that tau and GSK-3β are parts of an ~500 kDa tau phosphorylation complex in the brain. Within the complex GSK-3β interacts with tau through a phosphoserine-binding protein 14-3-3. 14-3-3 not only connects GSK-3β to tau within the complex but also facilitates GSK-3β catalyzed tau phosphorylation. In this study we have investigated the molecular mechanism by which 14-3-3 mediates interaction of GSK-3β with tau. We find that phosphorylation of GSK-3β on Serine-9 is essential for 14-3-3 to bind and connect GSK-3β to tau *in vivo*. Because GSK-3β is phosphorylated on Serine-9 during insulin signaling in neurons, our results suggest that deregulation of insulin-signaling pathway may result in tau hyperphosphorylation and induction of early stage of neurofibrillary pathology in AD brain.

A PROTEOMIC APPROACH TO BIOMARKER DISCOVERY IN ALZHEIMER'S DISEASE

Hanling Yu
Laboratory of Dr. Hyman M. Schipper
Co-authors: Howard M. Chertkow, Howard Bergman

Dept. of Neurology & Neurosurgery and Dept. of Medicine (Geriatrics), McGill University
Centre for Neurotranslational Research and Bloomfield Centre for Research in Aging
Lady Davis Institute for Medical Research
Sir Mortimer B. Davis Jewish General Hospital, Montreal, Canada

A proteomic approach was employed to elucidate possible differential expression of native and oxidized glycoproteins using pooled plasma samples derived from ten patients with sporadic AD and pooled plasma samples from nine normal elderly control (NEC) subjects. The plasma samples were fractionated by sequential affinity chromatography on heparin-agarose (HepA) and concanavalin A-agarose (ConA) columns followed by separation on 1D and 2D PAGE gels. Carbonylation (oxidation) of proteins was monitored by in-strip derivatization with DNP and anti-DNP immunoblotting. Nine spots representing glycoproteins which showed enrichment or high specific oxidation indices in AD HepA-ConA 2D-gels relative to NEC samples were analyzed by MALDI-TOF/MS and identified with high probability ($p < 0.001$) as isoforms of human transferrin (Tf), hemopexin (Hpx) and α-1-antitrypsin (α-1-AT). These glycoproteins were concentrated, respectively, 5-, 6.5- and 107-fold in HepA-ConA eluates derived from AD plasma relative to the NEC samples. Specific oxidation indices of the identified Tf and Hpx isoforms in AD plasma were, respectively, 7.4 and 2.8 relative to NEC. Our findings provide further evidence for *systemic* derangements in heme/iron/redox homeostasis and activation of the acute phase response in sporadic AD. Moreover, the data implicate isoforms of Tf, Hpx and α-1-AT as potential biological markers of this condition.

LA MODÉLISATION DE L'UTILISATION DE SERVICES HOSPITALIERS D'URGENCE AU SEIN DE SIPA

François Truchon (Candidat au Ph.D.) et François Béland (Directeur)
Santé publique, Université de Montréal

L'utilisation des services de santé et, par extension, des services d'urgence est souvent expliquée selon un modèle béhavioriste qui détermine une propension d'utilisation en fonction de trois éléments, à savoir : 1. des facteurs prédisposants (caractéristiques démographiques, structure sociale et croyances à l'égard des soins de santé); 2. des facteurs habilitants (ressources familiales et communautaires); et 3. des besoins (perçus ou évalués).

Tirée du modèle original d'Andersen-Newman, cette approche ne prend toutefois pas en considération les modalités de prestation des services. Une nouvelle version de ce modèle a été suggérée par Andersen et Aday pour y inclure la spécificité du système de santé, les politiques de santé et la satisfaction des utilisateurs. Or, le projet de soins intégrés pour les personnes âgées en perte d'autonomie (SIPA) fait l'hypothèse de diminuer l'utilisation de services d'urgence grâce à une modification de l'organisation des services. Plus précisément, le projet SIPA s'appuie sur : 1. l'intégration des services de santé et sociaux grâce à des ententes formelles de collaboration interorganisationnelle; 2. l'application de protocoles de soins de type gérontogériatriques élaborés par des équipes professionnelles interdisciplinaires; et 3. la coordination des services assurée par un gestionnaire de cas.

L'utilisation des services d'urgence au sein du projet SIPA peut donc être modélisée en mettant en relief des éléments issus de la propension à l'utilisation et d'autres issus de l'organisation des services.

