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Top Items

MGH Study Identifies Potential AD Risk Gene - Researchers from the MassGeneral Institute for Neurodegenerative Disorders (MIND) have identified a gene variant that may increase the risk of late-onset **AD**. They report that specific changes in **the gene for a protein called ubiquilin-1 are associated with an increased incidence of AD** in two large study samples. The discovery could lead to improved understanding of the disease mechanism and a new target for the development of preventive and treatment strategies. "We believe this variant moderately but significantly raises the risk of **AD**," says Lars Bertram, MD, of the Genetics and Aging Unit at MIND, lead author of the study. "**We now have to pinpoint the biological defects that accompany this finding, which also needs to be independently replicated in other AD sample groups**." Bertram is an assistant professor of Neurology at Harvard Medical School (HMS). The researchers studied brain tissue from **AD** patients and controls to see if the identified gene variants actually change the production of ubiquilin-1. In both groups, **the same gene variants that increased the risk of AD also led to increased production of a shorter form of ubiquilin-1**, an overproduction that was even more pronounced in the patients. "Now we **need to figure out what's wrong with too much ubiquilin-1 and with this different form**," says Tanzi. "We need to look at how this variant interacts with the presenilins and what effect that may have on the production of A-beta," the protein that accumulates in the amyloid plaques found in the brains of **AD** patients. Tanzi is a professor of Neurology at HMS. The MGH researchers estimate that the increased risk accompanying these ubiquilin-1 gene variants is less than half that conferred by ApoE4. They and other research groups **expect that 4 to 7 additional gene variants may be found that confer similar levels of risk**. *PR 3/2/05 New England Journal of Medicine 352(9):884-894 (March 3 2005*)

NICE Proposes to Withdraw AD Drugs from NHS - The **drugs donepezil (Aricept), rivastigmine (Excelon), galantamine (Reminyl), and memantine (Namenda) should no longer be prescribed on the UK National Health Service (NHS) to treat AD**, says new draft guidance from the National Institute for Clinical Excellence (NICE). NICE, the NHS prescribing watchdog for England and Wales, has retracted its previous guidance issued in 2001 and which said that these drugs should be prescribed for **AD** - after reviewing the latest evidence on efficacy and cost effectiveness. Patients currently receiving any of the drugs, however, can continue to do so. Memantine will be available only as part of a clinical trial with strict outcome criteria. Comments on the proposals are being accepted until 21 March, and final guidance is expected to come into force in July this year. **The NICE assessment group says** that, although donepezil, rivastigmine, and galantamine (collectively known as anticholinesterase inhibitors) have proved gains in cognitive and global scales compared with placebo in people with mild to moderate **AD**, **there is "limited and largely inconclusive" evidence on outcomes that are important to patients and carers, such as quality of life and time to admission to a nursing home**. *By Zosia Kmietowicz BMJ 2005;330:495(5 March)*

Drugs

Drug for Agitation Can Worsen Dementia - The antipsychotic drug Seroquel does not relieve agitation in elderly demented patients, and is actually associated with more rapid mental decline, investigators report. Antipsychotic drugs are often prescribed for agitated patients with dementia, Dr. Clive Ballard at King's College London and his associates note in the British Medical Journal. **Seroquel (technically known as quetiapine) is believed to cause fewer side effects than other antipsychotic**

agents. Also, some studies have also suggested that drugs called cholinesterase inhibitors may be an effective treatment for agitation. Ballard's group treated 80 nursing home residents who probably had **AD** and agitation with quetiapine or the cholinesterase inhibitor Exelon (rivastigmine) or an inactive placebo. The team found no differences in agitation scores at the beginning of the study or 26 weeks later in any of the groups. However, **compared with placebo, quetiapine was associated with a 15-point decline in cognitive function between the start of the study and 26 weeks later**. There was no significant difference between rivastigmine and placebo at either time point. **The findings "highlight concerns regarding the long-term use of antipsychotics in these patients," Ballard's group concludes, and says Seroquel should not be used**. *Reuters Health 2/18/05 British Medical Journal, Online doi:10.1136/bmj.38369.459988.8F (published 18 Feb 2005)*

