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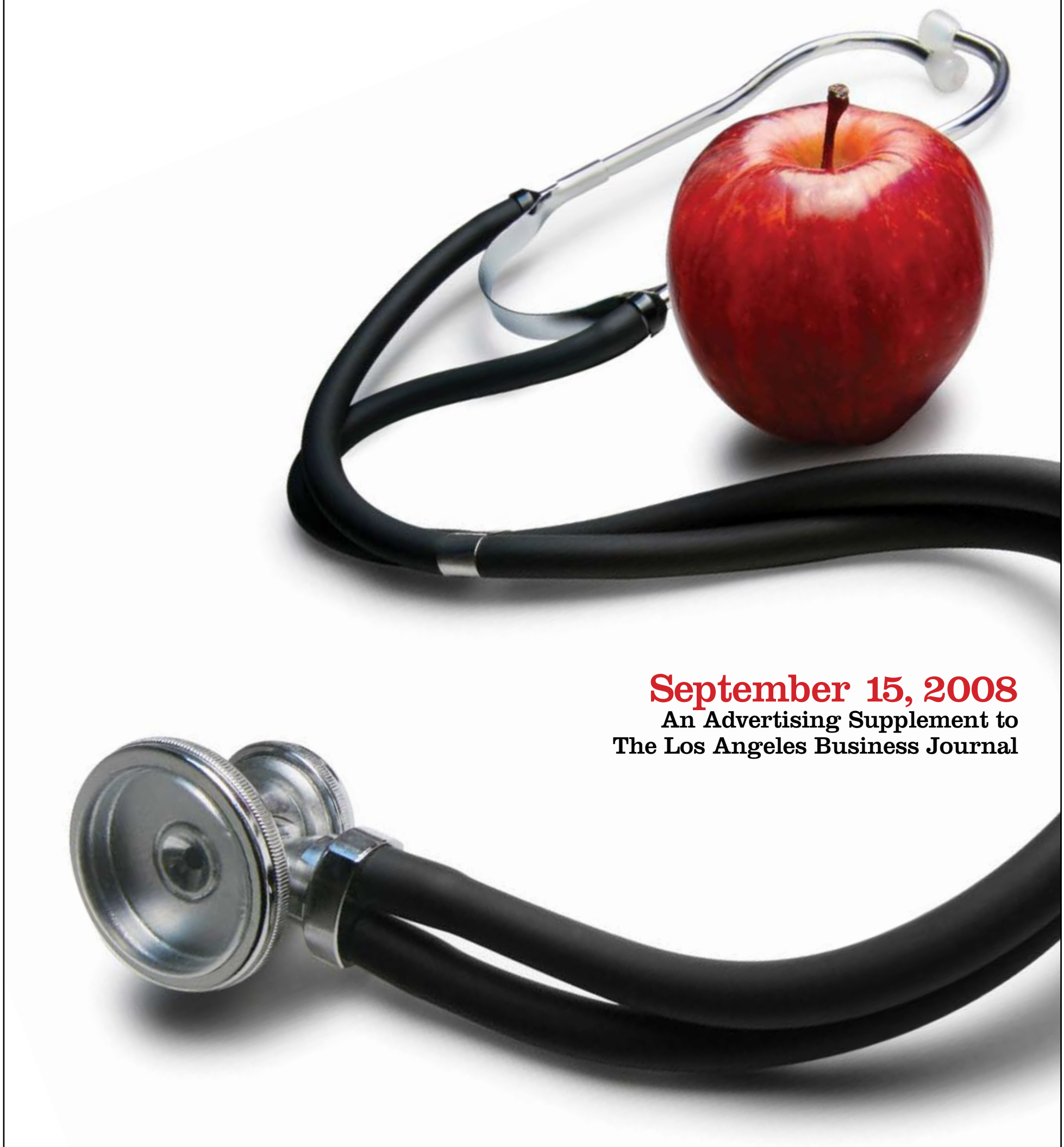

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HealthCare

No Slowdown for Healthcare M&A in 2008

By PAUL KACIK

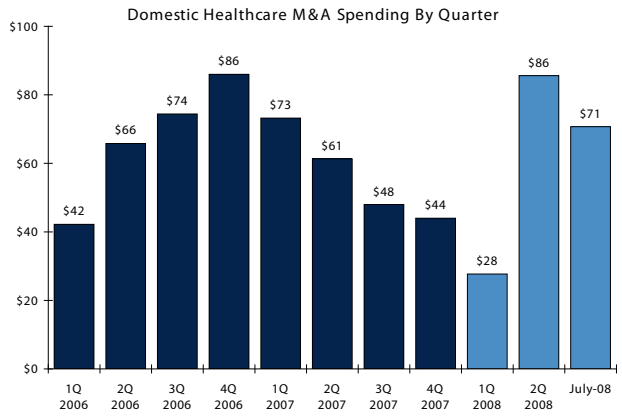
Despite the economy and the turmoil in the public equity and debt capital markets, Healthcare merger & acquisition activity has shown impressive strength in 2008. While M&A activity and spending in the overall market has declined 29.2% and 53.6%, respectively so far this year, Healthcare M&A activity remains even with last year's pace and acquisition spending has actually increased 9.4% over 2007 levels.