LIMITATIONS AND LESSONS LEARNED FOR ASSESSING AGREEMENT BETWEEN SELF-REPORTED PHYSICIAN UTILIZATION AND DATA OBTAINED FROM THE RAMQ MEDICAL SERVICES DATABASE

John E. Podoba
Department of Epidemiology & Biostatistics, McGill University

Physician utilization data can be obtained from self-reporting by patients or from government medical service databases. However, self-reporting relies on the respondent's recall of past events. In order to validate self-reported physician utilization, a random sample of elders 75 years of age and older from the Greater Montreal region that participated in the unmet needs study and consented to the release of medical utilization data from the Régie de l'Assurance Maladie du Québec (RAMQ) were used to compare self-report of physician visits to data obtained from the RAMQ medical service database. For assessing the reliability of physician utilization between questionnaire data and the RAMQ database, using the kappa statistic, careful attention should be paid to the type of data that are available from the RAMQ when developing medical utilization questions for a questionnaire. Otherwise, assessing reliability proves to be problematic. This presentation will discuss the types of questions that were not included in the unmet needs questionnaire but should have been and the resulting difficulty that results when attempting to assess reliability. Moreover, the problem of the kappa paradox will be discussed and how despite excellent agreement, values of the kappa statistic are substantially lower than would be anticipated.

CROSS-TALK BETWEEN CYCLIN-DEPENDENT PROTEIN KINASE 5 AND GLYCOGEN SYNTHASE KINASE-3β WITHIN A MICROTUBULE-ASSOCIATED TAU PHOSPHORYLATION COMPLEX

Tong Li, Hamid Y. Qureshi, Dong Han and Hemant K. Paudel
Bloomfield Centre for Research in Aging, Lady Davis Institute for Medical Research,
Sir Mortimer B. Davis-Jewish General Hospital, and Department of Neurology and Neurosurgery,
McGill University, 3755 Cote Ste-Catherine Road, Montreal, Quebec, H3T 1E2, Canada

In Alzheimer disease (AD), microtubule-associate protein tau is abnormally hyperphosphorylated. Hyperphosphorylation of tau causes miocrotubule insatiability, axonal transport loss and neurodegeneration. Cyclin-dependent protein kinase 5 (Cdk5) and glycogen synthase kinase-3β (GSK3β) phosphorylate tau in normal and AD brain. The mechanism by which these two kinases phosphorylate tau in the brain is not know. In this study, we find that when purified brain microtubules are analyzed by gel filtration chromatography, tau, Cdk5 and glycogen synthase kinase-3β (GSK3β) co-elute as an ~500 kDa complex. From fractions containing the ~500 kDa complex, tau, Cdk5 and GSK3β co-immunoprecipitate with each other. Similarly, when fractions containing the ~500 kDa complex are subjected to an anti-GSK3β immunoaffinity column chromatography, tau, Cdk5 and GSK3β bind to the column. In HEK-293 cells transfected in various combinations with tau, Cdk5 and GSK3β, tau binds to both Cdk5 and GSK3β but Cdk5 and GSK3β bind to each other only in the presence of tau forming a Cdk5-tau-GSK3β complex. Although tau is phosphorylated in HEK-293 cells transfected with tau and Cdk5 or tau and GSK3β, hyperphosphorylation of tau only occurs in HEK-293 cells transfected with tau, Cdk5 and GSK3β. Our data indicate that tau, Cdk5 and GSK3β are components of an ~500-kD brain microtubule-associated multiprotein complex. Within this complex, tau acts as the scaffold and connects GSK3β and Cdk5, whereas GSK3β and Cdk5 communicate with each other and phosphorylate tau together.

AN ^{15}O PET STUDY OF WORD MEANING. IN AD

C. Whatmough, H. Chertkow, L. Verret, K. Hanratty & V. Whitehead
Department of Neurology and Neurosurgery

It has been suggested that in neurodegenerative diseases patients recruit alternative systems to perform the same cognitive tasks as nondiseased individuals. We carried out a ^{15}O PET study which compared the cerebral blood flow (CBF) for word meanings in elderly normal subjects (ENs) with that of patients with Alzheimer's type dementia (ADs). Subjects made similarity judgments about pairs of words; two scans targetted concrete concepts and two abstract concepts. ADs displayed a category effect not seen in the ENs in that they were slower and less accurate on abstract concepts than on concrete concepts. Analyses of the rCBF indicated that both groups activated the ventral occipital-temporal cortex more for concrete than for abstract concepts, suggesting that activation of concrete concepts involves some type of figural processing. R-CBF was left lateralised in ENs but bilateral and more distributed in ADs. Even more striking was a right hippocampal CBF increase in ADs not found in ENs. Increases in the right hippocampal CBF in normal individuals generally occurs during episodic memory tasks requiring the encoding of figurative material. This finding is similar to a previous PET study in which ADs but not ENs activated the left hippocampus during difficult picture naming. We propose that in both of these semantic tasks (picture naming, judgement of meaning) ADs activate episodic memory circuits to supplement their degraded semantic memory system.