Study Finds Seroquel Effective and Well Tolerated - AstraZeneca announced results from a study involving elderly patients with **AD** treated with the atypical antipsychotic **Seroquel (quetiapine)** 3/5/05 at the annual meeting of the American Association of Geriatric Psychiatry in San Diego, USA. The study found that Seroquel at 200 mg/day **was effective in reducing agitation in elderly patients with AD without leading to a decline in cognitive function**. Seroquel was also generally well tolerated with no incidence of cerebrovascular adverse events during treatment, which have been associated with the use of other atypical antipsychotics in this patient population. In the 30-day follow up, one cerebrovascular event was reported in the 100 mg/day group. **Seroquel has been licensed for the treatment of schizophrenia since 1997** and is available in 82 countries for the treatment of this condition. Seroquel is also licensed in 63 countries for the treatment of mania associated with bipolar disorder, including the US, Canada and several European countries. **Seroquel has not been approved for the treatment of agitation in AD patients**. *PR 3/5/05*

Statins Don't Protect Against Dementia: Study -**The use of cholesterol-lowering drugs belonging to the statin family, such as Lipitor or Pravacol, does not seem to have any effect on the risk of dementia or AD, according to findings from a new study**. This supports the results of another study, **but run counter other study findings that have linked statin use with a reduced risk of dementia**. The current study involved elderly residents living in Cache County, Utah, who were evaluated for statin use and dementia between 1995 and 1997 and then again between 1998 and 2000. Dr. John C. S. Breitner, from the VA Puget Sound Health Care System in Seattle, and colleagues report their findings in the Archives of General Psychiatry. Of the 4,895 subjects evaluated at the initial assessment, 355 had dementia, including 200 with **AD**. In this analysis, statin use was associated with a 56-percent reduction in risk of dementia. During 3-year follow-up, 185 of 3308 at-risk survivors were diagnosed with dementia, including 104 with **AD**. In this analysis, statin use at the start of the study or at follow-up had no effect on the risk of dementia or **AD**. **One explanation for the different findings could be that after dementia sets in, patients may simply be less likely to use statins, along with other drugs**. Studies with sufficient statistical power are needed to assess the effect of statin use on dementia risk, the authors note. "Until such research is able to demonstrate more promising results, however, we suggest that costly randomized trials of statins are premature." *Reuters Health 2/10/05 Archives of General Psychiatry, 2005; 62:217-224*

Marijuana Ingredient May Stall Decline From AD - New research shows that **a synthetic analogue of the active component of marijuana may reduce the inflammation and prevent the mental decline associated with AD**. "This research is not only a major step in our understanding [of] how the brain reacts to **AD**, but may also help open a route to novel anti-**AD** drugs," says Raphael Mechoulam, professor emeritus of medicinal chemistry at Hebrew University in Jerusalem and discoverer of marijuana's active component. To show **the preventive effects of cannabinoids on AD**, researchers at the Cajal Institute and Complutense University in Madrid, led by Maria de Ceballos, conducted studies using human brain tissue, as well as experiments with rats. "These **findings that cannabinoids work both to prevent inflammation and to protect the brain may set the stage for their use as a**

therapeutic approach for [**AD**]," de Ceballos says. The scientists will now focus their efforts on targeting one of the two main cannabinoid receptors that is not involved in producing the psychotropic effects, or high, from marijuana. *PR 2/17/05 The Journal of Neuroscience, Feb. 23, 2005, 25(8):1904-1913*

Advisory Panel Discussion Points to Aleve® - Bayer HealthCare's Consumer Care Division said 2/27/05 it was pleased that discussions by the U.S. Food and Drug Administration (FDA) Arthritis and Drug Safety and Risk Management Advisory Committees clarified conflicting reports about the safety of Aleve® that have confused and, in some instances, alarmed consumers and healthcare professionals. The discussion at the Meeting of the Advisory Committees **affirmed the safety of Aleve and distinguished the safety profile of naproxen, the active ingredient in Aleve, from selective COX-2 inhibitors and other non-selective nonsteroidal anti-inflammatory drugs (NSAIDs**), based on the weight of clinical data presented at the meeting. Some members of the panel even suggested that naproxen should be the standard by which future pain relievers should be measured for cardiovascular safety. The presentations and discussions before the Committees also **clarified that the widely publicized suspension of the AD Anti-Inflammatory Prevention Trial (ADAPT) on December 20, 2004 was precipitated not by Aleve safety concerns, but rather by administrative and practical issues**. Bayer presented data to the Committees that underscored the nearly 30-year safety profile of naproxen. Bayer's naproxen sodium formulation has been sold as an over-the-counter (OTC) product under the trade name Aleve since 1994. *Medical New Today 2/27/05*

