

Research Highlights:

Discoveries underscore the predictive value of biomarkers and the potential influence of modifiable risk factors

Each year, researchers around the globe explore a diversity of topics in Alzheimer science. These topics are impressive in their breadth and depth. In 2009 topics ranged from the role of heat-shock proteins in the development of the tau tangles that characterize Alzheimer's disease to the influence of emotional closeness between an individual with Alzheimer's and his or her caregiver on the individual's rate of cognitive and functional decline.

But perhaps most visible in 2009 were discoveries supporting the potential role of biomarkers in early detection and diagnosis of Alzheimer's disease and the influence of lifestyle factors such as exercise and diet in modifying one's risk of developing Alzheimer's.

A biomarker is a substance or characteristic that can be objectively measured and evaluated as an indicator of normal body processes, disease processes or the body's response(s) to therapy. For example, blood pressure is a biomarker that indicates risk of cardiovascular disease.

During the Alzheimer's Association International Conference on Alzheimer's Disease (AAICAD) 2009, Ronald Petersen, Ph.D., M.D., chair of the Association's Medical and Scientific Advisory Council, provided the context for why Alzheimer biomarkers are needed. "With the continued aging of the population and the growing epidemic of Alzheimer's, early detection of the disease is crucial for risk assessment, testing new therapies and eventual early intervention with better drugs, once they are developed," he said.

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“It is widely believed that Alzheimer’s disease brain changes, including amyloid plaques and neurofibrillary tangles, begin many years before we see symptoms. It is critical to identify affected individuals while they are still relatively cognitively healthy so that future therapies can preserve healthy memory and thinking function. And, in order to develop those new therapies, we need to identify ‘at risk’ individuals now to steer them to clinical trials,” Dr. Petersen added.

Discoveries about biomarkers were matched by a wealth of findings suggesting that diet, exercise and other lifestyle choices can impact one’s risk of Alzheimer’s. Age and family history are known to be the top risk factors for Alzheimer’s disease.

“We can’t do anything about aging or family history, but research continues to show us that there are lifestyle decisions we all can make to keep

our brains healthier and that also may lower our risk of memory decline as we age,” said William Thies, Ph.D., Chief Medical and Scientific Officer at the Alzheimer’s Association, at AAICAD.



Biomarkers

Alzheimer’s disease biomarkers were one of the highest profile areas of research discovery in 2009. The Alzheimer science community believes that disease-modifying drugs will likely be most effective when given in the very early stages of the disease and that biomarkers will play an important role in determining which individuals should receive these drugs.

Biomarkers identified through imaging techniques and analysis of cerebrospinal fluid (CSF) gained particular attention in 2009, but were joined by coverage of other biomarkers as well.

To facilitate the identification of Alzheimer biomarkers, UC-San Diego researchers developed a rapid, automated method for measuring the volume of very specific sub-regions of the brain. The method, used in combination with magnetic resonance imaging (MRI), showed that the volume of the entorhinal cortex was especially susceptible to change in the early stages of the disease and that it may be a better biomarker of Alzheimer’s than

overall brain atrophy. The study involved data from 600 individuals participating in the Alzheimer’s Disease Neuroimaging Initiative (ADNI).

ADNI volunteers have also been instrumental in understanding whether levels of beta-amyloid and tau in CSF are biomarkers of Alzheimer’s disease. University of Pennsylvania researchers tested CSF from 410 ADNI volunteers and found that those with MCI and Alzheimer’s had higher concentrations of tau and lower concentrations of beta-amyloid as the disease progressed. Levels of beta-amyloid in CSF were 96 percent accurate in detecting Alzheimer’s among those whose Alzheimer’s was

confirmed on autopsy. CSF levels accurately predicted conversion from MCI to Alzheimer's in 82 percent of cases.

European researchers studying CSF samples from 168 volunteers from seven countries found that those with low beta-amyloid and high tau levels in CSF had 27 times the risk of cognitive deterioration



as those without this CSF pattern. The pattern was present in all individuals with MCI who went on to develop Alzheimer's.

A study conducted in the United States and Europe backed up the potential effectiveness of CSF as a biomarker for Alzheimer's. The study involved 750 people with MCI, 529 with Alzheimer's, and 304 without these conditions. During follow-up, 271 individuals with MCI developed Alzheimer's and demonstrated an "Alzheimer's pattern" of CSF levels at baseline: low levels of beta-amyloid and high levels of phosphorylated tau and total tau.

At AAICAD, U.S. researchers presented data from a study of 85 ADNI participants with MCI that examined the potential role of a variety of biomarkers in predicting progression from MCI to Alzheimer's. Of all potential biomarkers tested, glucose metabolism in the brain as measured by positron emission tomography (PET) scans and performance on a memory recall test called the Auditory-Verbal Learning Test most accurately predicted progression from MCI to Alzheimer's. Individuals with low glucose metabolism in the brain and poor performance on the memory test had a 15-fold increased risk of developing Alzheimer's in two years.

Using data from the Nurses' Health Study, investigators at Brigham and Women's Hospital, Boston, examined whether the ratio of beta-amyloid 1-40 to beta-amyloid 1-42 in plasma influenced the risk of developing Alzheimer's. They determined the ratio in mid-life (mean age, 63) and 10 years later for the 481 study participants. A high ratio in mid-life was associated with worse late-life cognitive decline, and a greater increase in the ratio over time was associated with faster cognitive decline.

PET combined with the tracer element Pittsburgh Compound B (PIB) provided some of the earliest evidence of potential biomarkers for Alzheimer's, and the imaging method continues to be influential. In two studies from Washington University, St. Louis, researchers found that high levels of beta-amyloid in the brains of healthy individuals are associated with a greater risk for developing Alzheimer's, loss of brain volume and declines in cognitive function.

Non-Biomarker Techniques for Early Detection

Advances were also made in non-biomarker techniques for early detection of Alzheimer's and other dementias.

Researchers examining data from 3,375 people aged 65 and older in the Cardiovascular Health Study found that after six years 480 had developed dementia. When the study began, researchers gathered data on the participants. Based on these data and which individuals went on to develop

Investigators following 444 individuals for an average of six years found that those who developed Alzheimer's experienced a decline in visuospatial skill three years before diagnosis.

dementia, the researchers created a 15-point scale to determine risk of developing dementia. People who scored eight points or more on the scale were at high risk of developing dementia. In addition to known risk factors such as older age and having the APOE-e4 gene, individuals who were underweight, did not drink alcohol, had undergone coronary bypass surgery and were slow at physical tasks such as buttoning a shirt were more likely to develop dementia. The scale was 88 percent accurate in identifying those who developed dementia.

Scientists in Britain developed a cognitive test that accurately detected 93 percent of people with Alzheimer's in a study of 540 healthy individuals and 139 with Alzheimer's or MCI. The test measured performance on 10 tasks, including ability to copy a

sentence and perform calculations and tasks that tested verbal fluency and recall ability. Healthy individuals had an average score of 47 out of 50, while those with Alzheimer's had an average score of 33.

While memory loss is often one of the first symptoms of Alzheimer's, investigators following 444 individuals for an average of six years found that those who developed Alzheimer's experienced a decline in visuospatial skill three years before diagnosis. Overall cognitive ability declined two years before diagnosis. Verbal and working memory declined just one year before diagnosis, suggesting that visuospatial skills may be an earlier indicator of cognitive decline than memory loss.

Modifiable Risk Factors

In addition to making significant contributions to the body of knowledge regarding early detection, researchers in 2009 shared study results reinforcing the association between lifestyle factors and the risk of developing dementia.

While some Alzheimer risk factors, such as genetic make-up, cannot be changed, lifestyle factors can be modified, and these modifications could lead to more years of healthy brain function.

Physical Activity

In a high-profile study commissioned by the National Football League, University of Michigan scientists found that former football players had rates of dementia, Alzheimer's and other memory-related diseases that were up to 19 times higher than national norms. Scientists conducted telephone surveys of 1,063 retired players who had played for at least three seasons. Among players age 50 or older, 6.1 percent reporting receiving a dementia-related diagnosis, five times higher than the national average. Among players ages 30 through 49, 1.2 percent reported receiving such a diagnosis, 19 times the national average. These data contribute to research linking serious head injury with an increased risk of dementia.

While physical activity in general is known to benefit both the heart and the brain, little research

has focused on the association between brain health and muscle strength in particular. To shed light on this, researchers measured the arm, leg, and abdominal strength of 970 people ages 54 to 100. Those who ranked in the top 10 percent for muscle strength were 61 percent less likely to develop Alzheimer's than those who ranked in the lowest 10 percent. The mental abilities of stronger individuals also declined at a slower rate over time.

The *Journal of the American Medical Association* reported that exercise, combined with a healthy

Researchers found that residents who were very physically active had a 33 percent lower risk of developing Alzheimer's than sedentary residents.

diet, was especially effective in lowering one's risk of developing Alzheimer's. The report was based on a study of 1,880 elderly New York City residents followed for five years. Researchers found that residents who were very physically active (1.3 hours a week of vigorous activity such as jogging or 4 hours a week of light exercise such as walking) had a 33 percent lower risk of developing Alzheimer's than sedentary residents. Residents who most often adhered to a Mediterranean diet rich in fruits, vegetables, cereal and fish but low in meat and dairy foods had a 40 percent lower risk than individuals who less frequently followed such a diet. The overall risk of developing Alzheimer's was 9 percent for those who were very active and followed a healthy diet, compared with 21 percent for those who were least active and less diet-conscious.



Diet

Another type of healthy diet called DASH (Dietary Approaches to Stop Hypertension) is similar to the Mediterranean diet and was associated with better cognitive function in a study of more than 3,800 people age 65 or older. Over the 11 years of the study, study participants' diets were scored at four different times. Scores were based on their consumption of fruits, vegetables, whole grains, low-fat dairy foods and fish (all recommended), as well as sodium, sweets and non-fish meat (recommended in limited amounts). The higher the DASH diet score, the more closely participants adhered to the diet. Investigators found that the higher the DASH score, the higher the participants' scores for cognitive function at the start of the study and over time. Four of the food groups—vegetables, whole grains, low-fat dairy food, and nuts/legumes—were independently associated with higher scores on the Modified Mini-Mental State Examination.

Drinking any amount of alcohol, be it small or large, was associated with faster cognitive decline in people with MCI.

DHA, an omega-3 fatty acid found in fish and other foods, has been the subject of much research over the years for its potential effect on Alzheimer's. In two studies reported at AAICAD 2009, researchers said that DHA did not slow memory decline over 18 months in 402 people with mild to moderate Alzheimer's, but that among 485 people with mild memory complaints, those who took a DHA supplement performed better on a computer memory test

after six months than those receiving a placebo. However, more data are needed before taking a DHA supplement can be recommended.

Like DHA supplementation, alcohol consumption is a topic of wide interest in terms of its potential impact on Alzheimer's. In a six-year study of more than 3,000 people aged 75 and older, researchers found that drinking one or two alcoholic beverages daily was associated with a 37 percent lower risk of developing dementia, but that individuals consuming more than 14 alcoholic beverages per week were twice as likely to develop dementia. Drinking any amount of alcohol, be it small or large, was associated with faster cognitive decline in people with MCI.

Co-existing Health Conditions

Diet is often a contributor to health conditions that previous studies have shown increase the risk of developing Alzheimer's. Results of large-scale studies published in 2009 add to the growing evidence of diabetes, high cholesterol and high blood pressure as risk factors for Alzheimer's. For example, a study supported in part by a grant from the **Alzheimer's Association** found that among 13,000 twins, those who developed diabetes before age 65 had a 125 percent increased risk of Alzheimer's disease. Twin studies are valuable in that they enable researchers to eliminate genetic differences that might cause disease.

Data from nearly 20,000 participants in the Reasons for Geographic and Racial Differences in Stroke study served as the basis for an evaluation of the role of blood pressure on brain function. In these participants, all age 45 or older, the higher one's blood pressure, the greater one's chances of having

cognitive impairment. In fact, with each 10-point increase in diastolic blood pressure, the chance of cognitive impairment increased 7 percent. Diastolic blood pressure measures the force on arteries



when the heart is at rest. When diastolic blood pressure rises, it can cause thickening of the arterial walls in the brain, decreasing blood flow. Systolic blood pressure, the force on arteries when the heart contracts, wasn't associated with impaired brain function.

In a remarkably long four-decade study of nearly 10,000 individuals who were followed beginning in their 40s, researchers found that high cholesterol (240 mg/dL or higher) in midlife is correlated with a 66 percent increased risk of Alzheimer's disease

People with metabolic syndrome, a condition that is characterized by several heart disease risk factors including high blood pressure and low levels of good cholesterol, are at higher risk of developing Alzheimer's.

later in life. Borderline high cholesterol (200 to 239 mg/dL) was correlated with a 52 percent increased risk. The results are another reminder that midlife health can foreshadow health in one's later years and that taking action on modifiable risk factors such as high cholesterol may have significant rewards in decades to come.

Likewise, people with metabolic syndrome, a condition that is characterized by several heart disease risk factors including high blood pressure and low levels of good cholesterol, are at higher risk of developing Alzheimer's, according to researchers. In a four-year study of nearly 5,000 women with an average age of 66, 36 percent of women with metabolic syndrome developed cognitive impairment, compared with just 4 percent of women without metabolic syndrome.

Post-traumatic stress disorder (PTSD) is a health condition that has gained increased attention over the years, and researchers in 2009 showed that PTSD is associated with a higher risk of dementia. They studied more than 180,000 veterans aged 55 and older over seven years and found that the rate of new cases of dementia was 10.6 percent in those with PTSD compared with 6.6 percent in those without. Results were similar when those with histories of traumatic brain injury, substance abuse and depression were excluded. Researchers note that much more research is needed to understand the link between dementia and PTSD but that evidence such as this underscores the importance of physicians paying particular attention to early signs of dementia in patients with PTSD.

Other Risk Factors

Smoking is a known risk factor for Alzheimer's disease, but is second-hand smoke a risk factor too? To find out, investigators tested saliva samples from 4,800 nonsmokers age 50 and older for levels of cotinine, a product of nicotine that stays in the

saliva for about a day after exposure to smoke. Investigators found that people with the highest levels of cotinine had a 44 percent higher risk of cognitive impairment than people with the lowest scores and that impaired cognitive function increased with the amount of exposure to second-hand smoke. The findings underscore the importance of limiting one's exposure to smoke in maintaining brain health.