According to data compiled by Barrington Associates, the Healthcare market witnessed 568 announced M&A transactions from January to July 2008. For the same period in 2007 there were 569 Healthcare deals, making 2008 essentially even with last year's performance through seven months. Furthermore, M&A spending in 2008 through July was $184 billion, an increase over the $168 billion spent during the same period in 2007. Considering that 2007 was one of the most active years in Healthcare M&A history, this level of activity in the 2008 is even more impressive.

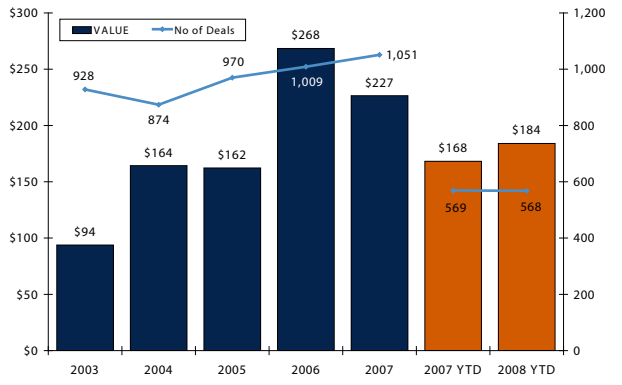
What is driving this resilient M&A activity? Here are a few of the most impacting trends:

Trend 1: Strategic Acquirer Appetite

The current debt market environment has returned the advantage in M&A processes to strategic acquirors. Coming off several years of robust earnings growth, leading strategic buyers are showing strong demand for acquisitions to continue their growth amidst a sluggish economy. While large biotech and pharma transactions have taken much of the spotlight this year, there is robust acquiror interest in mid-sized deals, especially among NASDAQ-listed companies in the healthcare services space.



Total Domestic Healthcare M&A



Trend 2: Technology Investment En Vogue

Technology-fueled sectors like biotech, medical devices, pharmaceuticals, contract research, and e-health are driving acquisition activity in 2008. While more traditional services have experienced consolidation, the most robust strategic growth plays have been for technology and innovation. With biotech leading the way (16 announced transactions worth $50 billion in July alone), technology-focused M&A activity has been a major driver of this year's surprising level of activity.

Trend 3: International Acquirer Activity

Whether or not the devaluation of the American dollar is a motivator in and of itself for cross-border deals, the truth is foreign buyers have been very active in 2008. In recent months France's Sanofi-Aventis, England's GlaxoSmithKline, Germany's Bayer, Switzerland's Roche, Sweden's LinkMed, and a host of other international buyers have made bids for U.S. companies. In July, nearly 30% of all announced acquisitions of U.S. companies were made by international acquirors, a trend to watch in the ensuing quarters.

Looking ahead, all signs point to continued activity in the technology sectors of the Healthcare industry. On the services side, growth via acquisitions remains a priority for many public companies, which should continue to drive activity in the middle market, in particular.

Paul Kacik is Head of Healthcare Investment Banking in the Newport Beach office of Barrington Associates, a division of Wells Fargo Securities, LLC (member FINRA/SIPC). Wells Fargo Securities LLC is a broker-dealer and full- service investment banking firm. The opinions expressed herein are solely those of the author and may not represent those of Barrington Associates. A transaction similar to those described in this article may not be suitable for you or your company. Data used is from sources Barrington Associates considers reliable, however Barrington does not guarantee its accuracy. For more information please contact Paul Kacik at (949) 719-6200 or pkacik@barrington.com.

Tendon Injuries: Common Problems Find a Futuristic Solution

Doctors Utilize Radiofrequency Technology to Help Heal Common Tendon Problems

By BRUCE HARTZELL

As more and more people of all ages take up "weekend warrior" activities such as tennis, golf, hiking, running and other outdoor sports, and as the fitness craze in general continues to grow, people tend to be healthier as a whole. But a passion for working out can be rudely interrupted by tendon-related aches and pains that can be bad enough to sideline even the fittest of us.

Some of the tendon problems fitness buffs can face include lateral epicondylitis (tennis elbow), plantar fasciitis (heel pain), achilles tendonitis and shoulder and knee pain. These are not uncommon afflictions either — plantar fasciistis is the most commonly reported complaint among patients visiting podiatrists today, with over 20 million Americans suffering from the condition, and tennis elbow is the most common elbow injury suffered by active adults including tennis players and other exercisers.