COMMUNICATIONS PAR AFFICHE – POSTER PRESENTATIONS

Ambassadeur B		
P1.	The Relevance of Caregivers in Economic Evaluations of Alzheimer's Disease Medications	Mark Oremus
P2.	An Assessment of Non-Response Bias in a Physician Survey of Drug Treatments for Alzheimer's Disease	
P3.	Physician Efficacy Requirements for Prescribing Drug Treatments for Alzheimer's Disease	
P4.	Detection and management of depression among seniors: A multidisciplinary research team project	Jane McCusker
P5.	G-AGE: A multidisciplinary research team to improve emergency department (ed) care of seniors	
P6.	Anthropometric characteristics of hospitalised female elderly	Slimane Belbraouet
P7.	Effects of cyclodextrine on t cell rafts composition with aging	Anis Larbi
P8.	Diète et stress oxydatif chez le sujet âgé atteint de diabète de type 2	Marie-Noelle Caron
P9.	L'altération de l'activité paraoxonase du pon1 est un indicateur de la réduction dans le potentiel antioxydant des hdl	Leila Jaouad
P10.	The McGill University/Jewish General Hospital Memory Clinic: A new approach to the management of patients with cognitive disorders	Kamadore Toure
P11.	Médecins de première ligne et les réseaux intégrés pour personnes âgées avec des incapacités: vision médicale comparative entre cliniciens SIPA, leaders de GMF et gestionnaires (protocole de l'étude)	Mathieu De Stampa
P12.	Undertaking a Population-Based Prospective Cohort Study on Community Dwelling Elderly: From Subject Recruitment to Follow up	Deborah Weiss
P13.	Canadian Longitudinal Study on Aging Protocol Development	Sathya Karunananthan

THE RELEVANCE OF CAREGIVERS IN ECONOMIC EVALUATIONS OF ALZHEIMER'S DISEASE MEDICATIONS

Mark Oremus
Centre for Clinical Epidemiology and Community Studies, S.M.B.D. Jewish General Hospital and Department of Epidemiology and Biostatistics, McGill University, Montreal, Quebec

Introduction: Drug treatments for Alzheimer's disease (AD) have been shown to delay cognitive decline in mildly to moderately affected patients, but they are not cures. Due to the aging population, researchers will seek to improve upon this early success, and economic evaluations will be an important component of the research process. There are several factors for economists to consider in AD, including the impact caregivers may have on drug utilization. This is important because caregivers play a major role in deciding how AD patients are treated.
Methods: MEDLINE was searched from 1984 to the fall of 2001 using the combined keywords 'caregiver and Alzheimer' and 'caregiver and dementia'.
Results: The search identified 42 articles of interest. Although many did not specifically have an economic theme, a thorough review allowed for the elucidation of points of interest for economists.
Conclusions: Caregivers are responsible for the day-to-day care of AD patients, and it is in this area where most resource consumption is incurred. Also, when the burden of caring becomes too great, many caregivers will consider institutionalizing the patient; it is primarily caregivers who bear these costs. Therefore, to obtain a more accurate estimate of the resource use and costs associated with AD medications, economists should consider the impact of these drugs on caregivers (e.g., does drug treatment lessen the amount of time a caregiver must devote to a patient, does drug treatment delay institutionalization). Economists should adopt a societal perspective, rather than a health care system perspective, when evaluating AD drugs.

