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Welcome to the first issue of our quarterly newsletter! 21<sup>st</sup> Century Neurology was founded in April of 2001 and has since grown tremendously.

Exciting things are happening in Neurology, the study of diseases which affect the brain and nervous system. At this time, researchers are engaged in many projects which are aimed at better means of diagnosing and treating diseases such as Alzheimer's disease, Parkinson's disease, multiple sclerosis, epilepsy, peripheral neuropathy, migraine and atypical pain syndromes like postherpetic and trigeminal neuralgias. At this time, Dr. Flitman and his staff are working on more than 15 clinical trials aimed at providing new therapeutic approaches to these diverse conditions. If you or someone you know is interested in a clinical trial, please call us or see our website for updated information.

lzheimer's disease (AD) is a common condition that affects Amostly people over age 65 but can happen as early as age 40. It occurs equally in men and women and leads to loss of short-term memory while long-term memory is preserved or is even better than normal. Treatments that are currently available include five prescription drugs, of which four are in common use, and herbal and vitamin therapies which may have value but remain controversial. The prescription drugs fall into two classes. The first were the cholinesterase inhibitors, drugs which prevent the breakdown of acetylcholine, a chemical messenger in the brain important to memory and thinking. Acetylcholine levels were observed to be low in the brains of patients with AD in the 1970s. The first drug approved in 1993 was Cognex (tacrine), which gave patients a mental boost but unfortunately caused liver damage which limited its use. The second drug approved in 1997 was Aricept (donepezil), which does not affect the liver and can have dramatic effects in about a third of patients. The third drug approved in 2000 was Exelon (rivastigmine), which adds a second enzyme inhibiting effect which makes it quite potent in improving memory and cognition. The fourth drug approved in 2001 was Reminyl, now renamed Razadyne (galanthamine), which actually was found in daffodils and so an herbal version exists. Razadyne ER is a once-daily version of the drug which became available this year.

The second class of drugs for AD are the selective NMDA antagonists. At this time the only approved drug in this class is Namenda (memantine), which works in a complementary way to the first class, so a drug in that class like Exelon or Aricept is often combined with Namenda for better effect. Namenda produces improvement in cognition and memory which is synergistic with the effect of a cholinesterase inhibitor, and can also work on its own. There is reason to believe that Namenda may have anti-amyloid effects which could slow down the course of the disease, but this has not been proven in patients.

Herbal therapies for Alzheimer's disease have included gingko biloba, which unfortunately causes unpredictable bleeding; Chinese club moss, which contains Huperzine A, a substance similar to donepezil with cholinesterase inhibitor effect; and turmeric, the curry spice, which has been shown to reduce amyloid production in mice. Of these, Dr. Flitman feels adding a little turmeric to one's diet is likely safe and may be beneficial, but studies need to be done. He has submitted a grant application to study this spice further. No good supportive data exists for either gingko or Huperzine at this time, and it is clear that prescription drugs are superior to herbal preparations because they provide a fixed and reproducible dose, where herbals tend to vary from dose to dose which is often detrimental to brain function.

Vitamins have been touted for nearly any disease state one can name. For AD, there has been a lot of focus on Vitamin C and Vitamin E which are both anti-oxidants, substances which eliminate free radicals which are naturally produced in the body and are toxic to DNA and cell membranes. At this time, Vitamin E at a high dose of 2000 IU daily has been shown to delay the progression of disease by up to a year, but a recently published analysis combining the results of many other studies has suggested increased risk to taking more than 400 IU daily. That analysis is limited because it is not new data, merely rehashing old data in a way which is not as scientific as a brand new double-blind and placebo-controlled study of the effects of Vitamin E. The high dose of 2000 IU daily was used safely in two published large studies.

Myriad Pharmaceuticals has a phase III trial underway of their unique compound Flurizan. According to the company's website <u>www.myriad.com</u> Flurizan changes the point at which brain cell enzymes cut the plaque protein. This makes a range of smaller proteins than the typical amyloid beta 42 protein which makes up the core of plaques in AD. Smaller proteins may disrupt accumulation of toxic plaque and enhance transport of plaque proteins into the bloodstream for disposal. The company has reported good results in earlier clinical trials and there is hope that the current large trial may be acceptable for FDA approval.

Neurochem, a Canadian company, has an alternative approach. Their current phase III trial of their unique compound Alzhemed promises to determine if existing plaque in the brains of AD patients can be reduced by making the protein more soluble, which may enhance clearance. According to the company's website <u>www.neurochem.com</u> the drug has so far demonstrated an excellent safety profile. The current trial has the potential to pave the way for FDA approvability. **\*** 

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