Numerous studies have suggested that completing more years of formal education produces a "cognitive reserve" that delays the onset of Alzheimer symptoms. But does this cognitive reserve affect the rate at which one's cognitive abilities decline once symptoms are present? Different studies have had varying answers to that question. Research conducted in 2009 involving 6,500 individuals age

72 and older suggests that it does not. Study participants' education levels ranged from eight or fewer years of schooling to 16 or more. Their memory and thinking skills were measured every

Researchers in 2009 showed that post-traumatic stress disorder is associated with a higher risk of dementia.

three years. While those with more years of education performed better on tests at the beginning of the study, once they started having memory problems their rate of cognitive decline was no slower than that of individuals with fewer years of education.

Genetic Risk Factors

Researchers believe that people develop Alzheimer's disease as the result of a combination of different factors, including genetic, lifestyle and environmental factors.

Mutations in three genes guarantee that individuals will develop Alzheimer's, but only a very small percentage of individuals with Alzheimer's (1–5 percent) carry these genes. The e4 form of the gene apolipoprotein E (APOE-e4) is carried by about 25 percent of individuals and increases the risk of developing Alzheimer's, but does not guarantee that individuals will develop the disease. Aware that genetics plays a role in Alzheimer's, researchers continue to study genetic variations and their association with Alzheimer's to better understand the disease and to identify factors that might aid in early detection.

Mayo Clinic researchers reported in the journal *Nature Genetics* the discovery of the first sex-specific gene that increases one's risk of Alzheimer's disease. Located on the X chromosome, PCDH11X

is a common gene that exerts its influence most strongly when a woman inherits it from both parents. Examining genetic data from 2,400 people with Alzheimer's and 3,800 without, they found that women with Alzheimer's disease were twice as likely to have two copies of the gene as women in the control group. Inheriting just one copy of the gene also increased one's risk, but to a smaller extent than having two. Researchers noted that the discovery does not necessarily mean women are at higher risk than men, as yet-undiscovered male-specific genetic risk factors may exist.

Pooling DNA data for 16,000 people across Europe and the United States, scientists identified three potential new genetic risk factors for late-onset Alzheimer's: variants of the genes PICALM, CLU and CR1. This was the largest genome-wide association

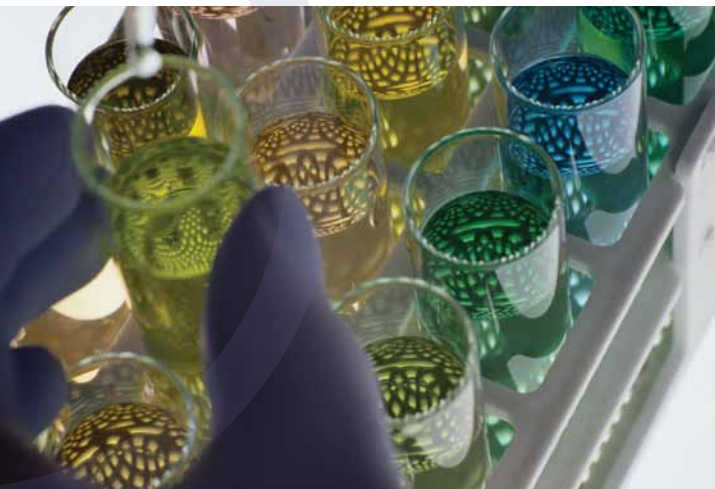
study reported to date for Alzheimer's. Genome-wide association studies aim to identify genetic associations with a disease by studying the DNA on all of the chromosomes in a specific population. PICALM is located on chromosome 11, CLU on chromosome 8 and CR1 on chromosome 1. These

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genes normally have helpful functions in the brain. CLU is thought to suppress the deposition of beta-amyloid, PICALM is believed to help keep synapses healthy, and CR1 may help remove beta-amyloid from the brain. However, the newly reported variants of these genes appear to have negative effects on the brain, with further research needed to understand how they might act to increase Alzheimer risk.

In a family carrying the mutant gene A673V, Italian researchers found that those carrying two copies of the gene were destined to develop Alzheimer's

while those with one copy or no copies of the gene did not develop the disease. The gene is the first recessive genetic trait found for Alzheimer's, meaning that two copies of the gene must be inherited for the disease to develop. Scientists studied cells from family members with zero, one or two copies of A673V, with fascinating results. While cells with two copies of the mutation produced more beta-amyloid, and the beta-amyloid was more likely to clump together, cells with one copy of A673V produced less beta-amyloid clumps than cells with no copies of A673V.



Drug Pipeline

Each year brings a remarkable growth in knowledge of Alzheimer's disease, and clinical trials of new drugs are essential to expanding that knowledge and identifying improved treatments.

Randy Nixon, Ph.D., professor of psychiatry and cell biology at New York University and vice chair of the Association's Medical and Scientific Advisory Council, remarked at AAICAD 2009, "There are currently dozens of drugs in Phase II and III clinical trials for Alzheimer's. This, combined with advancements in diagnostic tools, has the potential to change the landscape of Alzheimer's in our lifetime." Results of numerous Phase II and Phase III studies made headlines in 2009.

Docosahexaenoic acid (DHA), the most abundant omega-three fatty acid in the brain, has been of interest as a treatment for Alzheimer's for some time. Results of two studies presented at AAICAD 2009 showed that DHA did not slow cognitive decline in people with mild or moderate Alzheimer's but was associated with improved performance on a memory test in volunteers with mild memory complaints. "These two studies—and other recent Alzheimer's therapy trials—raise the possibility that treatments for Alzheimer's must be given very early in the disease for them to be truly effective," said William Thies, PhD., chief medical and scientific officer at the Alzheimer's Association.

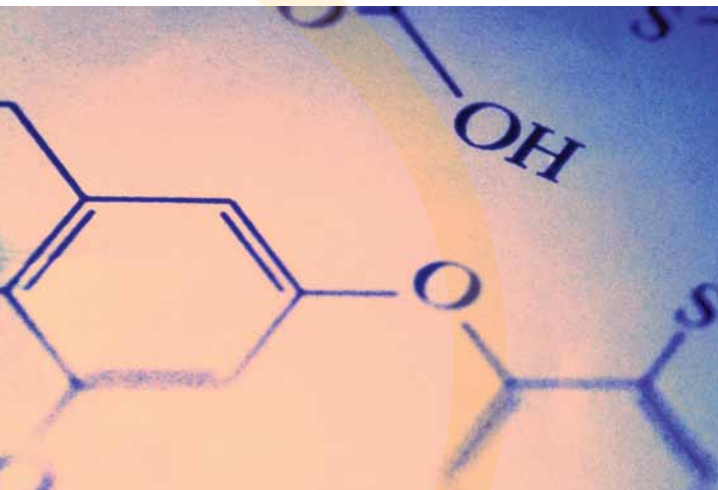
The larger of the two trials, funded by the National Institute on Aging, lasted 18 months and involved 402 people with Alzheimer's at 51 sites across the United States who received either a placebo or 2 grams of DHA daily. While DHA levels in the brain increased in the treatment group, it did not slow the rate of change on tests of mental function, dementia severity, activities of daily living or behavioral symptoms. Interestingly, it did slow the rate of decline on a mental function test in those with the APOE-e4 gene. "One of the issues raised by this study—and other recent Alzheimer's and mild cognitive impairment therapy trials—concerns a

possible interaction between certain therapies and genetic status. This issue needs to be explored more completely in future trials," Dr. Thies added.

The smaller of the two studies lasted six months and involved 485 older people who received either placebo or 900 milligrams of DHA daily. Volunteers' performance on a visuospatial memory test was measured at the beginning and end of the study. Those who received DHA made significantly fewer errors on the test at the end of the study than those who did not.

Beta-amyloid is a protein that is the main constituent of amyloid plaques found in the brains of people with Alzheimer's disease.

While Phase III clinical trials of dimebolin (Dimebon®) were under way in 2009, researchers shared results of a study aimed at shedding light on how the drug appeared to stabilize function in people with mild or moderate Alzheimer's who participated in earlier studies. Researchers conducted experiments in cells and in mouse models of Alzheimer's to assess the effects of dimebolin on beta-amyloid and other brain proteins known to be related to Alzheimer's disease. Beta-amyloid is a protein that is the main constituent of amyloid plaques found in the brains of people with Alzheimer's disease. It is widely considered a key player in the development and progression of Alzheimer's. The goal of anti-amyloid drugs in clinical trials is to reduce beta-amyloid levels in the brain. In a surprising result, researchers found that treatment with dimebolin caused an acute increase



in brain beta-amyloid levels in mice. “This result is highly unexpected in what may prove to be a clinically beneficial Alzheimer’s drug,” said one of the researchers. “We need more research to further clarify how dimebolin affects beta-amyloid levels in the brain.”

The makers of bapineuzumab, an Alzheimer vaccine designed to reduce levels of beta-amyloid in the brain, announced that the highest dose of the drug would be dropped from two Phase III clinical trials due to increased risk of vasogenic edema, a type of brain swelling caused by accumulation of water in brain tissue. The 0.5 mg/kg and 1.0 mg/kg doses in these two trials will continue as planned. The trials involve people with mild or moderate Alzheimer’s who do not have the APOE-e4 gene. The decision had no impact on two other ongoing studies testing a single 0.5 mg/kg dose of bapineuzumab in APOE-e4 carriers. The Phase III program for

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The two highest doses of ELND005, an Alzheimer drug from the makers of bapineuzumab, were dropped from a Phase II trial due to serious adverse events including an increased number of deaths in those receiving the highest doses. Nine deaths were reported in the groups receiving 1,000 mg or 2,000 mg twice daily. The Phase II trial enrolled approximately 353 patients with mild to moderate AD, who were divided into three treatment groups and one placebo group. ELND005 is designed to reduce deposits of beta-amyloid in the brain by preventing the formation of beta-amyloid oligomers, which recent research has shown may be the most toxic form of beta-amyloid.

Care for People with Dementia

Until new therapies to slow or stop the progression of Alzheimer’s disease are developed, more than 5 million Americans with Alzheimer’s will continue to require assistance from family or other caregivers to cope with the symptoms and declining function brought on by the disease.

The challenges experienced by people with the disease and their caregivers and physicians is an area of expanding investigation by the scientific community.

A study conducted in Australia involving 289 people with dementia aged 60 and older found that those whose care was person-centered and based on dementia-care mapping had less agitation when the study ended and four months after the study. Person-centered care makes the person with dementia a central part of care-planning and focuses on their individual needs. Dementia-care mapping is a tool to improve person-centered care that scores factors related to the individual’s well-being, such as enjoyment of eating, touching and interacting. While training in dementia-care mapping is expensive and labor-intensive, training in person-centered care is quickly taught and one-fourth the cost of dementia-care mapping. The authors suggest that patient-centered approaches to care be standard practice in residential care homes.

Death rates for individuals with Alzheimer’s who receive antipsychotic medication are significantly higher than for individuals who do not take this medication, reinforcing the guideline that the medication only be used as a last resort and for as short a period as possible. In a three-year study, 128 people with Alzheimer’s were assigned to either continue to receive one of several antipsychotic medications or to be switched to a placebo. At the end of the study, the risk of death was 42 percent lower among those on the placebo. After two years’ follow-up, 46 percent of those taking antipsychotics were alive, compared with 71 percent of those taking a placebo. After three years, 30 percent of

people receiving antipsychotics were alive, compared with 59 percent of those on placebo.

Half of family caregivers admitted to abusive behavior while caring for an individual with dementia, according to an article in the *British Medical Journal*. Of 220 caregivers surveyed, 52 percent reported occasionally screaming or yelling at the individual, 33 percent reported “significant” abuse such as frequently insulting or swearing at the individual, and 1 percent (3 caregivers) reported physically abusing a family member. As dementia progresses, individuals can become aggressive, and in some cases caregivers were reacting to being the subject of aggressive behavior. Some caregivers wished that physicians had asked them how they were coping with being a caregiver and said this might help prevent abusive behaviors.

Dementia-care mapping is a tool to improve person-centered care that scores factors related to the individual’s well-being, such as enjoyment of eating, touching and interacting.

While the study highlights the fact that it’s not paid caregivers alone who abuse vulnerable individuals, it also highlights the need for increased support services for caregivers.

Up to one-third of individuals with severe dementia receive nutrition via a feeding tube, yet a review of seven studies involving 409 such individuals found

that there was not significant evidence that feeding tube use increased survival or improved quality of life. Because individuals at this stage of dementia are unable to give informed consent, they often continue to receive tube feeding. The researchers highlighted the importance of individuals with dementia having advance directives to prevent what may be unwanted use of a feeding tube at this stage of their illness.

While cholinesterase inhibitors can temporarily help improve the memories of those with Alzheimer's disease, they do come with risks, one of them being an increased risk of fainting caused by slowed heart rates. Researchers used healthcare databases in Ontario, Canada, to identify nearly 20,000 people with dementia who were receiving cholinesterase inhibitors and 61,000 who were not and found that those taking the medications were almost twice as likely to be hospitalized for fainting. They were also 49 percent more likely to have a pacemaker implanted and 18 percent more likely to suffer hip fracture. The researchers said the study served as reminder that the benefits of cholinesterase inhibitors should be carefully weighed against their risks before being prescribed.



Individuals with Alzheimer's who are hospitalized may experience delirium as a result of a change in environment and daily routines, and according to scientists, the delirium may have unexpectedly serious consequences. The scientists studied 400 people with Alzheimer's over 15 years and found

that the rate of cognitive decline in those with an episode of delirium during hospitalization was three times that of those who had not experienced delirium. They noted that up to 40 percent of delirium episodes can be prevented by measures such as telling individuals that they are in the

Higher rates of emotional closeness were associated with significantly slower cognitive and functional decline.

hospital so they are better oriented to their surroundings, allowing as much uninterrupted sleep as possible and avoiding unnecessary medications.

