Howard Chertkow - selected publications

1 Chertkow, H., Feldman, H. H., Jacova, C., & Massoud, F. (2013). Definitions of dementia and predementia states in Alzheimer's disease and vascular cognitive impairment: consensus from the Canadian conference on diagnosis of dementia. *Alzheimers Research and Therapy, 5,* S2.
Notes: There have been several newly proposed sets of diagnostic criteria for Alzheimer's disease/mild cognitive impairment, advanced by the National Institute of Aging/Alzheimer's Association working groups in 2011 and by the International Working Group in 2007 and 2010. These sets each aim to provide broader disease stage coverage with incorporation of disease biomarkers into the diagnostic process. They have focused particular attention on the earlier identification of disease with focus on the preclinical and predementia stages. This paper reviews these diagnostic criteria and provides 2012 consensus recommendations from the Canadian Consensus Conference on the Diagnosis and Treatment of Dementia on their applications in both clinical and research settings

2 Nasreddine, Z. S., Phillips, N., & Chertkow, H. (2012). Normative data for the Montreal Cognitive Assessment (MoCA) in a population-based sample. *Neurology, 78,* 765-766

3 McKhann, G. M., Knopman, D. S., Chertkow, H., Hyman, B. T., Jack, C. R., Jr., Kawas, C. H. et al. (2011). The diagnosis of dementia due to Alzheimer's disease: recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. *Alzheimers and Dementia, 7,* 263-269.
Notes: The National Institute on Aging and the Alzheimer's Association charged a workgroup with the task of revising the 1984 criteria for Alzheimer's disease (AD) dementia. The workgroup sought to ensure that the revised criteria would be flexible enough to be used by both general healthcare providers without access to neuropsychological testing, advanced imaging, and cerebrospinal fluid measures, and specialized investigators involved in research or in clinical trial studies who would have these tools available. We present criteria for all-cause dementia and for AD dementia. We retained the general framework of probable AD dementia from the 1984 criteria. On the basis of the past 27 years of experience, we made several changes in the clinical criteria for the diagnosis. We also retained the term possible AD dementia, but redefined it in a manner more focused than before. Biomarker evidence was also integrated into the diagnostic formulations for probable and possible AD dementia for use in research settings. The core clinical criteria for AD dementia will continue to be the cornerstone of the diagnosis in clinical practice, but biomarker evidence is expected to enhance the pathophysiological specificity of the diagnosis of AD dementia. Much work lies ahead for validating the biomarker diagnosis of AD dementia

4 Chertkow, H., Massoud, F., Nasreddine, Z., Belleville, S., Joanette, Y., Bocti, C. et al. (2008). Diagnosis and treatment of dementia: 3. Mild cognitive impairment and cognitive impairment without dementia. *CMAJ, 178,* 1273-1285.
Notes: Bloomfield Centre for Research in Aging, Lady Davis Institute for Medical Research, Sir Mortimer B. Davis-Jewish General Hospital, McGill University, Montreal, Que. howard.chertkow@mcgill.ca
BACKGROUND: Mild cognitive impairment and cognitive impairment, no dementia, are emerging terms that encompass the clinical state between normal cognition and dementia in elderly people. Controversy surrounds their characterization, definition and application in clinical practice. In this article, we provide physicians with practical guidance on the definition, diagnosis and treatment of mild cognitive impairment and cognitive impairment, no dementia, based on recommendations from the Third Canadian Consensus Conference on the Diagnosis and Treatment of Dementia, held in March 2006. METHODS: We developed evidence-based guidelines using systematic literature searches, with specific criteria for study selection and quality assessment, and a clear and transparent decision-making process. We selected studies published from January 1996 to December 2005 that had mild cognitive impairment or cognitive impairment, no dementia, as the outcome. Subsequent to the

conference, we searched for additional articles published between January 2006 and January 2008. We graded the strength of evidence using the criteria of the Canadian Task Force on Preventive Health Care. RESULTS: We identified 2483 articles, of which 314 were considered to be relevant and of good or fair quality. From a synthesis of the evidence in these studies, we made 16 recommendations. In brief, family physicians should be aware that most types of dementia are preceded by a recognizable phase of mild cognitive decline. They should be familiar with the concepts of mild cognitive impairment and of cognitive impairment, no dementia. Patients with these conditions should be closely monitored because of their increased risk for dementia. Leisure activities, cognitive stimulation and physical activity could be promoted as part of a healthy lifestyle in elderly people and those with mild cognitive impairment. Vascular risk factors should be treated optimally. No other specific therapies can yet be recommended. INTERPRETATION: Physicians will increasingly see elderly patients with mild memory loss, and learning an approach to diagnosing states such as mild cognitive impairment is now warranted. Close monitoring for progression to dementia, promotion of a healthy lifestyle and treatment of vascular risk factors are recommended for the management of patients with mild cognitive impairment