Genes & Genetic Issues

AD-Risk Gene Makes Brain Work Harder - **Mental tasks take an extra effort for healthy non-demented older adults with a genetic variation called APOE-e4**, which has been linked to an increased risk of developing **AD**, research shows. On tests of learning and memory, brain scans show that **people with APOE-e4 apparently have to work harder to achieve scores comparable to those reached by people with the APOE-e3 variant**. "This study confirms alterations in brain activity during learning in healthy older people at genetic risk for **AD**," Dr. Mark W. Bondi from the VA San Diego Healthcare System told Reuters Health. Bondi and his colleagues had 20 non-demented adults (average age, 76) with normal learning and memory capabilities complete a picture-encoding task while undergoing magnetic resonance imaging. In multiple brain regions, the 10 people with the APOE-e4 gene displayed greater intensity and extent of brain activation while learning new pictures, compared with the 10 individuals with the APOE-e3 allele. The APOE-e4 group also displayed lower brain responses in another area during tasks of learning and memory, the researchers report in the journal Neurology. "**The implications of this finding**," Bondi told Reuters Health, "**include the possibility of providing new methods for identifying the earliest stages of AD**." Tests based these findings may "help us recognize brain changes early so that we can identify the people at highest risk for the disease, with the goal of providing them with treatment more quickly and efficiently," he added. *By Megan Rauscher Reuters Health 2/18/05 Neurology 2005;64:501-508*

UCF Stem Cell Research May Hold Promise for Treating AD - A compound similar to the components of DNA **may improve the chances that stem cells transplanted from a patient's bone marrow to the brain will take over the functions of damaged cells and help treat AD and other neurological illnesses**. A research team led by University of Central Florida professor Kiminobu Sugaya found that treating bone marrow cells in laboratory cultures with **bromodeoxyuridine**, a compound that becomes part of DNA, **made adult human stem cells more likely to develop as brain cells after they were implanted in adult rat brains**. Sugaya and his colleagues at UCF's Burnett College of Biomedical Sciences hope to eventually show that stem cells transplanted from a patient's blood or bone marrow will be an effective treatment for **AD** and other neurological diseases because they can replace cells that die from those ailments. The researchers are working with a $1.4 million grant from the National Institutes of Health. "**By using a patient's own stem cells instead of**

embryonic stem cells, we're able to avoid the ethical concerns many people have about stem cell research," Sugaya said. "We also don't have to worry about the immune system rejecting the new cells." *PR 2/10/05 Restorative Neurology and Neuroscience to be published*

Caregivers

New Patient Magazine from American Academy of Neurology to Launch in April - The American Academy of Neurology (AAN) is launching "Neurology Now" in April for patients and their caregivers. The premiere issue will be supported by a special promotional launch during the AAN's 57th Annual Meeting, held April 9 to 16 in Miami Beach. The magazine will be available to patients in the waiting rooms of neurologists across the United States and also by subscription for home delivery. Neurology Now will report on the latest advances in research and treatment in easy-to-read language. "Readers can expect a health magazine that has integrity, accuracy, and balance," said Robin L. Brey, MD, the editor-in-chief of the magazine. "Neurology Now will also foster greater energy for advocacy efforts on behalf of neurology patients." Each quarterly issue will highlight the latest advances in neurology research and treatment. Articles will provide tips for living and coping with disorders including **AD**, epilepsy, migraine, multiple sclerosis, neuropathy, Parkinson's disease, and stroke, among other conditions. For more information about Neurology Now, visit www.neurologynow.com . In addition to Neurology Now, the AAN offers a book series, Patient Pages in the journal Neurology, brochures, and www.thebrainmatters.org for patients and caregivers. *Medical New Today 3/2/05*