To better understand the effect of emotional closeness between caregivers and individuals with Alzheimer's disease, researchers studied 167 people with Alzheimer's and their caregivers every six months for up to four years. Those with Alzheimer's underwent physical, cognitive and functional tests, while caregivers were interviewed and completed a survey in which they were asked to rate their degree of emotional closeness to the individual with Alzheimer's. Researchers found that higher rates of emotional closeness were associated with significantly slower cognitive and functional decline and that the effect was similar to that of some of the cholinesterase inhibitors used to treat Alzheimer symptoms. More research is needed to understand the "closeness effect," but one of the investigators said it was possible that feelings of closeness result in caregivers being more attentive to the individual's needs and more likely to encourage them to participate in cognitively and socially stimulating activities that promote cognitive and functional health.

Basic Science Discoveries

Basic science discoveries form the foundation of advances in medicine. Advances in Alzheimer’s disease are no exception. Our understanding of the roles of beta-amyloid, tau and the amyloid precursor protein (APP) in the development of Alzheimer’s has evolved from science discoveries made in the lab. Likewise, science discoveries made in the lab hold the key to developing new treatments for Alzheimer’s disease and other dementias.

The plaques that characterize Alzheimer’s begin as individual fragments of APP called beta-amyloid 1-42 that clump together and go on to impede the functioning of synapses in the brain. In 2009, U.S. researchers studying why some nerve cells self-destruct during normal embryonic development discovered that a second APP fragment, N-APP, was a key part of the programmed cell death that occurs. They believe that the mechanism that causes excess nerves to be destroyed as the brain and spinal cord develop, a process that is supposed to stop early in life, may be turned on in Alzheimer’s, killing healthy brain cells. The researchers were able to block nerve destruction in human embryonic cells. The next step is to find out if the process can be stopped in adult brain cells. If successful, the method used to stop cell destruction could be tested as a potential new treatment for Alzheimer’s.

In a surprising discovery, investigators reported in the journal *Nature Neuroscience* that nerve cells in the brain make a form of collagen called collagen VI and that collagen VI attempts to protect nerve cells from the toxic effects of beta-amyloid. This may help explain why levels of collagen VI are increased in the brains of people with Alzheimer’s. Looking more closely, they found that small clusters of beta-amyloid called oligomers (which are much smaller than beta-amyloid plaques and are believed by many to be more toxic than plaques) bind to vulnerable neurons in the brain, but that collagen VI interrupts that binding and may help move the oligomers away from the neurons. If the role of collagen VI in cell models of Alzheimer’s is borne

out in more advanced models, collagen VI could prove to be a new weapon against Alzheimer’s disease.

Astrocytes, star-shaped nervous system cells that make up about half the volume of the brain, typically support normal brain function. However, researchers at the MassGeneral Institute for Neurodegenerative Disease in Boston found that



the beta-amyloid plaques of Alzheimer’s activate the astrocyte network in the brain and may cause the harmful effects of beta-amyloid to be spread cell by cell in waves to distant parts of the brain. Researchers are now trying to determine whether increased astrocyte signaling harms brain cells or may actually be an effort by the body to protect brain cells.

Researchers have known for some time that clusters of beta-amyloid contribute to the nerve cell damage that leads to Alzheimer’s. However, they haven’t always understood which clusters were most harmful: the large clusters called plaques, the small clusters called oligomers, or clusters somewhere between.



Recent studies have suggested that oligomers are most toxic, and in 2009 researchers at UCLA narrowed in on exactly how toxic they are. The researchers created beta-amyloid clusters in the lab that exactly matched those that form in the brains of people with Alzheimer's. They found that toxicity increases dramatically as the clusters grow from two to three or four beta-amyloid molecules. Clusters consisting of two molecules are three times as toxic as one-molecule clusters, and three- and four-molecule clusters are more than 10 times as toxic as one-molecule clusters. Detailed study of the atomic structure of these clusters will make development of anti-toxicity drugs much easier and likely more successful, said researchers.

The **Alzheimer's Association** played a key role in funding research showing that inhibiting a protein called heat-shock protein 70 (Hsp70) reduces levels of hyperphosphorylated tau in the brain. Hyperphosphorylated tau disrupts the movement of nutrients in brain nerve cells and threatens the very structure of nerve cells. Hsp70 is a "chaperone" protein that guides the activity of tau inside cells. The researchers originally thought that activating Hsp70 would cause the protein to remove hyperphosphorylated tau. However, instead of attaching to tau and removing it, Hsp70 attached to tau and continued to hold on to it, allowing it to accumulate

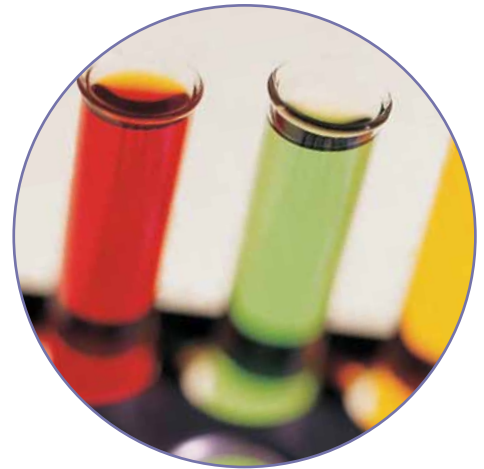
inside cells. Researchers are now working to identify a compound to effectively inhibit Hsp70 that could be tested as a treatment for Alzheimer's.

Research on the role of brain-derived neurotrophic factor (BDNF) was a focus of attention in 2009. In February, **Alzheimer's Association**-funded researchers reported in *Nature Medicine* that injecting the BDNF gene or protein slowed and even stopped the progression of Alzheimer's disease in animal models. BDNF is produced in the entorhinal cortex, which is involved in memory. Alzheimer's disease affects the entorhinal cortex and is associated with decreased production of BDNF. In September, a second group of researchers found that injection of neural stem cells into the brain in animal models of the disease resulted in improved performance in memory tests. The stem cells secreted BDNF,

The Alzheimer's Association played a key role in funding research showing that inhibiting a protein called heat-shock protein 70 (Hsp70) reduces levels of hyperphosphorylated tau in the brain.

which caused existing tissue to sprout new neurites, strengthening and increasing the number of connections between neurons. The discovery gives researchers hope that stem cells or a derivative of them, such as BDNF, may one day be used to treat Alzheimer's.

Perspectives in Alzheimer Science *timeline*



January

1

Brain “Exercises” as Dementia Therapy

In recent years, many games and exercises have been developed that aim to stimulate the brain and help prevent dementia. Researchers have analyzed data from numerous studies of such “cognitive training.” Their analysis found no clear evidence that cognitive training influenced cognitive loss. Current studies on this topic are small and inconclusive. The team recommends that future brain training research follows participants for a longer period and assesses the training’s effectiveness on a wider array of brain functions.

Alzheimer’s & Dementia: The Journal of the Alzheimer’s Association, January 2009;5(1):50–60.

Polyphenols in Red Wines May Reduce Alzheimer Pathology

Drinking red wine that contains cabernet sauvignon and muscadine grapes has been shown to significantly reduce the development of Alzheimer pathology and memory deterioration in mice by reducing amyloid accumulation in the brain. The study adds further support to the hypothesis that moderate consumption of red wines might facilitate disease-modifying interactions between polyphenolic compounds and beta-amyloid and suggests the possibility of developing a combination of dietary polyphenolic compounds for Alzheimer prevention and therapy.

Journal of Alzheimer’s Disease, January 2009;16(1):59–72.

Muscle-Building Protein Could Prevent Brain Cell Damage in Alzheimer’s

Collagen protein plays an essential role in building muscles and cartilage. Scientists discovered that a kind of collagen, called collagen VI, can protect brain cells from damage related to Alzheimer’s disease. Studying mice that were engineered to develop Alzheimer-like symptoms—as well as brain tissue from people who died of Alzheimer’s—the researchers observed that collagen VI levels were increased in a part of the brain called the dentate gyrus, which is vulnerable to Alzheimer damage. They then determined that collagen VI binds to beta-amyloid and may prevent toxic amyloid clumps called oligomers from harming brain cells. Future Alzheimer therapies may incorporate the potential protective effects of collagen VI.

Nature Neuroscience online (Print: February 2009;12(2):119–121.)

6

Genes Found that Increase Alzheimer Risk

Study results have revealed nine genes that may make people more likely to develop Alzheimer's disease. Researchers identified the genes by sequencing—or translating the genetic code—of thousands of gene variations from about 500 people with Alzheimer's and 500 healthy people. Discovering the genetic causes of Alzheimer's could lead to better methods of preventing it or diagnosing it at its earliest stages.

American Journal of Human Genetics, January 2009;84(1):35–43.

Imaging Technology Used to Detect Possible Early Signs of Dementia

Investigators have been using positron emission tomography (PET) imaging to search for two key protein clumps associated with Alzheimer's disease: beta-amyloid plaques and neurofibrillary tangles. The team injected 76 non-demented participants with FDDNP, a newly developed chemical that binds to plaques and tangles and can be detected on PET brain scans. According to the results, participants who showed high concentrations of FDDNP in their brains had other conditions that placed them at risk for Alzheimer's. Some had mild cognitive impairment (MCI), some had the Alzheimer-related APOE-e4 gene, and some had both MCI and APOE-e4. These results suggest that PET-FDDNP technology could prove a useful tool for early Alzheimer diagnosis.

Archives of General Psychiatry, January 2009;66(1):81–87.

7

Process of Nerve Cell Degeneration May Link Several Different Brain Diseases

Research results shed new light on how neurons die in Alzheimer's disease and other neurological disorders. The study, supported in part by the **Alzheimer's Association**, analyzed mice that lacked a neuronal protein called modifier of cell adhesion (MOCA). As the mice aged, protein clumps built up in their nerve cells' axons—the armlike extensions through which neurons communicate. This clumping led to axonal degeneration and eventual nerve cell death. In addition, the mice developed a motor coordination problem called ataxia. The researchers believe that this process may be involved in multiple brain diseases, including Alzheimer's, and could be targeted in a variety of disease therapies.

Journal of Neuroscience, January 7, 2009;29(1):118–130.

8

Antipsychotics Can Cause More Harm Than Good

Antipsychotic drugs have long been used to treat aggression and other mental problems related to Alzheimer's disease. However, a British study has found that these drugs may cause serious side effects. Elderly participants in the study were more likely to suffer stroke, chest infections and earlier death if they took antipsychotic drugs than if they took a placebo. Study researchers say that antipsychotic treatments are still useful for people with severe, dementia-related behavioral problems, but they do not recommend the drugs for most people with dementia.

Lancet Neurology online (Print: February 2009;8(2):151–157.)

Multiple Kinds of Statins May Help Prevent the Onset of Alzheimer's Disease

Researchers have found that people who take statins are 43 percent less likely to develop Alzheimer's than people who do not take these cholesterol-lowering drugs. The team used data from a large Dutch study assessing cognitive loss over time. Results showed that a variety of statins—including atorvastatin, simvastatin and pravastatin—had similar protective effects against Alzheimer's compared with a placebo. Moreover, the drugs were just as effective among people with the Alzheimer-related APOE-e4 gene as they were among people without the gene. These findings confirm earlier research on statins and could lead to statin-based Alzheimer therapies.

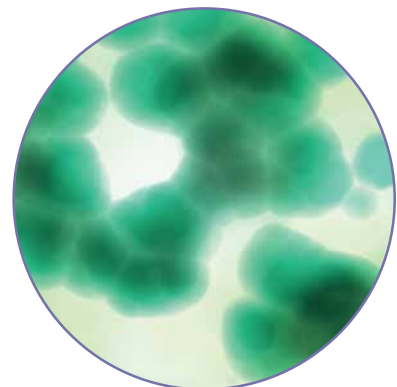
Journal of Neurology, Neurosurgery and Psychiatry, January 2009;80(1):13–17.

11

Gene Variant Boosts Alzheimer Risk

Investigators have found that women who inherit two copies of a gene variant possess a greater risk of developing Alzheimer's disease. Because this gene—a variant of the PCDH11X gene—occurs on the X chromosome, only women can inherit two copies. Women have two X chromosomes, while men have an X and a Y chromosome. However, even inheriting one copy of the gene has been shown to increase Alzheimer risk slightly. Normal PCDH11X genes encode a protein that promotes cell development and cell-to-cell communication in the central nervous system. According to the researchers, variant PCDH11X might be involved with presenilins, proteins linked to inherited forms of Alzheimer's. Further research could lead to novel methods of Alzheimer prevention or early diagnosis.

Nature Genetics online (Print: February 2009;41(2):192–198.)



12

Diabetes Treatment Linked to Brain Injury Patterns in Dementia

Individuals with dementia and diabetes who receive treatment for diabetes appear to suffer a different pattern of brain injuries than people with dementia and diabetes who do not receive treatment. Scientists have found that those who received treatment for diabetes had more damage to brain blood vessels and less damage caused by beta-amyloid and toxic oxygen molecules than those who did not receive treatment. Brain injury patterns among those with dementia but no diabetes were similar to those of people with dementia and untreated diabetes. If confirmed by future research, these findings could help scientists understand the causes of dementia and develop more precise therapies for this subpopulation of people with dementia.

Archives of Neurology online (Print: March 2009;66(3):315–322.)

15

Caffeine May Reduce Dementia Risk

People who drink coffee during midlife may decrease their risk of Alzheimer's by as much as 65 percent, Finnish researchers suggest. The researchers acquired their results after a long-term study of middle-aged participants who drank varying daily amounts of coffee. They found that the individuals who drank "moderate" amounts of coffee—3–5 cups per day—were least likely to develop dementia. These results, however, are preliminary and need to be confirmed by larger studies. The exact relationship between caffeine consumption and brain health remains unclear.

Journal of Alzheimer's Disease, January 2009;16(1):85–91.

20

Lifestyle Choices Could Prevent the Onset of Dementia

People who lead socially active lives with limited stress may reduce their risk of Alzheimer's disease. Researchers conducting a six-year study of more than 500 elderly participants with varying lifestyles found that the people who were both outgoing and calm were half as likely to develop dementia as those with only one of these positive lifestyle characteristics.

Neurology, January 20, 2009;72(3):253–259.