AN ASSESSMENT OF NON-RESPONSE BIAS IN A PHYSICIAN SURVEY OF DRUG TREATMENTS FOR ALZHEIMER'S DISEASE

Mark Oremus
Centre for Clinical Epidemiology and Community Studies, S.M.B.D. Jewish General Hospital and Department of Epidemiology and Biostatistics, McGill University, Montreal, Quebec

Introduction: Survey non-response bias--systematic differences between respondents and non-respondents--was examined in a study of physician attitudes and perceptions about drug treatments for Alzheimer's disease.
Methods: A postal questionnaire was sent to 803 Quebec physicians; non-response bias was assessed by comparing: (1) respondent/non-respondent demographics (sex, speciality, urban/rural, language); (2) early/late respondent questionnaire responses; and (3) questionnaire responses between respondents and a random sample of telephoned non-respondents.
Results: The overall response rate was 34% (226/658), excluding physicians who said they did not treat Alzheimer's disease (n=137) and invalid mailing addresses (n=8). For respondent/non-respondent comparisons, sex ($p=0.01$) and specialty ($p< 0.001$) were statistically significantly different. For early versus late respondents, only two of over 40 response variables were statistically significantly different ($p<0.04$). For non-respondents reachable by telephone (5 out of a sample of 100), only two of the response variables were statistically significantly different in comparison with respondents ($p<0.02$).
Conclusions: The impact of non-response bias appears minimal. However, contacting non-respondents by phone was difficult, and 144 physicians returned a blank questionnaire to expressly decline participation, meaning they could not later be contacted by telephone. The possibility of systematic bias cannot therefore be completely ruled out.

PHYSICIAN EFFICACY REQUIREMENTS FOR PRESCRIBING DRUG TREATMENTS FOR ALZHEIMER'S DISEASE

Mark Oremus
Centre for Clinical Epidemiology and Community Studies, S.M.B.D. Jewish General Hospital and Department of Epidemiology and Biostatistics, McGill University, Montreal, Quebec

Introduction: Ongoing research is aimed at developing new medications that improve upon the success of cholinesterase inhibitors (ChEIs) in the treatment of Alzheimer's disease (AD). Physicians were given two hypothetical scenarios and asked to specify their minimum efficacy requirements for prescribing newer AD medications.

Methods: A postal questionnaire was sent to 803 Quebec physicians: all geriatricians (n=51), all neurologists (n=223), all psychogeriatricians (n=54), and a random sample (n=475) of general practitioners. The two scenarios were: (1) a new AD drug having lasting positive effects on cognitive status, behaviour and mood (BM), and the ability to perform basic activities of daily living (bADL); (2) the drug does not halt or reverse disease progression, but stabilizes patients for longer than ChEIs.

Results: The response rate was 35.4% (233/658), excluding physicians who did not treat AD (n=137) and invalid mailing addresses (n=8). For scenario 1, 61.8% of respondents specified a requirement of stabilization of cognitive status, rather than a reversal of decline; 75.5% required that BM problems be either somewhat reduced (≤25% reduction in incidence) or substantially reduced (>25% reduction); 88.9% required either a permanent halt to further loss of ability to perform bADL or a resumption of 1-2 bADL. For scenario 2, the required increase in length of stabilization for mild AD patients was reported to be between 1-6 months for 22.7% of respondents, 7-12 for 44.2%, 13-24 for 28.2%, and 25-60 for 4.9%; for moderate AD patients, 1-6 months for 38.4%, 7-12 for 48.7%, 12-24 for 10.7%, and 36 for 2.2%.

Conclusions: Blocking further cognitive deterioration, and improvements to BM and the ability to perform bADL, were reported by physicians as important requirements for 'disease-reversing' AD medications. For medications that lengthen stabilization, respondents expressed more stringent requirements for mild AD. These data provide benchmark efficacy requirements for drug development and assessment.

DETECTION AND MANAGEMENT OF DEPRESSION AMONG SENIORS: A MULTIDISCIPLINARY RESEARCH TEAM PROJECT

Jane McCusker, MD, DrPH, Team leader and Epidemiologist, SMHC and McGill University.
Martin G. Cole, MD, FRCP(C), Psychiatrist , SMHC and McGill University.
Nandini Dendukuri, PhD, Biostatistician, SMHC and McGill University.
Michel Élie, MD, Psychiatrist, SMHC and McGill University.
Dina Giannopoulos, PhD, Psychologist, Concordia University.
Johanne Laplante, Rn, BSc, MSc(a), Clinical nurse specialist, SMHC.
Jacqueline Oxman-Martinez, PhD, Sociologist, School for Social Work, McGill University.
Louise Poulin de Courval, MD, Family physician, CLSC Côte-des-Neiges and McGill University.
François Primeau, MD, BPh, FRCP(C), Psychiatrist, SMHC and McGill University.
Mark Yaffe, MD, CM, Family physician, SMHC and McGill University.
Maida Sewitch, PhD, Research Associate
Tong-tong Wang, MSc, Research Assistant