National Council of Certified Dementia Practitioners Stress the Need for AD and Dementia Training for All Healthcare Workers and Law Enforcement - The National Council of Certified Dementia Practitioners is stressing the need for **AD** and Dementia training for all health care professionals. It is imperative that long-term care facilities provide competent trainers in the area of Dementia. The National Council is holding a nationally recognized **AD** and Dementia Train the Trainer Seminar on May 14th, 2005. The seminar is recommended for Corporate Trainers, In-Service Directors, Geriatric Care Managers, Nurses, Administrators, Activity Professionals, Social Workers and Consultants. The **AD** and Dementia Trainer Seminar will provide the student with all the tools to implement a comprehensive training program, Power Point, Overheads, 5 Text Books, Video and Handouts. The course will include Overview (Diagnosis, Prognosis, Treatment) Communication, Feelings and Repetitive Behaviors, Wandering, Hoarding, Paranoia, Hallucinations, Sun downing, Intimacy, Sexuality, Aggressive Behaviors, Catastrophic Reactions, Personal Care (Swallowing, Eating, Bathing & Dressing), Activities, Environment, Staff and family relationships, Stress and the Caregiver, Multicultural Considerations, Pastoral Care and End of Life. **The NCCDP was formed to promote standards of excellence in dementia education to professionals and other caregivers who provide services to dementia clients. The goal of the council is to develop and encourage comprehensive standards of excellence in the profession and delivery of dementia care**. To qualify for Certified Dementia Practitioners, the applicant must have the following credentials: 1. Certified or licensed in a health care profession 2. 3 years experience in health care 3. Completed a minimum of 7 hours of a comprehensive **AD** and Dementia course. The NCCDP also provides training to law enforcement as they are generally the first to respond to emergencies. For information please contact National Council of Certified Dementia Practitioners at toll free 1-877-729-5191 or visit their website http://www.nccdp.org *PR 2/22/05*

New Trials for Counseling Caregivers and Patients with AD Begin - Three studies are underway at the NYU School of Medicine **to find out whether short-term counseling can ease the psychological stress and depression of people with AD and their family members**. These studies were inspired by the success of a previous trial at the NYU School of Medicine that showed that even a short period of counseling can have a long-term beneficial impact on the emotional well-being of people taking care of spouses with **AD**. *Medical New Today 3/5/05*

Prevention

Heavy Bodyweight Raises Dementia Risk in Men - A link between body mass index (BMI) -- a measure of weight in relation to height -- and a hospital or death certificate diagnosis of dementia has been identified in a Swedish study. Drawing on data collected in the Primary Prevention Study that began in Goteburg in 1970, researchers analyzed 7402 men who were between 47 and 55 years old between 1970 and 1973. None of the men had a history of stroke or heart attack at the start of the study. Dr. Annika Rosengren of Sahlgrenska University Hospital in Goteburg and a multicenter team classified the subjects into four groups: 22 men diagnosed with **AD**; 78 men with a secondary diagnosis of dementia; 154 diagnosed with dementia as a primary diagnosis or cause of death; and 7148 men who had never been diagnosed with dementia. According to the **team's report they found that the likelihood of dementia rose linearly as body mass index increased**. That is, after factoring in smoking, blood pressure, cholesterol, diabetes, and social strata, men with a **BMI of about 20 at the start of the study had the lowest risk of developing dementia, and the risk rose steadily up to 2.5-times greater for men with a BMI of 30 or higher**. "Overweight and obesity," Rosengren's group says, "could be major preventable factors in the development of dementia." *Reuters Health 2/18/05 Archives of Internal Medicine 2005; 165:321-326 To determine your BMI see the calculator at http://www.nhlbisupport.com/bmi/bmicalc.htm*

Healthy Lifestyle Could Reduce AD Risk - A recent Finnish study showed that middle-aged people taking **regular exercise at least twice a week could reduce their risk of developing AD by 50 percent in old age**, neurologist Miia Kivipelto said 3/3/05 at a conference in Amsterdam. "An active lifestyle, both physical, mental and social, is preventive. It's never too early to start to prevent **AD**," said Kivipelto, an **AD** specialist at Stockholm's Gerontology Research Center. Studies have shown that **people with high blood pressure, high cholesterol and obesity could be running a greater risk of developing AD** and dementia than those with a more active, healthy lifestyle, she said. People could reduce the risk of developing the disease by going to their doctor for regular check-ups to monitor their blood pressure, cholesterol and weight, she said on the sidelines of a conference on old age organized by Britain's Royal College of Psychiatrists. Other recent **studies show that elderly people who take regular walks are less likely to suffer from dementia**. Mental activities such as reading and doing crossword puzzles also help to slow mental decline. *Reuters 3/3/05*