5 Chertkow, H., Whatmough, C., Saumier, D., & Duong, A. (2008). Cognitive neuroscience studies of semantic memory in Alzheimer's disease. *Progress in Brain Research, 169,* 393-407.
Notes: Semantic memory is the component of long-term memory that stores our concepts about the world. The disruption of semantic memory as a result of brain damage may have profound negative consequences on an individual's ability to name objects and process concepts. This can be disrupted as a result of many forms of brain damage, particularly Alzheimer's disease (AD). The current paper reviews research demonstrating that semantics deteriorates early in AD, particularly on effortful semantic tasks. There is a "category effect", meaning that AD preferentially affects concepts dealing with living things and abstract concepts compared to non-living objects and verbs/actions. While this pattern of deterioration, specific for AD, may reflect a breakdown within a distributed semantic system (where living things are distinguished by a high rate of inter-correlations between concepts or by a particular mode of being learned), it is equally possible that there is a regional distribution of semantic knowledge, with living things preferentially involving left temporal regions which become damaged early on in AD. Evidence from patients with strokes and semantic dementia, as well as activation studies in normal individuals, implicates the left posterior temporal region in semantic processing for pictures, abstract words, and concrete words. AD individuals, who are impaired in a variety of semantic tasks, show functional deficits in this area, and fail to activate it normally

6 Chertkow, H. & Black, S. (2007). Imaging biomarkers and their role in dementia clinical trials. *Canadian Journal of Neurological Sciences, 34 Suppl 1,* S77-S83.
Notes: There are five potential major roles for neuroimaging with respect to dementia; (1) as a cognitive neuroscience research tool, (2) for prediction of which normal or slightly impaired individuals will develop dementia and over what time frame, (3) for early diagnosis of Alzheimer's disease (AD) in demented individuals, (sensitivity) and separation of AD from other forms of dementia (specificity), (4) for monitoring of disease progression, and (5) for monitoring response to therapies. Focusing on the last role, no single imaging approach is yet ideal, as all trade-off speed, cost, and accuracy. Functional imaging (SPECT and PET) is best suited to tracking symptomatic therapy response, and anatomic (MRI volumetric) imaging or amyloid PET are more suited to reflect dementia modulation studies. The potential for imaging with respect to pharmacological studies of dementia--to provide surrogate markers for drug studies, to improve diagnosis, to speed evaluation of outcomes, and to decrease sample sizes--is huge. At the present time, however, no single measure has sufficient proven reliability, replicability, or robustness, to replace clinical primary outcome measures

7 Chertkow, H., Nasreddine, Z., Joanette, Y., Drolet, V., Kirk, J., Massoud, F. et al. (2007). Mild cognitive impairment and cognitive impairment, no dementia: Part A, concept and diagnosis. *Alzheimers and Dementia, 3,* 266-282.
Notes: Mild cognitive impairment (MCI) and cognitive impairment, no dementia (CIND) are controversial emerging terms that encompass the clinical state between elderly normal cognition and dementia. This article reviews recent work on the classification of MCI and CIND, their prognosis, and diagnostic approaches and presents evidence-based recommendations approved at the meeting of the Third Canadian Consensus Conference on the Diagnosis and Treatment of Dementia (CCCDTD3) held in Montreal in March, 2006. New short tools such as the Montreal Cognitive Assessment are making it easier for family physicians to confidently attach the label of MCI

8 Gauthier, S., Reisberg, B., Zaudig, M., Petersen, R. C., Ritchie, K., Broich, K. et al. (2006). Mild cognitive impairment. *Lancet, 367,* 1262-1270.
Mild cognitive impairment is a syndrome defined as cognitive decline greater than expected for an individual's age and education level but that does not interfere notably with activities of daily life. Prevalence in population-based epidemiological studies ranges from 3% to 19% in adults older than 65 years. Some people with mild cognitive impairment seem to remain stable or return to normal over time, but more than half progress to dementia within 5 years. Mild cognitive impairment can thus be regarded as a risk state for dementia, and its identification could lead to secondary prevention by controlling risk factors such as systolic hypertension. The amnestic subtype of mild cognitive impairment has a high risk of progression to Alzheimer's disease, and it could constitute a prodromal stage of this disorder. Other definitions and subtypes of mild cognitive impairment need to be studied as potential prodromes of Alzheimer's disease and other types of dementia

9 Chertkow, H. (2006). Emerging pharmacological therapies for mild cognitive impairment. In H.A.Tuokko & D. F. Hultsch (Eds.), *Mild cognitive impairment: International perspectives* (pp. 217-243). New York: Taylor & Francis.