Depression is a frequent and serious problem among seniors. In order to plan services for an increasingly diverse population of depressed seniors, we need better methods of detecting and understanding depression in different ethnocultural groups and better, culturally sensitive, models of care for use in primary care settings. The goals of this team are:

1. to study different sub-groups of seniors (ethnocultural, medically ill, cognitively impaired) according to factors that affect recognition and detection of depression, need for and access to care, (symptoms, distress, and functional status)
2. to investigate the effects of care delivery systems for depressed seniors on the process and outcomes of care;
3. to investigate the effects of depression in seniors on the burden of care and health of their informal caregivers.

The research is organized around 3 themes, 1) the population at risk, 2) care delivery sytems, and 3) caregiver outcomes. There are currently 7 specific research projects.

Ethnic and cultural risk factors for depression
Depression in patients with dementia
Estimation of disease prevalence from multiple non-gold standard tests
Enhancing the effectiveness of outpatient consultation
Shared care model for demented patients with depression
Quality of life of family caregivers of depressed seniors
Understanding and treating caregivers of depressed seniors

G-AGE: A MULTIDISCIPLINARY RESEARCH TEAM TO IMPROVE EMERGENCY DEPARTMENT (ED) CARE OF SENIORS

J.McCusker MD, DrPH (coordinator, epidemiologist), SMHC and McGill University
S. Cardin, PhD (epidemiologist), Universite de Montreal
N. Dendukuri, PhD (biostatistician), SMHC and McGill University
J. Verdon, MD, MSc (geriatrician), Cite de al Sante, Laval
N. Guimond, RN, MA (nurse), CHUM
K Berg, PhD (physiotherapist), McGill University

Objectives: Our group is one of four axes of the GIRU (Groupe Interuniversitaire de Recherche sur les Urgences). The objectives of the GIRU are to (1) develop knowledge regarding organization of health services and its effects on utilisation of hospital resources (hospitalizations and emergency care), health care trajectories of clientele of emergency departments (EDs), and also informational tools; (2) contribute to the development of research capacity (notably by establishing partnerships, developing joint projects or programs with other research groups); (3) promote transfer of knowledge (notably by establishing linkages with decision-makers, production and synthesis of knowledge).

The objectives of the G-AGE (GIRU – axe personnes âgées) group are:

1. To describe the patterns and determinants of ED utilization and trajectories of care among seniors.
2. To determine the effects of different care delivery models (including community-based case-management and other integrated approaches, and ED-based case-finding and liaison models) upon ED utilization, care trajectories, costs of care, and outcomes.
3. To determine the reliability and validity of different sources of information on ED utilization among seniors.

Methods: We have begun work on 7 projects relating to our 3 themes:

A. ED utilization: patterns and trajectories
   - Systematic review of the literature on determinants of ED utilization among seniors
   - Trajectories of care: longitudinal patterns of service utilization involving the ED

B. Care delivery systems
   - ED care of seniors: effects on early return visits
   - 2-step intervention for seniors: further development
   - Adaptation of tools for 2-step intervention for use with Minimum Data Set (MDS)

C. Information tools
   - Reliability and validity of information sources on ED utilization
   - Further validation of ISAR screening tool

ANTHROPOMETRIC CHARACTERISTICS OF HOSPITALISED FEMALE ELDERLY

S. Belbraouet[1,2,3], A. Tebi[1,2], N. Chau[2], K. Gray-Donald[4], and G. Debry[1]
[1]Centre de Nutrition Humaine, 40, rue Lionnois, 54000 Nancy, France
[2]INSERM, Unit 420, Faculté de Médecine, BP 184, 54505, Nancy, France
[3]ESANEF, Université de Moncton, Canada
[4]McGill University, Canada