Scientific Experts Meet to Discuss Safety and Benefits of Vitamin E - Scientific experts in pharmacology, toxicology and nutrition gathered at the University of Southern California (USC) on 2/26/05 for a forum to discuss the benefits and safety of vitamin E. **The group concluded that due to promising results from existing clinical studies, antioxidant supplements are safe and appear to confer a health benefit in certain individuals**. Future research in well-defined populations with both clinical and biomarker end-points needs to be undertaken. **Vitamin E, a fat-soluble vitamin, acts as an antioxidant to protect cells in the body against the effects of free radicals**, which are potentially damaging by-products of cell metabolism. Common food sources of vitamin E include vegetable oils, nuts, green leafy vegetables, and fortified cereals. Numerous scientific studies suggest vitamin E supplements offer a variety of health benefits including helping to reduce the risk of heart disease, cancer and **AD**. In November 2004, another John Hopkins meta-analysis found that older patients (47-84 years of age) with existing conditions such as heart disease, Parkinson's disease and kidney disease, who took more than 400 IUs of vitamin E or more per day, had an increased risk of all-cause mortality. But the study noted, "overall, vitamin E supplementation did not affect all-cause mortality." **The study also concluded, "... high dosage vitamin E trials were often performed in patients with various chronic diseases, and we could not evaluate the generalizability of our findings to healthy adult populations**." Referencing the body of clinical research on vitamin E safety, **scientists participating in the USC Vitamin E Forum agreed it would be premature to apply this study's isolated findings to the general population**. The group urged the scientific community to conduct long-term, large-scale trials on vitamin E supplementation in well-defined populations because they appear to be beneficial to

the health of certain individuals. *MedicalNew Today 3/3/05*

Other Items

UCI Researchers Identify Trigger for Onset of AD, Aiding Search for New Therapies - Researchers at UC Irvine have identified a trigger at the molecular level that marks the onset of memory decline in mice genetically engineered to develop brain lesions – in the form of plaques and tangles – associated with **AD**. **The trigger is a protein called "beta amyloid" that accumulates within neurons in the mice's brains**. Although several researchers have studied the association between beta amyloid and memory, the UCI research team is the **first to identify that early beta amyloid accumulation within neurons is the trigger for the onset of memory decline in AD**. "This finding has important and useful implications for the pharmaceutical industry in terms of developing drugs that can target beta amyloid as soon as it accumulates within the neurons," said Frank LaFerla, principal investigator of the research project, associate professor of neurobiology and behavior, and co-director of the UCI Institute for Brain Aging and Dementia. "Once the plaques and tangles form, it is too late." Lauren M. Billings, a postdoctoral researcher working with LaFerla, explained the genetically engineered mice were making more beta amyloid than their brains could clear naturally. When the researchers cleared away the beta amyloid within the neurons, however, they were able to correct the memory impairments in the mice. Moreover, the researchers found that a reemergence of beta amyloid inside the neurons in the mice marked again the onset of memory problems. Billings said the study "suggests strongly that these hallmarks of **AD** [plaques and tangles] contribute to cognitive decline only later and that the **intraneuronal beta amyloid is the molecular trigger for the onset** of this insidious disease." *PR 3/2/05 Neuron 45;675-688 3 March 2005*

Neuronal 'Traffic Jam' Marks Early AD - Early **AD** may be precipitated by a "traffic jam" within neurons that causes swelling and prevents proper transport of proteins and structures in the cells, according to new studies by a research team led by Lawrence S. B. Goldstein, a Howard Hughes Medical Institute investigator at the University of California, San Diego (UCSD). In mouse models of **AD** and in human brain samples from people with the disease, **researchers observed a characteristic breakdown in neurons that appears to prevent the normal movement of critical proteins to the communications centers of the nerve cells**. In a vicious cycle, the traffic jam also could increase production of an abnormal protein that clogs neurons, leading to their failure and eventual death. The researchers said their findings could provide information that might be used to develop drugs to preserve the molecular transport system and thus the viability of brain cells otherwise lost in **AD**. The findings also could ultimately lead to distinctive markers of early **AD** that could be used in early diagnostic tests for the disorder, they said. "So, our hypothesis is that in familial **AD** - or in disorders such as Down syndrome where beta-APP is overexpressed - those defects cause early failure in cellular transport," Goldstein said. "**And those failures then stimulate further production of A-beta peptide, which may further poison the machinery**." Goldstein theorized that **AD might develop spontaneously** in people without an overt genetic defect, **as the transport machinery in their neurons breaks down with age**. "A person could have a predisposition to the disease, or it could just be that as time progresses, one person could by chance accumulate these blockages more than another," said Goldstein. "And randomly, some people would accumulate more than others, enough to cross a critical threshold and tip the scale toward disease." Goldstein emphasized that any application of these findings to potential diagnostic tests or new therapies remains speculative at this time. "However, **if tracers could be developed that would reflect transport function, there could be imaging methods that might be helpful for diagnosis**," he said. "And, if these findings continue to hold for humans, the transport machinery could be a target for drugs to preserve that machinery." *Science Daily 3/3/05 Science 25 Feb. 2005: 1282-1288*

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