22

Verbal Abuse Common Among Caregiver Relatives of People with Dementia

After questioning more than 200 family caregivers of people with dementia, researchers found that more than half committed some form of verbal abuse toward the person in their care. Such abuse often consisted of harsh yelling, though some caregivers admitted to making verbal threats. Caregiver abuse usually occurs after the person with dementia has become aggressive or difficult to handle. The researchers hope their study's results will focus more attention on improving dementia care in the home, as well as in clinics and hospitals.

British Medical Journal, January 22, 2009;338:b155.

28

Developing Midlife Diabetes Boosts Alzheimer Risk

As part of an ongoing study of twins, Swedish researchers found that participants who developed diabetes before age 65 had more than double the risk of developing Alzheimer's disease as those who did not develop diabetes. These results suggest that many of the lifestyle choices that increase one's chances of getting diabetes, including overeating and lack of exercise, may also be risk factors for dementia. The team's study was supported, in part, by the **Alzheimer's Association**.

Diabetes, January 2009;58(1):71–77.

Nicotinic Receptor Is a Potential Therapeutic Target for Alzheimer's

Researchers have found that nicotinic receptors in the basal forebrain, the part of the brain responsible for memory and learning, are highly sensitive to blockage by low levels of beta-amyloid, and that small aggregates of beta-amyloid had this same blocking effect. The researchers hypothesize that as beta-amyloid begins to increase, it first blocks acetylcholine signaling at the nicotinic receptors, possibly triggering neurodegeneration.

Journal of Neuroscience, January 28, 2009;29(4):918–929.

February

1

Mediterranean Diet May Delay the Progression of Alzheimer's

A study testing the effects of a "Mediterranean" diet—one high in fish, olive oil and vegetables—on nearly 2,000 people with mild cognitive impairment (MCI) or no cognitive problems found that, among the participants with MCI, those on the diet were less likely to develop Alzheimer's disease than those not on the diet. Moreover, cognitively normal people on the diet were less likely than those not on the diet to suffer memory problems. These results suggest that a healthy diet, may help lower one's risk of dementia.

Archives of Neurology, February 2009;66(2):216–225.

3

Education May Not Affect the Rate of Mental Decline in Old Age

Contradicting earlier research, a large study found that education does not slow the rate of cognitive decline in the elderly. However, educated older people were shown to have higher than normal levels of cognition when they began to lose their mental faculties. Thus, the time it took for them to become mentally incapable of independent living was also longer than typical. The investigators followed more than 6,000 people for up to 14 years, conducting at least three mental assessments for each one. Their results highlight the potential importance of education in delaying advanced Alzheimer's disease. Such delays could save millions of dollars in medical costs.

Neurology, February 3, 2009;72(5):460–465.

6

Atrophy in Certain Brain Regions May Predict Alzheimer's

People with certain patterns of brain damage on MRI scans may be particularly susceptible to Alzheimer's disease. In a study of more than 300 participants, most of whom had mild cognitive impairment, researchers found that certain individuals showed considerable brain atrophy in regions called the medial and lateral temporal lobes and the frontal lobes. These people suffered dramatic declines in cognitive function and brain health one year later, declines that may lead to an Alzheimer diagnosis. The research sheds new light on what Alzheimer's may "look like" before clinical symptoms appear. Such efforts could lead to earlier and more targeted Alzheimer interventions.

Radiology online (Print: April 2009;251(1):195–205.)

8

Naturally Produced Brain Protein Reverses Alzheimer Progression in Animals

Brain-derived neurotrophic factor (BDNF), a protein that occurs naturally in the brain, has been shown to halt the progression of Alzheimer's disease in rats, mice and monkeys. When the animals were treated with BDNF, they showed improved brain cell function—including cell-to-cell communication—and improved cognitive ability compared with animals that did not receive treatment. These positive effects occurred even though BDNF did not slow beta-amyloid accumulation in the animals' brains. The researchers, whose work was supported in part by the **Alzheimer's Association**, hope that BDNF might be used in tandem with amyloid-reducing techniques to provide a more potent, multi-pronged Alzheimer therapy.

Nature Medicine online (Print: March 2009;15(3):331–337.)

10

Study Tests the Driving Ability of People with Alzheimer's

Scientists describe the results of a study identifying factors that may indicate when a person with Alzheimer's disease should stop driving. Researchers tested the driving ability of 40 individuals with early Alzheimer's and 115 cognitively normal older people. On average, the drivers with Alzheimer's made 42 errors, compared with 33 for the nondemented drivers. Many of the errors made by those with Alzheimer's involved swerving or other lane violations. Subsequent cognitive testing found that the drivers who made the most mistakes had suffered the steepest declines in visual and motor skills. These results may contribute to accurate, physician-administered exams to gauge whether Alzheimer's disease has made a person unsafe behind the wheel.

Neurology, February 10, 2009;72(6):521–527.

11

The Body's Immune System May Help Reduce Protein Build-Up in Alzheimer's

The innate immune system is an ancient self-defense mechanism that fights off microbial invaders in the body. Using a treatment to stimulate this system, scientists have dramatically reduced beta-amyloid levels in mice engineered to develop Alzheimer-like symptoms. The treatment involves immune system molecules called toll-like 9 receptors. These results, along with the findings of other studies, show that beta-amyloid "vaccination" therapies may prove an effective option for people suffering with Alzheimer's.

Journal of Neuroscience, February 11, 2009;29(6):1846–1854.

12

Dementia Risk Could Increase After Exposure to Second-Hand Smoke

According to a British study, high amounts of second-hand smoke may cause cognitive loss and put people at risk for Alzheimer's and other forms of dementia. The study assessed more than 4,800 people, finding that participants with the most second-hand smoke exposure were about 44 percent more likely to experience cognitive impairment than people with less smoke exposure. These results confirm findings of earlier research and highlight a potential new benefit of smoke-free homes and public places.

British Medical Journal, February 12, 2009;338:b462.

Two Antibodies in the Blood May Predict Alzheimer Severity

Scientists have found that levels of two antibodies in the blood directly correspond to levels of brain inflammation in Alzheimer's disease. These antibodies attack molecules that proliferate in Alzheimer's: the protein fragment beta-amyloid and the protein RAGE (receptor for advanced glycation endproducts). Beta-amyloid and RAGE may work together to hinder cell-to-cell communication in the demented brain. Further testing of these antibodies could lead to an effective Alzheimer blood test.

Journal of Gerontology: Medical Sciences, February 2009;64A(2):264–271.

19

A Mechanism Used in Early Brain Development Might Contribute to Alzheimer's

During embryonic development of the brain and spinal cord, a "pruning" mechanism is used to destroy excess nerve cells. Researchers have found that a protein fragment called N-APP is involved in this mechanism and may play a role in Alzheimer's disease. N-APP is clipped from APP, the same molecule from which the dementia-related beta-amyloid fragment is cut. During Alzheimer's disease, N-APP may "hijack" the embryonic pruning mechanism in order to kill vital adult nerve cells. The researchers have found that, in laboratory studies of embryonic cells, they can block the pruning mechanism. They are now testing their procedure in adult neurons. If successful, this procedure could lead to a novel Alzheimer therapy.

Nature, February 19, 2009;457(7232):981–989.

26

Prion Proteins Assist Beta-Amyloid in Causing Alzheimer Brain Damage

The protein fragment beta-amyloid is suspected of causing brain cell damage and death in Alzheimer's disease. In cell culture studies, researchers have found that this damage may occur after prion proteins bind to beta-amyloid molecules. Prions are best known to cause such neurological disorders as Creutzfeldt-Jakob disease and mad cow disease. This research indicates a role for prions in Alzheimer's disease as well.

Nature, February 26, 2009;457(7233):1128–1132.

27

Beta-Amyloid Plaques Linked to Damaged Astrocytes in Alzheimer's Disease

Astrocytes are cells that occur throughout the brain and assist neurons in conducting brain functions. Using sophisticated imaging techniques, researchers studied the effects of Alzheimer's disease on astrocytes in mouse brains and found that beta-amyloid plaques, a key hallmark of Alzheimer's, may cause astrocytes throughout the brain to develop higher than normal calcium levels. Abnormal regulation of calcium levels is another feature of Alzheimer's. This finding shows that plaques have more widespread effects on the brain than previously believed, causing damage to both neurons and astrocytes.

Science, February 27, 2009;323(5918):1211–1215.



March

1

Cardiovascular Risk Factors in Older Women May Increase Alzheimer Risk

Having a combination of risk factors for heart disease, including high blood pressure, obesity and high levels of bad (LDL) cholesterol, is known as the metabolic syndrome. Investigators recently analyzed data from a large group of older women to determine whether having the metabolic syndrome affected their risk of cognitive impairment. The results showed that cognitive decline occurred in about 7 percent of women with the syndrome, but only about 4 percent of women without the syndrome. These findings suggest that avoiding risk factors for heart disease could also reduce one's chances of developing dementia.

Archives of Neurology, March 2009;66(3):324–328.

Dementia Risk for the Obese Increased in Mid-Life, Decreased in Late Life

Researchers report that obesity has different effects on cognitive loss during middle age and old age. Among middle-aged study participants, obese people had a greater than average risk of developing dementia. Among the elderly, however, underweight people had the greatest dementia risk, while the obese had a lower than average risk. These findings suggest that dementia prevention strategies should be tailored to different age groups.

Archives of Neurology, March 2009;66(3):336–342.

High Cholesterol and Diabetes Hasten Decline in People With Alzheimer's

According to researchers, people with Alzheimer's disease tend to suffer faster than normal rates of cognitive decline if they also have diabetes or high levels of total cholesterol or bad (LDL) cholesterol. These findings suggest a strong association between Alzheimer progression and risk factors for cardiovascular disease.

Archives of Neurology, March 2009;66(3):343–348.

Accurate Alzheimer Biomarkers May Exist in CSF

Many researchers have been searching for accurate biomarkers, or molecular indicators, of Alzheimer's disease. In one such effort, Finnish investigators studied more than 100 participants with Alzheimer's and other brain disorders. They focused on levels of beta-amyloid and tau in the cerebrospinal fluid (CSF) surrounding the brain. Results showed that when levels of CSF beta-amyloid became low and CSF tau became high, corresponding increases occurred in the development of beta-amyloid plaques and tau-based neurofibrillary tangles—two Alzheimer hallmarks in the brain. This finding suggests that CSF amyloid and tau can be used to detect the onset and progression of dementia.

Archives of Neurology, March 2009;66(3):382–389.

Alzheimer's Disease May Destroy the Brain's "Helper" Cells

Astrocytes are helper cells in the brain, and they play a vital role in maintaining the synaptic channels through which brain cells communicate. One research group studying astrocytes in mice that were engineered to develop Alzheimer-like symptoms found that the astrocytes near beta-amyloid plaques grew in size, possibly to protect the affected nerve cells. But astrocytes farther away from the plaques appeared to shrink and die. These results contradict earlier studies that found astrocytes becoming inflamed throughout the Alzheimer brain and may influence future studies of inflammation and Alzheimer's disease.

Cell Death & Differentiation, March 2009;16(3):378–385.

12

Anesthesia Linked to Protein Tangles in Alzheimer's

Neurofibrillary tangles, a key hallmark of the Alzheimer brain, are produced after tau protein becomes abnormally modified. In two studies with mice, researchers found that anesthesia promotes this abnormal modification of tau. Moreover, the modification occurs at sites where tau tangles usually form in Alzheimer's disease. This finding suggests a mechanism by which anesthesia can boost dementia risk.

Journal of Alzheimer's Disease, March 2009;16(3):619–626, and
The *FASEB Journal* online (Print: August 2009;23(8):2595–2604.)

Procedures Reduce Agitation Among People with Dementia

Researchers are working to improve the care of people with dementia who live in residential care facilities. One study assessed the effectiveness of two care procedures: person-centered care and dementia-care mapping. Both procedures devote more individual attention to residents in order to ameliorate such behaviors as agitation, screaming and pacing. The results of this study found that the procedures reduced agitation levels among residents. However, neither procedure was shown to improve other aspects of resident well-being or quality of life.

Lancet Neurology online (Print: April 2009;8(4):317–325.)

13

APP Variant Causes Alzheimer's Disease in Some People and Prevents It in Others

Scientists report on their discovery of a rare gene variant for amyloid precursor protein (APP) in an Italian family. Members of this family who inherited two copies the gene developed dementia early in life, while members who inherited only one copy were protected against the disease. The researchers produced laboratory cells that expressed this variant gene to measure the cells' production of toxic beta-amyloid from APP. Results showed that the cells with two copies of the gene produced extensive clumps of beta-amyloid. Cells with only one copy produced far less beta-amyloid, even less than cells that lacked the gene.

Science, March 13, 2009;323(5920):1473–1477.

17

MRI Technology Predicts Alzheimer Risk

Researchers have found that damage to the hippocampus can predict the risk of a cognitively normal person developing Alzheimer's disease. The team administered magnetic resonance imaging (MRI) scans over time to a group of elderly participants with no cognitive loss. Results showed that those whose hippocampuses were shrinking fastest had an Alzheimer risk two to four times greater than average. The investigators believe that brain cell loss in the hippocampus could be an effective biomarker for early Alzheimer diagnosis.

Neurology, March 17, 2009;72(11):999–1007.

Study Assesses the Ability of CSF Molecules to Predict Alzheimer's

Another study has found that cerebrospinal fluid (CSF) levels of beta-amyloid and tau may prove useful as Alzheimer biomarkers. The researchers showed that people with high levels of CSF tau tended to have increased brain cell degeneration. People with low CSF beta-amyloid tended to have more beta-amyloid clumping in the brain. The team also found that people with two copies of the APOE-e4 gene, a known risk factor for Alzheimer's, had particularly low concentrations of CSF beta-amyloid, indicating increased beta-amyloid accumulation in the brain.

Annals of Neurology online (Print: April 2009;65(4):403–413.)

23

Abnormal Tau and Beta-Amyloid May Work Together to Hinder Cell Function in Alzheimer's

Researchers have discovered a mechanism by which nerve cells become dysfunctional in Alzheimer's disease. Toxic clumps of beta-amyloid and tau molecules activate enzymes that prevent the transport of vital proteins from one part of a cell to another. These activities also hinder communication between brain cells and eventually lead to brain cell death. Understanding how such Alzheimer processes work may lead to more effective disease therapies.