This study assessed the anthropometric status (weight, mid-arm circumference, triceps skinfold thickness, weight/height, body mass index, arm muscle circumference, arm muscle area) of 451 hospitalised female patients aged 70 or more, at their admission to hospital, in reference to 77 healthy women of the same age. The most frequent diseases were the circulatory diseases (40.8%), the mental disturbance (29.9%), the respiratory diseases (12.4%), the endocrine and metabolic diseases (11.5%), the osteomuscular diseases (8.4%), traumatisms (6.9%). The patients with various categories of diseases had values lower than the healthy people except for the subjects suffering from infectious or genitourinary diseases; the differences being significant for mid-arm circumference, triceps skinfold thickness, weight, weight/height, and body mass index. The patients with cancer, blood disease, mental disturbance, respiratory disease, digestive disease, or traumatism had the lowest values. All the indices similarly negatively correlated with age (correlation coefficient of about -0.20). The frequency of the patients with decreased values (below 5th percentile values in the healthy people) equalled 35.1% for triceps skinfold thickness, 33.7% for mid-arm circumference, about 28% for weight and body mass index, 23.8% for weight/height, and 17.5% for arm muscle area. It increased with age. The frequencies of decreased values did not significantly differ between the patients with various categories of diseases except for those with respiratory diseases who had a higher frequency for triceps skinfold thickness. It is useful to evaluate regularly their nutritional status with the indices studied especially as they are easy to use, and to try to ensure them a good nutrition.
Key words: Anthropometric indices. Malnutrition. Diseased elderly women.

EFFECTS OF CYCLODEXTRINE ON T CELL RAFTS COMPOSITION WITH AGING

A.Larbi, G. Dupuis∗, N. Douziech, A. Khalil, T. Fulop Jr.
Institut Universitaire de Gériatrie de Sherbrooke, Center on Aging Research, ∗ Department of biochemistry, Faculty of medicine, Université de Sherbrooke, Qc, J1H 4C4 Canada

The immune response is altered with aging, mainly that of T cells. One of the reasons is the alteration of the early stage of the signal transduction mediated by the TcR/CD3 complex. We have shown that with aging we assist to an alteration of the composition of lipid rafts. There is a significant increase in the cholesterol content in rafts of T cells of elderly. This is accompanied by the decrease of tyrosine phosphorylation of key signalling molecules such as LAT, Lck. The aim of this work was to study wether the application of Methyl-β-cyclodextrine (MBCD) could modulate the cholesterol content of T cells of elderly as well as their function. We pre-treated the separated T cells, obtained from young and elderly healthy subjects, with MBCD for 30 or 60 min. We studied the T cells function after TCR stimulation. We also separated their lipid rafts. We measured in these lipid rafts their composition in lipid and in signalling proteins. Our results show that we are able to restore by the extraction of the cholesterol the function of T cells, but never the same extent than in T cells of young. This increase in function was correlated to the decrease in cholesterol content in lipid rafts. Moreover, the phosphorylation of LAT and Lck increased also. The coalescence of lipid rafts measured by confocal microscopy increased also. These results indicate that there is a possibility by the decrease in the cholesterol content of lipid rafts to increase T cell functions., however this does not seem to be the only mechanism involved.

DIÈTE ET STRESS OXYDATIF CHEZ LE SUJET ÂGÉ ATTEINT DE DIABÈTE DE TYPE 2

MN Caron, T Fülöp, D Tessier, A Carpentier, A Khalil
Centre de recherche sur le vieillissement, Institut Universitaire de Gériatrie de Sherbrooke

Problématique : Le diabète est une maladie caractérisée par une plus grande prédisposition à l'athérosclérose et ses complications. Le stress oxydatif (SO), augmenté chez les diabétiques, serait un facteur d'athérogenèse. Un des déterminants du stress oxydatif est la composition de la diète en lipides et en antioxydants. C'est pourquoi nous nous intéressons aux effets de la diète sur les marqueurs du stress oxydatif chez les sujets diabétiques. Méthodologie : Étude transversale comparant 15 sujets avec DM âgés de 65 ans et plus et 15 sujets âgés sans DM comparables. Échantillon de convenance. Évaluation nutritionnelle par journal alimentaire de 3 jours. Évaluation des apports en acides gras et en antioxydants à l'aide du logiciel CANDAT. Échantillons sanguins recueillis pour analyses biochimiques des marqueurs du SO : hydroperoxydes lipidiques, diènes conjugués, acide ascorbique et alpha-tocophérol. Résultats : Diète comparable entre les groupes. Différences au niveau des taux d'alpha-tocophérol plasmatique, qui sont plus faibles chez les diabétiques. Des apports plus élevés en acides gras saturés et en glucides semblent entraîner une déplétion de l'alpha-tocophérol et de l'acide ascorbique. Les concentrations d'acide ascorbique diminuent dans un milieu favorable à la glycation. Conclusion : Les différences en antioxydants rencontrées chez les sujets diabétiques sont plutôt la conséquence de la physiopathologie du diabète que de la composition de la diète. Néanmoins, certaines composantes nutritionnelles semblent avoir une influence sur certains antioxydants.