For many people, the answer is rest, bracing, physical therapy, medicines or injections. In some cases, however, where tendons don't properly heal, patients are often left considering invasive surgery that can involve significant recovery time. That is, until recently.

A new medical technique referred to as "Topaz" is enabling a less invasive alternative based on radiofrequency technology and is being quickly adopted by sports medicine specialists around the country. The technology offers an innovative advancement in the treatment of tendons and fascia and yields significantly faster recovery times.

The physician places the patient under mild sedation. After two small ½ inch incisions are made (dramatically smaller than what would be made in a traditional invasive tendon surgery), the doctor then treats the problem area with Topaz technology, removing tiny fragments of the problematic tendon, which stimulates a healing response. The treated area is rinsed and closed and medication is given. From start to finish, the whole process takes about 15 minutes. Patients are ready to leave the clinic once recovered from light anesthesia.

"By using Topaz to treat tendon injuries, we're able to help people return to their normal routines much faster than using traditional surgery," said Dr. Bob Baravarian, a foot and ankle surgeon based at Santa Monica/UCLA Medical Center. "The surgical procedure takes only minutes to perform and recovery

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times are much shorter than with traditional surgery."

Coblation: The Innovative Science Behind Topaz

Topaz is a procedure that utilizes the science of Coblation technology – now a widely utilized alternative to standard surgical techniques for removing and treating tissue in a number of specialties. Topaz enables the micro-debridement of soft tissue, such as tendons in the knee, shoulder, elbow, the ankle and foot. The Topaz procedure uses Coblation technology to preserve the anatomical structure of the tissue while delivering a precisely controlled amount of radiofrequency energy – which is what stimulates the healing response in the tissue.

While most radiofrequency-based surgical products, lasers, and electrosurgical devices use heat-driven processes to remove or cut tissue, Topaz's Coblation-based radiofrequency wand operates at a lower temperature, allowing for more precise procedures than would be performed by traditional surgical tools. Instead of exploding tissue structures under high temperatures, Coblation technology gently dissolves target tissue, minimizing damage to surrounding healthy tissue.

In the case of Topaz technology, the gentle tissue-dissolving process provided by Coblation is applied specifically for the microdebridement of soft tissues such as tendons and fascia.

Clinical Study

The results of a recently completed two-year study published in Arthroscopy: The Journal of Arthroscopic & Related Surgery showed Topaz to be especially effective in treating chronic lateral epicondylitis (tennis elbow).

Pain relief was achieved rapidly in all participating patients and diminished even further with time.

The study consisted of patients of the San Diego Sports Medicine & Orthopaedics Center (SDSM) who had been suffering from the symptoms of tennis elbow for six months or longer. Each of the patients had failed to achieve relief after conservative treatment, yet each reported "significantly reduced" pain only seven to 10 days after Topaz procedures. In fact, the vast majority of subjects reported noticeable reduction in pain only one or two days after the procedure.

"Our findings from the study demonstrate this procedure is technically simple to perform and is associated with a rapid and uncomplicated recovery," said SDSM founder James P. Tasto, MD, one of the study's authors and Clinical Professor of Orthopedic Surgery at UCSD. "Pain relief was achieved rapidly in all participating patients and diminished even further with time. Based upon our results, the procedure is safe and effective for at least two years, post-op. Treatment utilizing the Topaz MicroDebrider offers a new, minimally invasive alternative for millions of patients for whom conservative therapies have failed."

With tennis elbow, the tendons involved are responsible for anchoring the muscles that extend or lift the wrist and hand. Patients often complain of severe, burning pain on the outside part of the elbow. In most cases, the pain starts in a mild and slow fashion. It gradually worsens over weeks or months.

"This study's results are particularly meaningful because they center around a technology and treatment that have the opportunity to help a large population," Tasto said. "Tennis elbow is the most common injury among patients seeking help for elbow pain. It should also be noted that over the same period of time that our data was collected for this particular study, patients with tendinosis of the medial epicondyle of the elbow (a different elbow tendon condition), the Achilles and patellar tendons were also treated with Topaz – and yielded similar results. We're certainly not limiting this kind of treatment to tennis elbow cases. We've seen similarly positive results among patients suffering from tendon problems in other parts of the body, such as the shoulder and foot. I see great promise for this technology in an array of applications."

In short, Topaz provides patients with a treatment option that is less invasive and less traumatic, resulting in a potentially dramatic reduction in recovery time. For example, a patient suffering from a problem such as plantar fasciitis, exhibited by heel pain and a painful stiffening of the arch of the foot would be faced with the traditional surgical treatment, which is to cut a large incision at the bottom of the foot which can flatten the arch and decrease foot stability, requiring a lengthy and somewhat painful recovery. Because TOPAZ is minimally invasive, only a small incision is required, and since the Topaz treatment itself preserves the anatomical structure of the patient's foot while inducing a healing response, recovery times can be significantly shorter.