Proceedings of the National Academy of Sciences online (Print: April 7, 2009;106(14):5907–5912.)



April

1

MRI Can Detect Alzheimer-Related Shrinkages in the Brain

People with mild cognitive impairment (MCI) who go on to develop Alzheimer's typically develop physical changes in the brain before the first cognitive symptoms of the disease appear. These changes include shrinking of the hippocampus and other dementia-affected brain areas. Investigators report that they have developed a computer-based technology called volumetric magnetic resonance imaging (MRI) that can accurately detect shrinkages in the hippocampus, amygdala and temporal horn regions. The team used volumetric MRI to measure the brain volumes of 269 people with MCI. They found that those with smaller hippocampus and amygdala volumes performed poorly on subsequent cognitive tests. Scientists suspect that early changes in brain volume may be biomarkers in detecting conversion from MCI to Alzheimer's disease.

Alzheimer Disease & Associated Disorders, April/June 2009;23(2):139–145.

3

Scientists Reveal a Key Alzheimer Protein in Mitochondria

Researchers have discovered a mechanism by which beta-amyloid may hinder cell-to-cell communication in the Alzheimer brain. In cell culture studies, the team found that small beta-amyloid clumps increase levels of a toxic oxygen molecule called nitric oxide. This molecule, in turn, chemically alters a protein in mitochondria called Drp1. Mitochondria are cellular structures that use oxygen and nutrients to provide energy for a cell. When Drp1 becomes altered, it causes mitochondria to break apart, damaging the tiny channels through which brain cells send and receive messages. Ultimately, this damage causes brain cells to die. If further research validates these results, Drp1 could prove an important target for Alzheimer therapies.

Science, April 3, 2009;324(5923):102–105.

8

Young Adults With an Alzheimer Gene Show Abnormal MRI Brain Activity

The gene variant APOE-e4 puts people at greater risk for developing Alzheimer's disease. According to researchers, young adults with APOE-e4 were shown to have abnormally increased brain activity on MRI scans. This activity occurred in the hippocampus, one of the first brain regions affected by Alzheimer's. Such findings suggest that Alzheimer-related changes may begin decades before clinical symptoms occur, but much additional research is needed.

Proceedings of the National Academy of Sciences online (Print: April 28, 2009;106(17):7209–7214.)

Proteins, Cholesterol and Calcium Interact to Kill Aging Neurons in Alzheimer's

As brain cells age, they become more susceptible to processes associated with Alzheimer's disease. In cell culture studies, researchers found that older neurons can develop high levels of both calcium and cholesterol. Abnormal cholesterol levels can make brain cells more vulnerable to damage by toxic beta-amyloid, a key suspect in Alzheimer's. Such damage includes the production of the toxic tau protein. Moreover, high calcium levels can put brain cells under stress and cause cell death. The researchers found that by removing cholesterol, they could prevent some of the damage caused by beta-amyloid. This study suggests that Alzheimer's disease involves complex relationships between beta-amyloid, tau, calcium and cholesterol and that effective therapies will need to target multiple systems. *Journal of Neuroscience*, April 8, 2009;29(14):4640–4651.

14

Statins May Not Decrease the Risk of Dementia

Scientists reviewing two large studies of the role that statin drugs may play in people at risk for Alzheimer's disease found that two statins—simvastatin and pravastatin—had no significant effect in lowering Alzheimer risk. Participants in the studies who took statins showed no better results on cognitive tests than participants who took a placebo. These findings contradict the results of other studies that support the role of statins in Alzheimer treatment. *Cochrane Database of Systematic Reviews*, April 2009;2:CD003160.

Tube Feeding Not Recommended for People with Late-Stage Dementia

Hospitals often use enteral feeding, or tube feeding, for people in advanced stages of Alzheimer's disease and other dementias, but an analysis of several studies suggests that this may cause more harm than good. The analysis found that tube feeding may lead to pneumonia, dangerous abdominal disorders and increased aggressive behavior. Other evidence suggests that withholding food may not cause pain in people with advanced dementia. These findings highlight the need for further research into how people with dementia are treated near the end of life. *Cochrane Database of Systematic Reviews*, April 2009;2:CD007209.

15

Dementia Risk Increases in Diabetics with Low Blood Sugar Attacks

People with type 2 diabetes can experience dangerously low blood sugar levels, often as a result of taking medication that overproduces insulin in the body. Researchers report that these hypoglycemic attacks can increase the risk of dementia in the elderly. Using data from thousands of older diabetics, researchers found that one hypoglycemic attack can increase dementia risk by 26 percent. Two or three attacks increase the risk by 115 percent and 160 percent, respectively. These results suggest that aggressive insulin treatment can be harmful for the elderly. Whenever possible, diabetics' blood sugar levels should be controlled with diet and exercise. *Journal of the American Medical Association*, April 15, 2009;301(15):1565–1572.

Blocking Beta-Amyloid Production at the Right Time May Delay Alzheimer's

Researchers have found that by suppressing beta-amyloid production for a short time, they may significantly delay the onset of Alzheimer's disease and other dementias. Using mice engineered to develop beta-amyloid, the team injected some of the mice with amyloid antibodies for six months. After the treatment was stopped, the animals began producing beta-amyloid again—but their overall amyloid levels never reached those of the mice that had not been treated. The researchers believe that such short-term amyloid suppression, if administered early in life, could delay the onset of amyloid-related diseases in both mice and humans.

Journal of Neuroscience, April 15, 2009;29(15):4964–4971.

16

Brain Diseases are Associated With Specific Nerve Cell Pathways

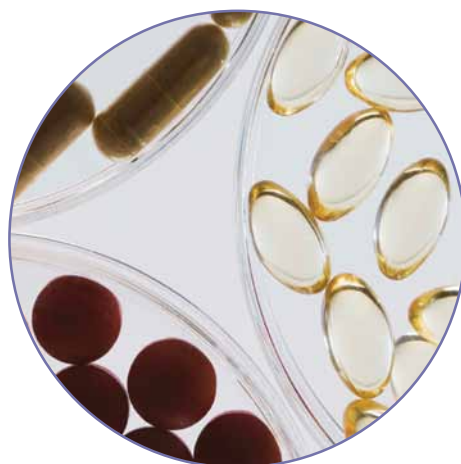
Using sophisticated imaging methods, scientists have found that different brain disorders—including Alzheimer's disease and frontotemporal dementia—spread along different “neural networks.” These networks are pathways that connect nerve cells in various parts of the brain. Normally, neurons use the pathways to communicate with one another and produce healthy proteins. But in diseased brains, the pathways can be “hijacked” to create molecules that harm brain cells. In Alzheimer's disease, such molecules include toxic forms of the protein fragment beta-amyloid and the protein tau. The results of this study could lead to better, more targeted methods of treating brain disease.

Neuron, April 16, 2009;62(1):42–52.

Abnormal Calcium Regulation May Be Related to Cell Death in Alzheimer's Disease

Researchers have identified a mechanism by which beta-amyloid can cause abnormal calcium levels in brain cells, a key feature of Alzheimer's disease. In cell culture studies, beta-amyloid was found to create pores in the neuronal membranes—enabling calcium ions to build up in the cells and damage cellular functions. These results contradict earlier research that found membrane thinning to be responsible for higher calcium levels in Alzheimer cells. The study team, funded in part by the **Alzheimer's Association**, hopes their work may lead to more effective ways of slowing Alzheimer progression.

Neurotoxicity Research online (Print: July 2009;16(1):1–13.)



A Natural Survival Mechanism Could Help Prevent Alzheimer's Disease

When oxygen levels become low in the body, cells protect themselves with a mechanism called the hypoxic response. This response is “turned off” after adequate oxygen levels are restored. In a study involving worms, researchers found that by keeping the worms’ hypoxic response “on”—even when oxygen levels were normal—they could extend the animals’ lives by about 30 percent. These worms were engineered to lack a protein called VHL-1, which normally destroys another protein that regulates hypoxic response. Worms that lacked VHL-1 also remained healthy in old age and developed few of the clumps of toxic proteins associated with neurodegenerative diseases of aging such as Alzheimer’s and Huntington’s disease. The researchers believe that similar hypoxic response treatments may be useful in preventing dementia in humans. Their work was supported in part by the **Alzheimer’s Association**.

Science online (Print: May 29, 2009;324(5931):1196–1198.)

22

Molecules May Destroy Toxic Beta-Amyloid in Alzheimer's Disease

In a cell culture study of neurons, researchers found two chemicals—called Ia1 and Ia2—that boost by 700 percent and 400 percent, respectively, the activity of insulin-degrading enzyme (IDE), which breaks down beta-amyloid in the brain. These results could spur further research into the effectiveness of IDE treatments for human Alzheimer’s disease.

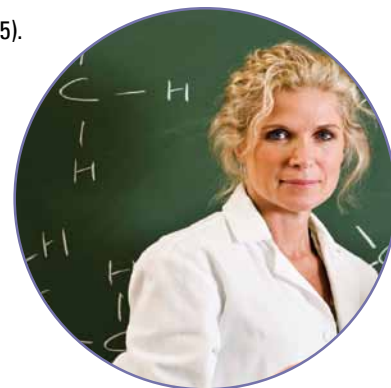
PLoS ONE, April 22, 2009;4(4):e5274.

27

A Protein Thought to Promote Alzheimer's Disease Could Have Protective Abilities

Researchers report the results of a study involving mice engineered to develop beta-amyloid but lack the protein p75, which normally regulates the growth and programmed death of nerve cells. Earlier research found that, in Alzheimer’s disease, p75 may bind to beta-amyloid and cause abnormal brain cell death. Researchers expected that the genetically engineered mice would be protected from the toxic effects of amyloid-p75 interactions. Instead, the animals developed abnormally formed nerves outside the brain, nerves that made their hearts and other organs more vulnerable to stress. Most of the mice died at a young age—around three weeks. These results indicate that p75 can help maintain the structure of the nervous system against beta-amyloid damage. Future studies of p75 could lead to novel treatments that take advantage the molecule’s protective abilities.

Proceedings of the National Academy of Sciences online (Print: May 12, 2009;106(19):7870–7875).



May

1

CSF Proteins and Alzheimer Risk

Researchers report study results showing that among people with very mild Alzheimer's disease who were followed for more than three years, those with the lowest levels of beta-amyloid and highest levels of tau in cerebrospinal fluid (CSF) suffered the steepest cognitive declines. Changes in the beta-amyloid and tau proteins are hallmarks of Alzheimer's. These findings support the role of protein levels of CSF as potential predictors of disease progression.

Archives of Neurology, May 2009;66(5):638–645.

5

Cognitive Loss Accelerates After an Episode of Delirium

Delirium, or a severe episode of mental confusion, often affects older hospitalized individuals. In assessments of data from hospitalized people with Alzheimer's disease, a research team found that delirium episodes can double or even triple a person's rate of cognitive decline. The team believes that such episodes can be prevented in hospitals. Study author Tamara Fong, M.D., recommends that hospitals try to "orient the patient to his or her surroundings, to allow for as much uninterrupted sleep as possible by not waking patients ... at night, and to get patients out of bed and walking as soon as their medical condition allows." This study was funded in part by the **Alzheimer's Association**.

Neurology, May 5, 2009;72(18):1570–1575.

11

Prescription Drugs for Alzheimer's Disease Can Cause Harmful Side Effects

In a study of people with Alzheimer's, Canadian researchers found an increased risk of health problems in those taking cholinesterase inhibitors. Researches analyzed information from healthcare databases that included more than 19,000 people with dementia who were taking cholinesterase inhibitors and more than 61,000 people nondemented individuals who were not taking these medications. They found that those taking cholinesterase inhibitors had a 100 percent increased risk of fainting, 69 percent increased the risk of a dangerously slowed heart rate, 49 percent increased risk of needing a pacemaker and 18 percent increased risk of hip fractures. Researchers urge physicians to examine the risks and benefits of cholinesterase inhibitors before prescribing them and to be especially careful in monitoring the health of patients on this medication.

Archives of Internal Medicine, May 11, 2009;169(9):867–873.

18

Risk Factors for Dementia Revealed by New Assessment Tool

Researchers have developed a diagnostic tool aimed at predicting dementia. This “risk index” tool assesses various disease risk factors. Some of the factors are well known, including old age and poor scores on cognitive tests. Other, novel factors were identified by the research team, which studied 480 people who progressed from cognitive health to dementia over six years. The novel factors include being underweight, not drinking alcohol and being slow at performing dexterous physical tasks. The researchers found that their risk index correctly identified 88 percent of study participants who developed dementia. Further testing of the index could lead to an effective, and relatively inexpensive, method of detecting those at increased risk of dementia.

Neurology online (Print: July 21, 2009;73(3):173–179.)

19

Low Weight and Weight Loss Could Make the Elderly More Susceptible to Alzheimer’s

In a study of about 2,000 older Japanese Americans, researchers found that thinner people were 79 percent more likely than heavier people to develop dementia. Moreover, individuals who had lost extensive weight—or who had lost weight quickly—were more likely to develop dementia than those whose weight had remained stable. These results suggest that being underweight is a Alzheimer risk factor in the elderly.

Neurology, May 19, 2009;72(20):1741–1746.

23

Novel Mechanism May Underlie the Creation of Abnormal Tau in Alzheimer’s

Investigators share results of a study showing how the addition of a single phosphate molecule to a particular amino acid may be responsible for creating the harmful tau tangles of Alzheimer’s. Tau protein normally plays a crucial role in maintaining the structural framework and transport systems within nerve cells. The protein is modified when phosphate molecules are added to it. In Alzheimer’s disease, however, too many phosphate molecules are added to tau, causing the protein to become abnormally modified and no longer able to carry out its helpful functions. The researchers suggest that the addition of a single phosphate to the Ser202 amino acid in tau is the principal culprit responsible for the tau tangles of Alzheimer’s. Future Alzheimer therapies could target the enzyme responsible for depositing this phosphate on Ser202.

Journal of Biological Chemistry, May 2009;284(20):13422–13433.