10 Saumier, D. & Chertkow, H. (2002). Semantic memory. *Curr.Neurol.Neurosci.Rep., 2,* 516-522.
Our concepts about objects, states, and events are stored in a cognitive structure termed semantic memory. There are several types of neurologic disorders that may cause impairments of semantic memory. Clinical evaluations of these impairments are complex, because semantic memory is linked to other cognitive systems that, when damaged, may produce related syndromes or difficulties. In an attempt to gain further understanding of these breakdown patterns, we review data from both neuropsychologic and brain activity research that have been concerned with how object concepts are represented and localized in the brain. Although these data have spawned varying and controversial views regarding the content and organization of semantic knowledge, converging evidence suggests that semantic memory is mainly localized in the posterior region of the left temporal lobe, and that particular categories of knowledge may be represented in different but overlapping regions within this area

11 Chertkow, H. & Bub, D. (1994). Functional activation and cognition: The ^{15}O PET subtraction method. In A.Kertesz (Ed.), *Localization and neuroimaging in neuropsychology* (pp. 151-184). San Diego: Academic Press.
Notes: (The authors explore the methodological pitfalls of the subtraction method, and other methodological limitations, before a review of PET results in sensory processing and visual cognition, attention, language, and frontal lobe processes)

12 Chertkow, H., Bub, D., & Caplan, D. (1992). Constraining theories of semantic memory processing: Evidence from dementia. *Cognitive Neuropsychology, 9,* 327-365.
Notes: In this paper we analyze the performance of ten patients with Dementia of the Alzheimer's Type (DAT) who show a pattern of performance suggesting a deficit at the level

of semantic memory in the face of normal visual perceptual processing. We use the results of their performance on probe questions for pictures and words to evaluate several hypotheses arising from recent theories concerning semantic memory. We assess whether these patients demonstrate better performance on pictures rather than words (they do), and whether this can be explained away as a by-product of the perceptual nature of the items tested; pictures whose items have many discernible object parts would tend to contact more residual information in semantic memory, thus producing apparent superior performance from pictures. In fact, we find no suppoprt for this explanation. Rather, we are able to demonstrate, in the semantic category of animals, that it is only the items that are correctly identified (as a whole) that will give rise to evidence of better performance on pictures. We then go on to demonstrate that, in contrast to theories suggesting the presence of multiple stores within semantic memory, error analysis of our patients suggests that associative conceptual knowledge is stored amodally - loss of such functional knowledge for pictures is usually accompanied by equal loss of the same information for words

13 Chertkow, H. & Bub, D. (1990). Semantic memory loss in dementia of Alzheimer's type. What do various measures measure? *Brain, 113,* 397-417.
Notes: This paper examines three methodological issues concerning the measurement of semantic memory impairment in brain-damaged patients. Ten carefully selected patients with dementia of Alzheimer's type (DAT) and anomia were studied. A battery of perceptual tests and direct tests of semantic memory led to the conclusion that these patients represented a homogeneous group having a prominent deterioration of their semantic memory store without visual perceptual deficits. The first issue addressed in this patient group was whether verbal fluency impairment accurately reflected the loss of semantic memory. It was found that verbal fluency (generation of semantic category lists) was impaired due to two major constraints: deterioration of semantic memory store, and variable difficulties in semantic search. Verbal fluency, therefore, reflects semantic memory loss to some degree, but is not a direct test of semantic memory store in DAT. The second issue was whether semantic memory impairment in our patients conformed to the 'semantic storage disorder' syndrome hypothesized by Shallice (1987). It was shown that, consistent with this hypothesis, the patients demonstrated co-occurrence of consistency of errors, loss of semantic cueing, and preserved superordinate knowledge with loss of detailed knowledge of concept items. The third issue was whether semantic cueing and semantic priming are altered in a similar manner in DAT. It demonstrated that semantic cueing and semantic priming, using the same words whose concepts were degraded in semantic memory, yielded an entirely different pattern of results. Cueing and priming therefore may not be used interchangeably in the study of semantic loss after brain damage

14 Bub, D. & Chertkow, H. (1988). Agraphia. In F.Boller & J. Grafman (Eds.), *Handbook of neuropsychology, Vol.1* (pp. 393-415). Amsterdam: Elsevier.