Thanks to this modern technology, more and more people suffering from tendon complaints are working out again – and faster than they expected to.

To learn more about Topaz, or to fond a surgeon in your area utilizing the technology, visit www.TopazInfo.com. Bruce Hartzell is a freelance writer.

Scientists Isolate a Toxic Key to Alzheimer's Disease in Human Brains

Soluble Beta-Amyloid Protein Fragments May Damage Brain Cells, Study Finds

SCIENTISTS have long questioned whether the abundant amounts of amyloid plaques found in the brains of patients with Alzheimer's actually caused the neurological disease or were a by-product of its progress. Now, using new research techniques, scientists have shown that a two-molecule aggregate (or dimer) of beta-amyloid protein fragments may play a role in initiating the disease. The study, supported by the National Institutes of Health, suggests a possible new target for developing drug therapies to combat the irreversible and progressive disorder.

Ganesh M. Shankar, Ph.D., and Dennis J. Selkoe, M.D., of Brigham and Women's Hospital and Harvard Medical School, conducted the study in collaboration with other researchers at Harvard and in Ireland at University College Dublin, Beaumont Hospital and Royal College of Surgeons Ireland, and Trinity College Dublin. The National Institute on Aging (NIA), part of NIH, funded the study which appeared in the June 22, 2008, Nature Medicine.

Alzheimer's disease is marked by the build-up of plaques consisting of beta-amyloid protein fragments, as well as abnormal tangles of tau protein found inside brain cells. Early in the disease, Alzheimer's pathology is first observed in the hippocampus, the part of the brain important to memory, and gradually spreads to the cerebral cortex, the outer layer of the brain. In this study, researchers tested cerebral cortex extracts from brains donated for autopsy by people aged 65 and older with Alzheimer's and other dementias, as well as those without dementia. The extracts contained soluble one-molecule (monomer), two-molecule (dimer), three-molecule (trimer) or larger aggregates of beta-amyloid, as well as insoluble plaque cores. The researchers then injected the extracts into normal rats or added the extracts to slices of normal mouse hippocampus.

Shankar, Selkoe and colleagues discovered that both the soluble monomers and the insoluble plaque cores had no detectable effect on the hyppocampal slices. However, the soluble dimers induced certain key characteristics of Alzheimer's in the rats. The dimers impaired memory function, specifically the memories of newly learned behaviors. In the mouse hippocampal slices, the dimers also reduced by 47 percent the density of the dendrite spines that receive messages sent by other brain cells. The dimers seemed to be directly acting on synapses, the connections between neurons that are essential for communication between them.

To confirm this effect, the researchers then injected certain antibodies against beta-amyloid protein fragments. These latched onto and inactivated the dimers, preventing their toxic effects in the animal models. However, much work remains to be done before inactivation of dimers could move into the clinic.

"Scientists have theorized for many years that soluble beta-amyloid may be critical to the development and progression of this devastating disease. Now these researchers have isolated a candidate causative agent from brains of people with typical Alzheimer's and directly tested it in an animal model," said NIA Director Richard J. Hodes, M.D. "While more research is needed to replicate and extend these findings, this study has put yet one more piece into place in the puzzle that is Alzheimer's."

The animal findings were consistent with what the researchers found when they examined the brain tissues of people who had been clinically diagnosed with Alzheimer's and those without dementia. They detected soluble dimers and some trimers of amyloid in the brains of patients with Alzheimer's, but none or very low levels in those free of the disorder. Some people free of the disorder, however, did have insoluble amyloid plaques in their brains.

"These findings may help explain why people with normal cognitive function are sometimes found to have large amounts of amyloid plaques in their brains, which has been a puzzle for some time," said Marcelle Morrison-Bogorad, Ph.D., director of the NIA Division of Neuroscience. "Their findings noted that the brain of an individual who was never clinically diagnosed with dementia was found with abundant insoluble Alzheimer's plaques, but no soluble beta-amyloid."

Selkoe and Shankar noted that further insights into the early stages of this disease process may answer questions not only about Alzheimer's, but also about age-related memory impairments. "The approaches we used to isolate dimers and the widespread availability of tissues from brain banks, open new avenues of investigation into how these aggregates induce Alzheimer's disease," said Selkoe. "We still need to find out why dimers in particular are so destructive to neurons."

NIA leads the federal government effort conducting and supporting research on the biomedical and social and behavioral aspects of aging and the problems of older people. For more information on aging-related research and the NIA, please visit www.nia.nih.gov. The NIA provides information on age-related cognitive change and neurodegenerative disease specifically at its Alzheimer's Disease Education and Referral (ADEAR) Center site at www.nia.nih.gov/Alzheimers. To sign up for e-mail alerts about new findings or publications, please visit either Web site.

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