25

Computer-Based MRI Technology Could Better Predict Early Alzheimer's

Using an imaging software package, researchers have compared MRI scans from 216 people with Alzheimer's disease, mild cognitive impairment (MCI) or no cognitive loss. They analyzed changes in three brain areas that are affected early in Alzheimer's: the hippocampus, entorhinal cortex and supramarginal gyrus. This technique correctly distinguished people with Alzheimer's disease from people with MCI 95 percent of the time. When distinguishing people with Alzheimer's from cognitively normal people, the program achieved 100 percent accuracy. These encouraging results show the potential value of automated imaging technology in Alzheimer diagnosis.

Brain online (Print: August 2009;132(8):2048–2057.)

27

Vitamin D is Linked to Brain Health

In an analysis of several vitamin D studies, researchers find that people with low levels of vitamin D in blood are more likely to develop heart disease, diabetes, osteoporosis and tooth loss, conditions that are risk factors for dementia. In addition, low vitamin D levels may make the brain more susceptible to inflammation, which has been associated with Alzheimer's disease. Given this evidence, the researchers suggest that more studies be conducted to reveal the mechanisms underlying vitamin D's role in brain health. They also recommend that older people at risk for dementia have their vitamin D levels checked by a physician and take supplements if necessary.

Journal of Alzheimer's Disease, May 2009;17(1):151–159.

June

1

Older Whites and African-Americans with Cognitive Loss Have Similar Survival Rates

A study of 1,700 older adults, about half of whom were white and half African-American, finds that people with mild cognitive impairment were 50 percent more likely to die over 10 years than cognitively healthy people. Participants with Alzheimer's were nearly three times more likely to die over that period than healthy participants. These dementia-related increases in risk of death did not differ significantly between whites and African-Americans.

Archives of Neurology, June 2009;66(6):767–772.

2

Alzheimer Risk Might Increase, Not Diminish, After Anti-Inflammatory Treatment

A study evaluating the effectiveness of non-steroidal anti-inflammatory drugs (NSAIDs) in nearly 3,000 older participants with minimal cognitive problems showed that participants on heavy NSAID treatment were 66 percent more likely to develop Alzheimer's than people taking little or no NSAIDs. The researchers noted that in earlier NSAID trials, participants tended to be younger and healthier—a fact that might have accounted for the trials' positive results.

Neurology, June 2, 2009;72(22):1899–1905.

8

New Blood Analysis Method Could Detect Alzheimer's Disease

Using a light-based analytical technique called near-infrared (NIR) spectroscopy, researchers studied blood samples of healthy people and people with Alzheimer's disease. Specifically, the team measured blood levels of oxidative stress, or damage caused by toxic oxygen molecules. This technique distinguished people who had Alzheimer's from those who did not with 80 percent accuracy. The researchers believe NIR spectroscopy may also detect whether certain people with mild cognitive impairment are likely to develop Alzheimer's.

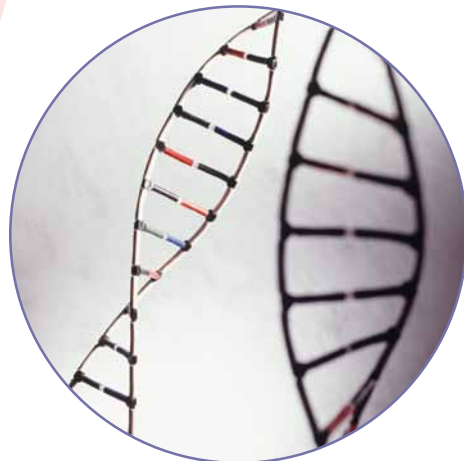
Journal of Alzheimer's Disease, June 8, 2009;17(2):391–397.

9

Novel Cognitive Test for Alzheimer's May Supplant Standard Tests

British researchers have developed a short, easy-to-use cognitive test for detecting early Alzheimer's disease. Known as "test your memory" (TYM), the assessment was administered to about 680 individuals who were cognitively normal or had mild Alzheimer's or mild cognitive impairment. The participants also underwent other memory tests, including the Mini-Mental State Examination (MMSE). Results showed that TYM correctly identified 93 percent of participants with Alzheimer's, compared with 52 percent for the MMSE. These results suggest that TYM might prove a good alternative to standard cognitive tests.

British Medical Journal, June 9, 2009;338:b2030.



10

APP Promotes Brain Health

Amyloid Precursor Protein (APP) is the parent molecule of beta-amyloid, a key suspect in Alzheimer's disease. Yet the protein may also help facilitate cell-to-cell communication in the brain. In cell culture studies of neurons, researchers found that APP stabilized the synapse channels through which brain cells communicate. Moreover, APP worked with a protein called reelin to promote the development of axons and dendrites, armlike extensions of neurons from which cells send chemical messages. Maintaining levels of "good" APP in the brain may be an important strategy for ensuring cognitive health.

Journal of Neuroscience, June 10, 2009;29(23):7459–7473.

14

Human Blood Stem Cell Growth Factor Reverses Alzheimer Symptoms in Mice

Granulocyte-colony stimulating factor (GCSF)—a human growth factor that stimulates blood stem cells to proliferate in bone marrow—significantly reduced levels of beta-amyloid in the brains of mice genetically engineered to develop Alzheimer's, increased the production of new neurons and promoted nerve cell connections. The growth factor could eventually be a powerful new therapy for Alzheimer's disease.

Neuroscience online (Print: September 29, 2009;163(1):55–72.)

16

Inflammation May Not Lead to Alzheimer's

Investigators report results of a study that contradict the long-held theory that beta-amyloid causes microglia—a group of helper cells in the brain—to become inflamed during Alzheimer's disease. The researchers devised a chemical that binds to microglia in Alzheimer brain tissue, making the cells easier to see under a microscope. Analysis of this tissue found that the microglia were not inflamed, but instead had begun to degenerate. This may affect future studies addressing the connection between brain inflammation and Alzheimer's.

Acta Neuropathologica online (Print: October 2009;118(4):475–485.)

Donepezil and Depression in MCI

Researchers report results of a study examining whether the Alzheimer drug donepezil delays the onset of Alzheimer's disease in people with mild cognitive impairment (MCI) and depression. Previous studies have shown that those with MCI and depression may be more likely to develop Alzheimer's disease than those with MCI alone. The researchers reported that after more than two years, 14 percent of the people on donepezil had developed Alzheimer's, compared with 29 percent of people receiving a placebo. These findings suggest that donepezil may prove useful in slowing dementia progression among individuals with MCI and depression. The study was supported in part by the **Alzheimer's Association**.

Neurology, June 16, 2009;72(24):2115–2121.

19

An Alzheimer's Disease Profile May Exist in CSF

Investigators report that among people with minimal memory impairment, having a “cerebrospinal fluid AD profile” increased one’s risk of severe cognitive decline 27-fold. This profile includes low levels of the protein beta-amyloid and high levels of the protein tau. This profile can be detected long before Alzheimer symptoms appear, which may help physicians identify people who should receive preventive treatments for Alzheimer’s disease, once such treatments are available.

Lancet Neurology online (Print: July 2009;8(7):619–627.)

28

Statins Can Lessen Brain Cell Damage and Cognitive Loss in Dementia

In studies with mice, researchers found that cholesterol-lowering statin drugs can protect brain cells from the effects of Alzheimer’s disease. One such effect, called excitotoxicity, overexcites nerve cells and causes them to die. Using a kind of statin called lovastatin, researchers prevented the death of mouse neurons that they had artificially overstimulated. This treatment also prevented cognitive loss in the animals. If proven effective in human clinical studies, statins may become a therapeutic option for Alzheimer’s.

Journal of Alzheimer’s Disease, June 2009;17(2):327–336.

29

Beta-Amyloid May Cause Brain Blood Flow Problems in Alzheimer’s

Beta-amyloid may play a role in restricting blood flow in the brain, a hallmark of Alzheimer’s disease, say researchers. In cell culture studies, scientists found that beta-amyloid increases the expression of a protein called endothelin converting enzyme-2 (ECE-2). This enzyme produces the protein endothelin-1, which constricts blood vessels and decreases blood flow. Drugs have already been produced to combat endothelin-1, which has been implicated in high blood pressure. Such drugs might be given new uses as Alzheimer therapies.

American Journal of Pathology online (Print: July 2009;175(1):262–270.)

Closeness of Caregiver-Care Recipient Relationship Can Impact Disease Progression

Slower cognitive and functional decline occurs in people with Alzheimer’s disease who have a close relationship with their caregivers. This is especially true when the caregiver is a spouse, researchers found in a 6-month study.

Journal of Gerontology: Psychological Sciences and Social Sciences online (Print: September 2009;64B(5):560–568.)

July

1

Anti-Inflammatory Drug Prevents Malfunction Linked to Beta-Amyloid Accumulation

Scientists report that in mouse studies, indomethacin—a nonsteroidal anti-inflammatory drug—prevented inflammation from turning off a molecular mechanism called the lipoprotein receptor-related protein (LRP) pump that allows beta-amyloid to exit the brain. When LRP malfunctioned, toxic levels of amyloid protein accumulated in the brains of study mice. This suggests that anti-inflammatory therapies may have a role in Alzheimer treatments.

Journal of Alzheimer's Disease, July 2009;17(3):553–570.

2

Marriage and Cohabitation Lower Dementia Risk

A study of marital status and dementia risk reveals that people who live alone have twice the risk of developing dementia and Alzheimer's disease in later life as people who are married or cohabiting. Individuals who are widowed or divorced in midlife have three times the risk of developing dementia.

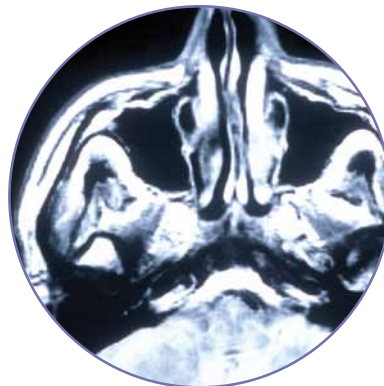
British Medical Journal, July 2009;339(7712):b2462.

5

MiRNA-145 May Protect Against Vascular Disease and Decrease Alzheimer Risk

Researchers report that a ribonucleic acid (RNA) molecule called miRNA-145 may have a role in vascular disease and Alzheimer's. The study suggests that miRNA-145 may limit the growth of vascular muscle cells that cause narrowing of arteries and can lead to vascular disease. The study also revealed that miRNA-145 encourages the expression of the protein myocardin. Myocardin activates genes that may influence the rate at which the brain can remove amyloid-beta. This finding could explain why myocardin occurs in higher levels in Alzheimer's disease. Delivering miRNA-145 into vessel walls may normalize levels of myocardin and counter its negative effects.

Nature online (Print: August 6, 2009;460:705–710.)



6

Antibodies Could Hold Promise in Preventing Alzheimer's

Investigators share results of a study suggesting that antibodies in blood could play a role in preventing or slowing the progression of Alzheimer's disease. Researchers studied blood samples from more than 250 individuals aged 21–89 with and without Alzheimer's. In both groups, they found antibodies targeting many forms and aggregation-states of beta-amyloid, which is toxic to neurons in the brain. The researcher also revealed that overall levels of these antibodies decline with age and with advancing stages of Alzheimer's. The findings suggest that therapies that increase antibody levels may have a role in preventing Alzheimer's.

Proceedings of the National Academy of Sciences online (Print: July 2009;106(29):12145–12150.)

Two Studies Support Benefits of Caffeine in Mouse Models of Alzheimer's

Large quantities of caffeine reversed memory impairment in mice genetically engineered to exhibit the symptoms of Alzheimer's disease, report researchers. Mice were given the equivalent of five cups of coffee a day. Additionally, caffeine reduced abnormal levels of beta-amyloid by nearly 50 percent. Caffeine appears to restore memory by reducing enzymes needed to produce beta-amyloid. It may also suppress inflammatory changes in the brain that lead to an overabundance of beta-amyloid. More research is needed to determine if caffeine has a role in treating Alzheimer's in humans.

Journal of Alzheimer's Disease, July 2009;17(3):661–680 and 681–697.

8

Language Abilities in 20s Could Predict Alzheimer Risk

Women with more sophisticated language abilities in their 20s had a lower risk of developing Alzheimer's disease later in life, according to scientists. This was true despite the fact that these women, who had no symptoms of Alzheimer's, had evidence of Alzheimer brain changes on autopsy. Scientists reported that their brains had larger, more functional neurons, which might compensate for the beta-amyloid plaques and tau tangles that are hallmarks of Alzheimer's. These results lend support to the "cognitive reserve" hypothesis that suggests that greater years of education in early life helps the brain find alternative routes of neuron-to-neuron communication when the neurons originally used die because of Alzheimer's.

Neurology online (Print: September 2009;73(9):665–673.)

Nicotinic Receptor May Help Trigger Alzheimer's Disease

Researchers report that the combination of beta-amyloid and the nicotinic receptor alpha-7 may exacerbate Alzheimer's symptoms. Eliminating alpha-7 seems to cancel out beta-amyloid's harmful effects. The findings suggest that therapies that block the function of the alpha-7 receptor or beta-amyloid's access to it may be beneficial in Alzheimer's.

The Journal of Neuroscience, July 8, 2009;29(27):8805–8815.

12

Omega-3 Supplement Fails to Slow Alzheimer's

Findings from an 18-month study showed that taking supplements of the omega-3 fatty acid docosahexaenoic acid (DHA) did not slow cognitive decline in individuals with mild-to-moderate Alzheimer's disease, said researchers. However, a six-month study conducted by makers of a DHA supplement found that DHA helped restore some mental acuity in individuals without Alzheimer's. Additional research is needed to determine if DHA has a role in treating or preventing Alzheimer's.

Alzheimer's Association International Conference on Alzheimer's Disease

PTSD Increases Dementia Risk

Veterans aged 55 years or older who experienced post-traumatic stress disorder (PTSD) develop dementia at a higher rate than those without PTSD, say researchers. Those with PTSD developed dementia at a rate of 10.6 percent over seven years compared with 6.6 percent for veterans without PTSD. The research suggests that physicians should be especially alert to the potential signs of dementia in this population.