L'ALTERATION DE L'ACTIVITE PARAOXONASE DU PON1 EST UN INDICATEUR DE LA REDUCTION DANS LE POTENTIEL ANTIOXYDANT DES HDL

L Jaouad, A Khalil, C Milochevitch

Département de Physiologie et Biophysique, Faculté de médecine, Université de Sherbrooke

L'activité antioxydante des HDL est due en grande partie à l'activité peroxidasique de la paraoxonase 1 (PON1), une enzyme qui leur est associée.

L'activité paraoxonase du PON1 peut être altérée lors d'un stress oxydant, ce qui pourrait affecter les propriétés antiathérogène des HDL.

Objectif: étudier l'effet de l'oxydation des HDL sur l'activité paraoxonase du PON1 d'une part, et la corrélation entre l'activité enzymatique et les propriétés antioxydante des HDL d'autre part.

Méthodologie: 10 sujets âgés de 25 à 39 ans ont été recrutés pour cette étude.

L'activité du PON1 est évaluée par la vitesse d'hydrolyse du paraoxon. Pour initier l'oxydation des HDL trois systèmes d'oxydation ont été utilisés: 1) oxydation induite par les cellules THP1, 2) oxydation induite par les ions cu^{2+} et 3) oxydation induite par les radicaux libres oxygénés. $^{\cdot}OH$ et $O_2^{\cdot -}$ produits par la radiolyse gamma de l'eau. L'oxydation des HDL est suivie par la mesure de la formation des diènes conjugués et par la migration électrophorétique des lipoprotéines.

Résultats: Nos résultats montrent que l'oxydation des HDL induit une réduction de l'activité paraoxonase du PON1.cette diminution de l'activité paraoxonase est positivement corrélée avec le potentiel antioxydant des HDL.

Conclusion: La réduction dans l'activité du PON1 avec l'âge peut être un facteur non négligeable dans l'augmentation du risques d'incidences des maladies cardio-vasculaires chez les personnes âgées.

THE MCGILL UNIVERSITY/JEWISH GENERAL HOSPITAL MEMORY CLINIC: A NEW APPROACH TO THE MANAGEMENT OF PATIENTS WITH COGNITIVE DISORDERS

Touré Kamadore[1,3]; Bacher Yves[2]; Hosein Chris[2]; Chertkow Howard[2]; Windholz Sylvia[2]; Zunzunegui Maria Victoria [1]; Bergman Howard[2].
[1] GRIS/Department of Social and Preventive Medicine, Faculty of Medicine, University of Montreal, Canada.
[2] Memory Clinic, Division of Geriatric Medicine, McGill University, Jewish General Hospital, Montréal, CA
[3] University Cheikh Anta Diop of Dakar, Senegal

Objective: to compare the clientele of patients who have consulted at the McGill University/Memory Clinic of the Jewish General Hospital during the year 1992 and 2000.
Methodology: retrospectively, 100 patients from each year, 1992 and 2000, were selected using the systematic sampling method from the list of new patients. Sociodemographic, source of referral, past medical history, medication use, diagnosis features, diagnostic procedures, treatment and prognosis data were collected through patient records.
Results: there were no significant differences in the sociodemographic patterns of the patients with a mean age of 73.3 years (8.9) and 74.1 years (8.1) respectively in 1992 and 2000. The clientele was composed mostly of women, married subjects with at least completed primary education. There were statistically significant differences between the two years in the source of referral, the past medical history, the medication, the diagnosis, the diagnostic procedures, the treatment and prognosis of the clientele.
Conclusion: The McGill University/Memory Clinic of the Jewish General Hospital is a referral center for memory problems. Primary care physicians and neurologists increasingly use this clinic to obtain a diagnosis and to establish treatment for their patients. Research activities on MCI are facilitated by the operation of the memory clinics.
Keywords: memory clinic, dementia diagnosis, dementia treatment.