Alzheimer's Association International Conference on Alzheimer's Disease

Study Gives New Understanding on Successful Clinical Study Recruitment

Partnering with local physicians, working with local clinics and conducting educational seminars and health fairs are the most effective tools in recruiting people for Alzheimer clinical studies, according to researchers. Patient registries and Internet recruiting are much less successful recruitment strategies. Among African-Americans, the most powerful incentives for participating in clinical research were having a relative with the disease, receiving monetary compensation and interacting with underrepresented study personnel during the recruitment process.

Alzheimer's Association International Conference on Alzheimer's Disease

13

Some ACE Inhibitors May Lessen Cognitive Decline

Data from the long-term Cardiovascular Health Study reveals that participants who took ACE (angiotensin-converting enzyme) inhibitors that crossed the blood-brain barrier had 65 percent less cognitive decline per year than participants who took other blood pressure medications. ACE inhibitors that did not cross the blood-brain barrier increased one's risk of dementia, and the people taking them were more likely to develop difficulty performing daily activities. The study was funded in part by the **Alzheimer's Association**.

Archives of Internal Medicine, July 13, 2009;169(13):1195–1202.

14

ADNI Studies Identify Predictors of Alzheimer Risk

Data from the Alzheimer's Disease Neuroimaging Initiative (ADNI) continue to shed light on Alzheimer risk, say researchers. In a study of older people without memory or thinking problems, researchers found that those with the fastest rate of growth of white matter hyperintensities, or small areas of brain damage, were more likely to later develop permanent thinking problems that in many cases led to dementia. In a second study, researchers found that participants with low scores on a memory recall test and low glucose metabolism in certain areas of the brain (detected by positron emission tomography [PET]), had a 15-fold greater risk of developing Alzheimer's than those with higher memory scores and brain glucose metabolism.

Neurology, July 14, 2009;73(2):120–125 and *Alzheimer's Association International Conference on Alzheimer's Disease*

Controlling High Blood Pressure Through Diet May Reduce Cognitive Decline

Researchers report that individuals with high blood pressure, a potential risk factor for Alzheimer's, who adhered to the Dietary Approaches to Stop Hypertension diet had higher scores of cognitive function at the beginning of the study and over time. The results suggest that a diet of whole grains, vegetables, low-fat dairy foods and nuts may offer cognitive benefits in late life.

Alzheimer's Association International Conference on Alzheimer's Disease

Two Studies Find Being Active in Late Life May Slow Cognitive Decline

Researchers studying the physical activity and cognitive function of older adults in their 70s for over seven years report that those who were sedentary throughout the study had the lowest levels of cognitive function at the beginning of the study and experienced the fastest rate of cognitive decline. Those whose physical activity declined during the study period experienced a faster rate of cognitive decline than those with consistent activity levels. The good news is that sedentary elders who began aerobic exercise programs during the study experienced improvements in cognitive function, especially in their ability to process complex information quickly. In another study, researchers found that long-term strenuous activity may increase the risk of cognitive impairment in recently postmenopausal women. On the other hand, moderate long-term physical activity may improve late-life cognition.

Alzheimer's Association International Conference on Alzheimer's Disease

Potential Predictive Gene for Alzheimer's Discovered

Scientists shared results of a study in which inheriting the long-repeat version of the Tomm40 gene, in addition to the e3 form of the apolipoprotein E (APOE) gene, was associated with an increased risk of developing Alzheimer's and an increased risk of developing it at an earlier age. Individuals in the study carrying both genes developed Alzheimer's an average of seven years earlier—at about age 70—than individuals who inherited the APOE-e3 gene but not the Tomm40 gene. If this association is confirmed in larger studies, the presence of both genes could prove a tool for identifying those at increased risk of Alzheimer's.

Alzheimer's Association International Conference on Alzheimer's Disease

Detailed X-Ray Imaging May Help Detect Early Alzheimer's Disease

Individual beta-amyloid plaques can be seen in a mouse-brain model using diffraction-enhanced imaging (DEI), report researchers. DEI uses extremely bright X-ray beams that show not only bone, but also soft tissue in a way not possible using standard X-rays. Researchers say this is the first study to test DEI's ability to show the beta-amyloid plaques that are a hallmark feature of Alzheimer's disease. They hope to further develop this imaging tool so that it can be used to determine the presence of beta-amyloid plaques in humans.

NeuroImage, July 15, 2009;46(4):908–914.

Moderate Alcohol Consumption Lowers Dementia Risk

Investigators report that people who consume 8 to 14 alcoholic drinks per week had a 37 percent lower of developing dementia, while those who consumed more than 14 drinks per week had twice the normal risk of developing dementia. The research supports findings from other studies that suggest moderate alcohol consumption confers a lower risk of dementia.

Alzheimer's Association International Conference on Alzheimer's Disease

Blocking Endothelin-1 May Offer Benefit in Treating Alzheimer's

The enzyme endothelin converting enzyme-2 (ECE-2) may constrict blood vessels and reduce blood flow in the brain, potentially contributing to Alzheimer disease, according to researchers. This finding suggests that ECE-2-blocking drugs, already approved for treating other diseases, may be a potential treatment for Alzheimer's disease.

American Journal of Pathology, July 2009;175(1):262–270.

15

PMX205 Improves Memory Loss in Mice

Mice genetically engineered to exhibit Alzheimer symptoms ("transgenic" mice) that were treated with the drug PMX205 performed almost as well as normal mice on learning and memory tests, report scientists. In addition, treated mice had fewer Alzheimer's lesions and inflammatory immune cells than untreated transgenic mice. PMX205 prevented inflamed immune cells from clustering in brain regions with amyloid plaques. This inflammation causes brain cell damage and worsens the disease. These findings suggest that PMX205 may have potential in slowing or treating Alzheimer's.

Journal of Immunology, July 15, 2009;183(2):1375–1383.

Valproate Shows No Benefit in Treating Alzheimer-Related Neuropsychiatric Symptoms

Valproate, an anticonvulsant medication, does not prevent or delay the emergence of agitation or psychosis in Alzheimer's patients, say researchers, who compared groups who received valproate or a placebo. There were also no differences between valproate and placebo in tests of behavior, cognition or global functional status.

Alzheimer's Association International Conference on Alzheimer's Disease

16

Alzheimer Risk Knowledge Is Not Associated with Increased Distress

Results of the REVEAL (Risk Evaluation and Education for Alzheimer's Disease) study, the first to analyze the psychological effects of disclosing information about one's genetic risk of developing Alzheimer's, demonstrated that no significant short-term psychological distress occurred when test results were revealed. Those who learned they carried the APOE-e4 gene variant, which is associated with an increased risk of developing Alzheimer's, did not experience significantly greater anxiety, depression or test-related distress than non-carriers. The results provide potentially helpful information for individuals considering undergoing testing for the APOE-e4 gene, which, while increasing one's risk of Alzheimer's, does not guarantee that individuals will develop the disease.

New England Journal of Medicine, July 16, 2009;361:245-254

APOE-e4 Carriers Have Significantly Higher Risk of Alzheimer's

Having one copy of the gene variant apolipoprotein E-e4 (APOE-e4) results in a 29 percent lifetime risk of developing Alzheimer's disease, report researchers. Study participants without the gene had a 9 percent lifetime risk. Compared with non-carriers, those with the APOE-e4 gene also had earlier memory impairment—developing impairment as young as in their 50s. Those with two copies of APOE-e4 gene are at even great risk of developing Alzheimer's.

The New England Journal of Medicine, July 16, 2009;361:255-263.

21

Immunotherapy Could Offer Protection Against Alzheimer's Disease

Study results show that people who received immunotherapy in the form of intravenous immunoglobulin (IVIg) had a 42 percent lower risk of developing Alzheimer's disease over four years than those who did not receive IVIg. Researchers studied the medical records of 847 people who received IVIg treatments for other conditions as well as the records of nearly 85,000 people who did not receive IVIg. IVIg, which pumps good antibodies into the bloodstream, is being studied on a larger scale to determine whether it may be an effective treatment for Alzheimer's.

Neurology, July 2009;73:180-185.

22

BDNF Replacement a Potential Therapy for Alzheimer's

Research suggests that large amyloid-beta oligomers (clusters of beta-amyloid that precede plaque formation) are responsible for the decrease in brain-derived neurotrophic factor (BDNF) levels in mouse models of Alzheimer's disease and that replacing BDNF could be a potential treatment for the disease.

Journal of Neuroscience, July 22, 2009;29(29):9321-9329

Inhibiting RTN3 Aggregation May Help Treat Alzheimer's

The protein reticulon 3 (RTN3) has been shown to hamper the accumulation of the Alzheimer protein beta-amyloid by inhibiting the enzyme beta-secretase that is essential for beta-amyloid development. But researchers report that in mice genetically engineered to develop Alzheimer symptoms, RTN3's positive effects only occur if it does not aggregate and distort neurons. Researchers suspect that blocking RTN3 aggregation could be a potential treatment for Alzheimer's. This study was funded in part by the **Alzheimer's Association**.

Journal of Neuroscience, July 22, 2009;29(29):9163–9173.

CSF Biomarkers Show Promise in Predicting Conversion from MCI to Alzheimer's

A multicenter clinical trial shows that levels of beta-amyloid, total tau and phosphorylated tau in cerebrospinal fluid (CSF) have a high degree of accuracy in predicting which individuals with mild cognitive impairment will go on to develop Alzheimer's disease. While the results are a significant step forward in detecting who will develop Alzheimer's, further research is needed before the biomarkers can be used by physicians as a tool for early detection.

Journal of the American Medical Association, July 22, 2009;302:385–393.

24

Neuronal Stem Cells Restore Memory Loss in Alzheimer Mice

Researchers report that administering neuronal stem cells to mice with symptoms of advanced Alzheimer's resulted in significant improvements in memory tests. The stem cells did not replace lost neurons or reduce the amount of beta-amyloid plaques and tau tangles, but instead increased the production of brain-derived neurotrophic factor (BDNF), which in turn increased the number of synapses in the hippocampus of the brain. BDNF levels are decreased in the hippocampus and cortex of people with Alzheimer's. The findings lend support to the use of stem cells as a potential therapy for the disease.

Proceedings of the National Academy of Sciences online (Print: August 11, 2009;106(32):3594–13599.)

August

1

For People with Cognitive Loss, Pictures Enhance Memory Better than Words

Researchers report the results of a study testing the ability of people with mild cognitive impairment or no cognitive loss to recognize subjects in pictures and words. During the testing, researchers monitored participants' brain activity. Results showed that memory-related activity in the brain was similar for both groups when looking at pictures. When listening to words, however, the people with MCI showed less brain activity than cognitively normal people. Further research is needed to determine why people with memory loss respond better to pictures than to words. The researchers hope to use these findings to develop interventions to help people with memory problems.

Neuropsychologia, August 2009;47(10):2044–2055.

11

Enzyme's Benefit Could Offer New Direction for Alzheimer Treatment

The enzyme superoxide dismutase (SOD-2) reduces levels of superoxide (reactive oxygen) in cells and improves cognitive function in mice genetically engineered to exhibit signs of Alzheimer's, report researchers. The study, funded in part by the **Alzheimer's Association**, links superoxide to the disabling effects of Alzheimer's and suggests that SOD-2 may have a beneficial effect in treating Alzheimer's.

Proceedings of the National Academy of Sciences, August 11, 2009;106(32):13576–13581.

12

Eating a Mediterranean Diet and Being Physically Active Lowers Alzheimer's Risk

Scientists report that study participants who consumed a Mediterranean diet—consisting of olive oil, red wine, fish and fresh produce—and were the most physically active had a 60 percent lower risk of developing Alzheimer's disease than those who didn't follow the diet or exercise. This is the first study to look at the benefits of the Mediterranean diet and exercise combined.

Journal of the American Medical Association, August 12, 2009;302:627–637.

Formal Education Could Be Protective Against Alzheimer's

Researchers report that education diminishes the impact of Alzheimer's disease on cognitive function even if brain volume loss has already occurred. This research supports the theory that those with more formal years of education have a "cognitive reserve," or resilience against the brain damage of Alzheimer's.

Journal of Alzheimer's Disease, August 2009;17(4):855–862.

High Intake of Fruit and Vegetables Linked to Better Cognitive Performance

Researchers studying the impact of diet on cognitive function find that healthy people aged 45 to 102 who consumed 400 grams of fruits and vegetables daily had higher antioxidant levels, less evidence of free radical damage and better cognitive performance than those consuming less than 100 grams of fruits and vegetables. This finding supports other data suggesting that modifying lifestyle factors such as diet may decrease one's risk of cognitive impairment.

Journal of Alzheimer's Disease, August 2009;17(4):921-927.

24

People With High Blood Pressure Have Increased Alzheimer Risk

A study of nearly 20,000 people over age 45 shows that for each 10-point increase in diastolic blood pressure, a person's likelihood of developing memory problems increases 7 percent. A rise in diastolic blood pressure can cause arterial walls in the brain to thicken more quickly than normal, potentially causing reduced blood flow and tissue death. The results of this study strengthen the belief that modifying lifestyle factors such as blood pressure may help reduce one's risk of cognitive dysfunction.

Neurology, August 2009;73:589-595.

MRI Finds Brain Hyperactivity Might Compensate for Disease-Related Deterioration

Using functional magnetic resonance imaging (fMRI) to monitor the brain activity of cognitively normal individuals, scientists find that those with a family history of Alzheimer's disease or genetic markers of the disease had increased activation in certain areas of the brain when asked to recall people's names. This hyperactivity may indicate that these brain areas must work harder to compensate for very early brain changes caused by Alzheimer's.

Neurology, August 2009;73:612-620.

Keeping the Brain Active May Help Delay Onset of Dementia

Researchers report that staying mentally active may help delay the onset of dementia. They interviewed almost 500 healthy people in their late 70s to find out how many cognitive activities (reading, crossword puzzles, card games, group discussions, or playing music) they participated in and for how many days a week. Among individuals who went on to develop dementia, those with the highest activity level (about 11 activities a week) developed dementia an average of 15.5 months later than those with the lowest activity level (four activity days per week). The finding supports others that suggest that staying mentally active may impact cognitive decline.

Neurology, August 2009;73:356-361.