MÉDECINS DE PREMIÈRE LIGNE ET LES RÉSEAUX INTÉGRÉS POUR PERSONNES ÂGÉES AVEC DES INCAPACITÉS: VISION MÉDICALE COMPARATIVE ENTRE CLINICIENS SIPA, LEADERS DE GMF ET GESTIONNAIRES (PROTOCOLE DE L'ÉTUDE)

De Stampa M.,[1] Bergman H.,[1] Henrard J.C.[2]

[1]Division of Geriatric Medicine, McGill University, Montreal; [2]Université René Descartes, Paris V

La rationalisation des trajectoires d'aide et de soin autour de la personne âgée a permis la mise en place de nouveaux modèles d'organisation qui reposent sur l'intégration des services et où la coordination entre les partenaires est une des dimensions centrales du fonctionnement. Au regard de l'expérience SIPA (Système d'Intégration pour Personnes Agées), tout comme dans d'autres programmes similaires, les médecins de première ligne sont les professionnels de santé qui ont le moins bien participé alors qu'ils apparaissent comme des intervenants indispensables au fonctionnement des réseaux intégrés et qu'ils semblent favorables vis-à-vis de cette forme d'organisation.
Même si la littérature nous apporte un éclairage sur certaines caractéristiques des médecins liées a leur pratique, il existe peu de données sur leurs expériences dans des réseaux intégrés.
A partir d'une étude qualitative auprès de 25 médecins (participants et non participants dans SIPA, leaders des Groupes de Médecins de Famille et responsables d'organisation), notre étude a pour objectif de comparer leurs perceptions sur les obstacles et les incitatifs d'ordre professionnel, organisationnel, économique et politique liés à la participation dans les réseaux intégrés dans le contexte de la mise en place des GMF.
Le modèle d'analyse de Triandis (modèle du comportement interpersonnel) nous permettra de prendre en compte différents facteurs pour expliquer le passage de l'intention au comportement au niveau individuel.

UNDERTAKING A POPULATION-BASED PROSPECTIVE COHORT STUDY ON COMMUNITY DWELLING ELDERLY: FROM SUBJECT RECRUITMENT TO FOLLOW UP

Deborah Weiss, John E. Podoba, Josette Dupuis, Chritina Wolfson
Center for Clinical Epidemiology and Community Studies, Jewish General Hospital
Department of Epidemiology and Biostatistics, McGill University

Background: The study on unmet needs for community-based services for the elderly aged 75 years and over is a population-based prospective cohort study comprising a sample of 839 randomly selected residents of the island of Montreal and the South Shore.
Methodology: The recruitment process was conducted by Leger Marketing, a market research firm based in Montreal. Trained recruiters conducted brief telephone recruitment interviews to identify potential study subjects who met the study eligibility criteria. Of those seniors contacted by Leger Marketing, 1300 met the eligibility criteria of the study, and 946 agreed to participate. When contacted by study interviewers, 839 subjects were enrolled in the study. Each subject who consented to participate in the study underwent an extensive in-home baseline interview, a brief 6 month telephone interview, an extensive in-home 12 month interview and a telephone interview 18 months after baseline. To date, losses to follow-up rates for the 18 month interview are only 8%. This low rate of attrition was due in large part to the careful management of study subjects. This presentation will describe the process of subject recruitment, processes that were put in place to minimize losses to follow-up as well as processes to minimize data errors, including: the creation of a database to manage follow-up and maintaining regular contact with study subjects.

CANADIAN LONGITUDINAL STUDY ON AGING PROTOCOL DEVELOPMENT

Sathya Karunananthan for the CLSA investigators
Supervisor: Dr. Christina Wolfson
Department of Epidemiology & Biostatistics, McGill University

The Canadian Longitudinal Study on Aging (CLSA) will be one of the largest longitudinal studies of its kind undertaken to date. The CLSA will examine ways in which the social and physical environment, genetic, biological, clinical, lifestyle and behavioral factors, economic prosperity, and the health care system are interrelated and how they influence disease, health and well-being. The aims of the CLSA are to understand mechanisms underlying the process of aging, to understand the influences of various factors in relation to each other, and to distinguish aging from effects of disease processes, cohort effects, and secular changes among Canadian seniors. A cohort of more than 50,000 Canadians aged 45 and over will be recruited and followed as they as they enter the senior population.

The protocol development phase began in October 2002 and the final protocol will be submitted in the spring of 2004. 3 Principal Investigators supported by a team of more than 200 co-investigators and collaborators from across Canada are working to develop this innovative, transdisciplinary study. This presentation describes some of the strategies being used to meet the challenges of planning a study of this magnitude. The issues discussed include refining the objectives, selecting a sample size, sampling frame and sampling strategy; developing recruitment methods to maximize response rates; and designing feasible and economical methods of data collection to ensure proper coverage and to minimize attrition rates.