High Cholesterol in 40s More Than Doubles Risk of Late-Life Dementia

A 40-year study of nearly 10,000 men and women reveals that having high cholesterol in one's 40s increases the risk of developing Alzheimer's disease later in life by 66 percent. The study also showed that even moderately elevated cholesterol levels raise dementia risk. These data lend support to the idea that modifiable lifestyle factors such as diet and exercise may influence cognitive health.

Dementia and Geriatric Cognitive Disorders, August 2009;28(1):70-74.

September

3

RanBP9 Protein Increased in Alzheimer Brains, Offers a Potential Drug Target

Researchers find that the N60 fragment of the protein RanBP9 increases the production of the amyloid precursor protein (APP), which is present in great amounts in the Alzheimer brain. Targeting RanBP9 expression and/or the N60 fragment may lead to novel strategies to combat Alzheimer's disease.

The Journal of the Federation of American Societies for Experimental Biology, September 2010;24:119–127.

6

Discovery of Two Gene Variants Advances Understanding of Alzheimer Risk

Researchers pooling 16,000 DNA samples from European and U.S. databases discover that two gene variants—CLU (ApoJ/clusterin, located on chromosome 8) and PICALM (phosphatidylinositol-binding clathrin assembly protein, located on chromosome 11)—are associated with increased Alzheimer risk. Thirteen other potential gene variants were identified and warrant further study.

Nature Genetics online (Print: December 2009;41(12):1308-1312.)

Drug in a Family of Cancer Compounds Improves Memory in Mice

Researchers report that using a drug from a family of compounds now used to treat cancer resulted in improved memory in mice genetically engineered to develop Alzheimer's. Administering the drug, a histone deacetylase inhibitor, improved memory performance to the level found in normal mice. More research is needed to determine if the drug would have the same effect in humans.

Journal of Alzheimer's Disease, September 2009;18(1):131–139.

21

Individualized Immunotherapy for Alzheimer's Could Be on the Horizon

Research on a vaccine for Alzheimer's has revealed that the brain triggers a natural immune response when beta-amyloid is introduced. How the body responds to beta-amyloid depends on key genes of the immune system. This study, partially funded by the **Alzheimer's Association**, helps lay the groundwork for developing an individually based immunotherapeutic approach to Alzheimer's disease, since different populations will respond differently to a vaccine based on their genetic backgrounds.

Journal of Immunology, September 2009;183:3522–3530.

22

Even Mild Infections Hasten Decline With Alzheimer's

Temporary illness or conditions that can trigger inflammation in the body, such as a respiratory infection or a bruise, are associated with an increased rate of memory loss in people with Alzheimer's disease, report researchers. The reason may be that people with Alzheimer's can have high levels of tumor necrosis factor-alpha (TNF-a)—a protein associated with inflammation—in their blood. Individuals who had high levels of TNF-a or chronic inflammatory illness at the beginning of the study had 10 times the rate of memory decline as those who did not.

Neurology, September 2009;73:768–774.

Phone-Based Cognitive Assessments Could Be Effective

Study results show that telephone and in-person cognitive assessments in elderly individuals were comparable in effectiveness, suggesting that telephone assessment may be a useful, cost-effective and time-efficient alternative to in-person assessment of cognition in the elderly. Greater use of telephone assessments could provide cognitive evaluations to a wider range of people, including those who live in rural areas or at great distances from medical centers.

International Journal of Geriatric Psychiatry, September 2009; 25(5):531–539.

24

Lack of Sleep May Contribute to Alzheimer's

Researchers monitoring beta-amyloid levels in the brains of mice report that sleep deprivation boosted beta-amyloid levels and were associated with increased plaque formation. Although the research is preliminary, the possible link between sleep deprivation and Alzheimer's raises the prospect of possible treatments that target sleep-related pathways in the brain.

Science online (Print: November 13, 2009;326(5955):1005–1007)

29

Decreased Heart Rate Associated with Use of Cholinesterase Inhibitors

After analyzing medical information from 1.4 million people aged 67 and older, researchers report that people who recently started on cholinesterase inhibitors for Alzheimer's were nearly twice as likely to be hospitalized with bradycardia, or slowed heart rate, as other individuals. The study highlights the potential adverse effect of cholinesterase inhibitors on heart rate, and researchers urge professionals to reassess the benefits of continuing cholinesterase inhibitor therapy in people who develop bradycardia while taking these drugs.

PLoS Medicine, September 2009;6(9):e1000157.

30

NFL Study Shows Players Have Increased Dementia Risk

A study commissioned by the National Football League (NFL) shows that former NFL players ages 30–49 were diagnosed with Alzheimer’s and related memory-related disease at a rate 19 times that of the general population. The results support the link between head injury and increased dementia risk, however, additional research is needed to better understand dementia risk in these former athletes.

National Football League

Inhibiting Hsp70 a Novel Path in the Development of Alzheimer Therapies

Researchers report that inhibiting the protein Hsp70 clears the tau tangles of Alzheimer’s in mouse studies. Their goal is to develop an Hsp-70 inhibitor that will prove safe and effective in humans.

This study was partially funded by the **Alzheimer’s Association**.

Journal of Neuroscience, September 2009;29:12079–12088.

October

6

PP5 Enzyme May Protect Against Beta-Amyloid Toxicity

The enzyme protein phosphatase 5, or PP5, may protect neurons from cell death caused by reactive oxygen species such as free radicals that are linked to beta-amyloid, report researchers. In cell culture studies, they found that overexpression of PP5 prevented neuronal death by stopping harmful processes that occur with the generation of reactive oxygen species. The excess beta-amyloid production of Alzheimer’s has been associated with increased generation of reactive oxygen species. The finding could mean that PP5 may be protective against other health issues caused by reactive oxygen species, such as stroke and heart attack.

Journal of Neurochemistry, October 2009;111(2):391–402.



Decline in Cognitive Skills, Not Memory Loss, May Be First Clue to Alzheimer's

Researchers report that loss of cognitive skills such as visuospatial abilities—being aware of one's surroundings and how objects relate to each other in space—may be an early symptom of Alzheimer's disease, occurring even before memory loss. The study reveals that a sharp decline in visuospatial abilities may be seen three years before clinical diagnosis of Alzheimer's disease, and that a sharp decline in overall cognitive ability occurred two years before diagnosis. Verbal and working memory declined one year before diagnosis. The findings suggest that evaluation of visuospatial abilities may be especially important in early detection of Alzheimer's disease.

Archives of Neurology, October 2009;66:1254–1259.

12

Higher Beta-Amyloid Levels in Plasma Are Associated with Cognitive Decline

Study results show that people who have high ratios of beta-amyloid 1-40 to beta-amyloid 1-42 in plasma in midlife and who experience an increase in these ratios 10 years later are at greater risk for cognitive decline later in life than individuals without elevated ratios. If confirmed in other studies, this ratio could serve as a biomarker for Alzheimer's and help identify Alzheimer risk before symptoms develop.

Archives of Neurology, October 2009;66(10):1247–1253.

16

Activation of Microglia Removes Beta-Amyloid Plaques in Mice

Researchers report that when microglia, the brain's immune cells, are activated by the protein interleukin-6, they eliminated beta-amyloid plaques instead of causing or worsening them. This study, conducted in mice genetically engineered to develop Alzheimer's, could lead to the development of Alzheimer's disease treatments that manipulate the brain's immune response.

The Federation of American Societies for Experimental Biology Journal online (Print: February 2010;24(2):548–559.)

November

10

Greater Muscle Strength Associated with Less Risk of Alzheimer's

Older people who have greater muscle strength are less likely to develop Alzheimer's disease, report researchers. Their study results further support the connection between physical health and cognitive function. Researchers studied 970 people over age 54 and found that those who were in the top 10 percent for muscle strength were 61 percent less likely to develop Alzheimer's than the weakest 10 percent. Stronger people also showed a slower decline in mental abilities over time.

Archives of Neurology, November 2009;66:1339–1344.

Ability to Multitask May Differentiate Depression from Alzheimer's

Study results show that a person's ability to multitask may be a distinguishing factor between early Alzheimer's disease and depression, which can have common symptoms. Researchers found that, compared with depressed people and healthy, non-depressed individuals, people with Alzheimer's performed significantly worse when given multiple tasks to perform, despite being given allowances for memory deficits.

Journal of Neurology, November 2009;256:1860–1868.

11

Dementia Risk Elevated After Multiple Strokes

Researchers report that the number of strokes experienced are tied to dementia risk. People who had a recurrence of stroke were three times more likely to develop dementia within a few months than those who had one stroke. The finding suggests that physicians be especially alert to the signs of dementia in patients with a history of multiple strokes.

The Lancet Neurology, November 2009;8(11):1006–1018.

17

Protein Attempts to Repair Alzheimer Brain Damage

Researchers report that the protein Vimentin, which is released from neurons in the brain when the neurons' dendrites and synapses degenerate in Alzheimer's, attempts to repair the brain damage caused by Alzheimer's. A similar damage-response mechanism has been seen after traumatic brain injury, suggesting that therapeutic agents could be developed to enhance repair both for sudden brain trauma and progressive neurodegenerative diseases. This study was partially funded by the **Alzheimer's Association**.

Brain Research, November 17, 2009;1298:194–207.

18

Down Syndrome Study Could Shed Light on Alzheimer's Disease

Boosting norepinephrine signaling in the brains of mice genetically engineered to develop symptoms of Down syndrome improves their cognitive function, report scientists. Norepinephrine is a neurotransmitter that nerve cells use to communicate. If intervention occurred at an early age in children with Down syndrome, it could lead to an improvement in cognitive abilities. Most individuals with Down syndrome ultimately develop Alzheimer's disease, and results of this study could shed light on methods to improve cognitive function in Alzheimer's as well. This study was partially funded by the **Alzheimer's Association**.

Science Translational Medicine, November 18, 2009;1(7):7–17.

20

MRI Technique Aids in Early Detection, Tracking Alzheimer's Progression

Scientists describe how, using magnetic resonance imaging (MRI), they were able to measure atrophy in very precise areas of the brain. These sub-regional brain volume measurements outperformed other measures used for tracking Alzheimer severity, including tests of overall brain atrophy and some common cognitive tests for the disease. Brain atrophy in some areas is a particularly sensitive measure of the early stages of Alzheimer's. Measurements of these areas could aid in early detection of the disease.

Proceedings of the National Academy of Sciences online (Print: December 8, 2009;106(49):20954–20959.)

22

Beta-Amyloid Helps Maintain Normal Brain Function, Study Reports

Research results show that beta-amyloid plays an important role in maintaining the day-to-day function of the brain. Removing beta-amyloid from the brain, which is the goal of many Alzheimer drugs being developed, can impair neuronal function, say researchers. In cell culture and mouse studies, researchers found that an optimal amount of beta-amyloid is needed for healthy neuronal function and that the smallest imbalance in beta-amyloid production impairs neuron-to-neuron communication. Study findings highlight the importance of examining multiple potential causes of Alzheimer's disease, not just beta-amyloid.

Nature Neuroscience, November 2009;12:1567–1576.

Imaging Technique Shows Healthy APOE-e4 Carriers Have Same Brain Changes as People with Alzheimer's

Using automated neuroimaging analysis techniques, researchers find that cognitively healthy older people with the APOE-e4 Alzheimer risk gene had reduced cognitive performance and decreased brain volume in the hippocampus and amygdala (regions important for memory processing) compared with people without the APOE-e4 gene. These brain changes are also found in people with Alzheimer's and suggest that these cognitively normal individuals may already be experiencing the early, presymptomatic stages of the disease.

Journal of Alzheimer's Disease, November 2009;18(3):553–564.

December

11

Reducing the IGF-1 Signaling Pathway Slows Aging, May Delay Alzheimer's

Researchers report that altering the IGF-1 (insulin-like growth factor 1) signaling pathway, which is known to slow aging in mice, also improved animals' ability to function on various cognitive tests. When IGF-1 activity was cut in half, mice lived up to 35 percent longer. Although the long-lived mice tended not to show any of the cognitive or behavioral impairments typical of people with Alzheimer's, their brains were riddled with highly compacted beta-amyloid plaques. This suggests that beta-amyloid plaques may not be key players in Alzheimer's disease.

Cell, December 11, 2009;139:1157–1169.

14

Beta-Amyloid Raises Alzheimer Risk in People without Cognitive Problems

Two studies show that cognitively healthy people with high levels of beta-amyloid deposits in the brain have a greater risk of developing Alzheimer's, as well as a greater risk of decreasing brain volume and cognitive decline. The findings suggest that beta-amyloid accumulation may be a sign of Alzheimer's disease even before symptoms have developed.

Archives of Neurology, December 2009;66:1469–1481.

16

High Leptin Level Linked to Lower Risk of Alzheimer's Disease

A study of 200 older individuals shows that those with high levels of leptin, a natural hormone produced by fat cells, had a decreased likelihood of developing Alzheimer's. Individuals who are obese typically have low levels of leptin. This finding supports previous research connecting Alzheimer's risk and obesity.

Journal of the American Medical Association, December 16, 2009;302:2565–2572.

23

Ginkgo Biloba Does Not Improve Memory

Ginkgo biloba, an extract from the ginkgo tree, failed to improve memory and prevent cognitive decline in cognitively normal older people and older people with mild cognitive impairment, report researchers. The Ginkgo Evaluation of Memory study, conducted at six medical centers and involving more than 3,000 people between ages 72 and 96 for seven years, was larger than all previous ginkgo studies combined. Study results published in 2008 found that ginkgo was not effective in preventing Alzheimer’s dementia or dementia overall, while this study examined whether ginkgo had any effect on cognitive decline, specifically memory, visual-spatial construction, language, attention, psychomotor speed and executive function.

Journal of the American Medical Association, December 23/30, 2009;302(24):2663–2670.

27

Overproduction of Beta-Amyloid Decreases Neuronal Plasticity

Researchers report that overproduction of the Alzheimer protein beta-amyloid decreases the ability of brain cells’ dendrites to grow and change—referred to as “plasticity”—which in turn decreases the transmission of information throughout the brain cell. This weakens the individual brain cell or neuron, as well as circuits of neuron-to-neuron communication that are essential to learning and memory. These findings provide new insight into beta-amyloid’s potential role in Alzheimer’s.

Nature Neuroscience online (Print: February 2010;13(2):190-196.)Volume:

