Trends-in-Medicine

November 2003
By Lynne Peterson

SUMMARY

Elan/Wyeth's Alzheimer's Disease vaccine, AN-1792, may be revived. ♦ The outlook is for widespread use both on-label and off-label of Forest Lab's Namenda (memantine) for Alzheimer's disease. ♦ The various atypical antipsychotics perform quite differently from each other in bipolar disorder and in Parkinson's Disease. ♦ The failure of Biogen's antegren in Crohn's Disease does ***not*** predict how the drug will do in multiple sclerosis. ♦ Both Teva's Copxaone and Ares Serono's Rebif are expected to continue to gain market share, mostly at the expense of Biogen's Avonex. New research also suggests that Copaxone may work in MS – and other neurodegenerative diseases – when given monthly or even less frequently, and investigator-sponsored trials are being planned. ♦ Pfizer's pregabalin for neuropathic pain is generating little excitement and is viewed by many doctors as a me-too drug.

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AMERICAN NEUROLOGICAL ASSOCIATION
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San Francisco, CA

The American Neurological Association (www.aneuroa.org) is an invitation-only society of academic neurologists and neuroscientists. Requirements for membership include a doctoral degree in medicine or neurological science, excellence in teaching and research in clinical neurological science, and at least 10 scientific papers published in national and international journals.

Among the topics discussed at the ANA annual meeting were:

ALZHEIMER'S DISEASE

Elan/Wyeth's vaccine, AN-1792

Will this vaccine be revived? Perhaps, said researchers at the ANA meeting, in some form. The vaccine appeared to be dead when, in January 2002, Elan halted a trial of its experimental vaccine against Alzheimer's Disease due to brain and spinal cord inflammation and swelling. Then, in March 2003, an autopsy of one of the patients in that trial found that the vaccine did reduce brain plaques, but T cells had infiltrated the woman's brain, suggesting an immune overreaction that could have damaged normal brain tissue and caused brain inflammation. However, several experts at the ANA meeting were hopeful that the vaccine research will be resumed. One said, "I think Elan's vaccine will get revived. Nothing has reversed plaques in mice the way this did, and I have a friend in Europe who used it on humans and had the same results. We will need to treat the brain inflammation, but prednisone may do that."

In August 2003, Elan filed an IND for a humanized monoclonal antibody as part of its Alzheimer's immunotherapy program with Wyeth. The antibody is directed against A-beta amyloid and is intended for the treatment of mild to moderate Alzheimer's disease. A Phase I clinical trial could be initiated in the fourth quarter of this year.

Forest Laboratories' Namenda (memantine)

Namenda was approved by the FDA on October 17, 2003, just a day before the ANA meeting, but there was no signage at the Forest booth. Forest sales reps were pushing the antidepressant Lexapro (escitalopram) instead. Neurologists at the meeting predicted Namenda will find widespread use. Every source questioned said he plans to use Namenda a broad range of Alzheimer's patients, not just moderate-to-severe disease. They also said they plan to use it as monotherapy when patients cannot take an acetylcholinesterase inhibitor (AChEI). However, no source plans to switch patients from an AChEI to Namenda. There is likely to be strong patient and caregiver demand for Namenda. An Arizona doctor said,

"Patients have been asking for memantine for six months. I'll use it in all Alzheimer's patients, not just moderate-to-severe patients, and not just in combination with an AChEI." A New York neurologist said, "I'll use it as monotherapy as well as combination therapy." Another New York doctor said, "A number of patients are already getting it from overseas. Most moderate-to-severe patients will get it. There will be huge family pressure, and there has been nothing for severe patients. I'll probably also prescribe memantine to many mild patients. A lot of patients will get it, but insurance and cost will be the issue." A Louisiana doctor said, "There is a tremendous amount of interest in memantine. People are grasping at straws. There will be a lot of pressure to use it off-label, and I will do that. If there is demand from patients – and I expect there will be – I will use it in any Alzheimer's patient as add-on therapy."

Data is expected before the end of the year (by press release) from two monotherapy trials. Doctors questioned at the ANA meeting had not heard anything about the results yet, and there were only sales reps (not senior officials) at the Forest booth. In fact, the booth didn't even have any Namenda signage.

1. **MEM-MD-10:** monotherapy in mild-moderate Alzheimer's. This is a 24-week trial in 300-400 patients. The primary endpoints are ADAS-COG and CIBIC+. The results may be presented at the American College of Neuropsychopharmacology (ACNP) meeting in San Juan, Puerto Rico, December 7-11, 2003.
2. **MEM-MD-01:** monotherapy in moderate-severe Alzheimer's. This also is a 24-week trial in 300-400 patients. The primary endpoints are SIB and ADL. Complete results may be presented at the American Geriatrics Society meeting in Las Vegas from May 17-21, 2004.

PFIZER'S Aricept (donepezil)

Shortly after the ANA meeting, Duke University researchers reported that a randomized, double-blind, placebo-controlled study found that Aricept appears to cause physical improvements in the hippocampus and other brain regions of patients with mild to moderate Alzheimer's Disease. They used MRI technology to track brain changes in 67 patients taking Aricept over 24 weeks (followed by a six-week period in which all participants received only placebo), and they found that levels of *N*-acetylaspartate increased and the hippocampus deteriorated more slowly than among placebo patients. The author of the study said, "The implication is that we may be able to do something to change the progression of this disease…When someone has Alzheimer's disease, the brain begins to deteriorate as the gray matter shrinks, and the disease progresses…We are unsure of why and how donepezil slowed the loss of hippocampal volume, but we think the drug may help to improve cognition by increasing the levels of *N*-acetylaspartate in the brain, at least temporarily." This suggests a medication could be developed that would affect the progression of brain changes in Alzheimer's Disease.

BIPOLAR DISORDER

In 2000, **Lilly's Zyprexa** (olanzapine) became the first atypical antipsychotic to gain FDA approval for the short-term monotherapy treatment of acute bipolar mania. Recently, it was approved in combination with other mood stabilizers. Other atypical antipsychotics are also seeking approval for bipolar mania.

Sources at ANA insisted that the atypical antipsychotics differ from each other more in bipolar disorder than they do in schizophrenia. One source said, "In bipolar disorder, the more sedating atypicals – like olanzapine-- appear to do better…It is too early to say how Abilify (Bristol-Myers Squibb, aripiprazole) will do, but I understand it can cause mania, which is not good in bipolar disorder, so the jury is still out on Abilify."

MULTIPLE SCLEROSIS

Among the unanswered questions about MS are:

- Is there a virus?
- What causes progression?
- What is benign MS? Why do some patients do well and others don't?
- What is altered in the immune system of MS patients? What is wrong?
- How does MS start?

Some experts insisted that a virus is the causative agent in MS. Others are equally convinced that MS is a degenerative disease as well as an inflammatory disease. An expert said, "Any infectious agent -- a virus, bacteria -- could be a trigger for the immune system, or there may be a chronic infection in the brain of MS patients that we need to find…We don't know what causes MS…We need to keep an open mind." Another expert said, "Inflammation in MS may be a sign of repair, and reducing inflammation may interfere with repair."

Doctors were impressed with a study which showed that there is a wide variation in the rate at which MS patients progress from an EDSS score of 0 to 4.0, but once MS patients reach an EDSS score of 4.0, then progression to EDSS 7.0 occurs at the same rate. This raises the possibility of pre-programmed neurodegeneration, a speaker said. An expert commented, "It may be that once things start (happening) in the brain the effect at other sites is not the driving factor."

Researchers know that some MS patients have a benign form of the disease that does not appear to progress, but identifying these patients has been impossible. A Mayo Clinic researcher presented a study showing that patients with an EDSS ≤2.0 after 10 years have benign disease and don't need treatment.

MRI imaging

Doctors continue to believe that MRI imaging is valuable in MS, but the results still cannot be used as a long-term outcome predictor or a surrogate marker. An expert said, "Most of the field believe it is not a proven surrogate. We are nowhere near FDA-approvability for use of MRI in short-term trials."

Combination therapy

A few sources said they are increasingly using combinations of different MS drugs – when insurance carriers will pay for it – but generally not an interferon plus Copaxone.

BIOGEN'S antegren

No information was available on the upcoming interim look at the Phase III data; no one has any idea what it will look like, and a Biogen official insisted nothing will be made public unless the DSMB finds the results so negative that the trial must be halted. The final data is expected at the American Academy of Neurology meeting in Miami in April 2005.

The failure of antegren in Crohn's Disease does ***not*** predict how the drug will do in multiple sclerosis, experts agreed. Sources are not excited about antegren; they are taking a very measured wait-and-see attitude. An expert said, "Animal models are notoriously unreliable in MS, so antegren could fail in Crohn's and do well in MS – or not." Another expert said, "A positive Phase II trial doesn't assure Phase III success. But what happened in Crohn's has no bearing on antegren in MS. They are substantially different diseases." A California doctor said, "The results in Crohn's were not good, but they are not really negative either. T cells in MS may be different than in Crohn's. So, the Crohn's results don't impact the results in MS."

BIOGEN'S Avonex

Rebif and Copaxone share gains are coming mostly at the expense of Avonex, and that trend is likely to continue.

ITERATIVE THERAPEUTICS

This company was founded just a month ago by University of Chicago researchers to commercialize Fc receptor ligands, which have a potential therapeutic role in MS.

SERONO/PFIZER'S Rebif

Rebif market share has not peaked. Sources predicted it will continue to gain market gradually. A New England doctor said, "Rebif is still new, and use is continuing to increase." A Wisconsin doctor said, "Rebif use increased, then plateaued and is now going up again."

Several sources mentioned that they are seeing a few cases of elevated liver enzymes with Rebif. No one has stopped using Rebif or cut back on usage as a result, but doctors said they are keeping an eye on this issue. A West Coast doctor said, "I had a patient on Rebif that had liver failure. The liver abnormality side effects need to be watched." Serono's sales reps insisted the incidence of liver enzyme elevations is no higher with Rebif than with other interferons and suggested that the level of "noise" over this issue may be due to counter-marketing by competitors. A Canadian doctor said, "I'm concerned about the occasional Rebif side effects. Antibodies are worse than with other interferons. There are injection site reactions and malaise. And there have been a couple of reports of ALT <3xULN, and that is a bit of a concern." A Midwest doctor said, "We've seen some ALT problems. When that occurs, we reduce the dose to half. Only one patient has had to discontinue Rebif completely as a result of liver abnormalities."

TEVA PHARMACEUTICALS' Copaxone (glatiramer acetate, copolymer-1)

Copaxone market share will increase over the next year, sources generally agreed. When Copaxone is used in lieu of an interferon, it is generally because of lifestyle issues, side effect reasons, or "insufficient" response to one of the interferons. A Texas neurologist said, "People are getting more experience with it, are surprised it works, and are using it more."

An MS researcher presented some animal data suggesting that Copaxone may be effective in other neurodegenerative diseases, such as ALS. Copaxone may be more effective when given less frequently, perhaps monthly, quarterly or yearly. A researcher said, "Vaccination with copolymer-1 leads to neuroprotection…A single injection, unlikely daily injections, is beneficial. Daily injection may lead to anergy, but a single injection may be neuroprotective." Other experts said they were intrigued with this animal data, and they said investigators will start human trials of different dosing regimens.

NEUROPATHIC PAIN

PFIZER'S pregabalin

Sources expressed little excitement about pregabalin for neuropathic pain. They also indicated that pregabalin is poorly differentiated from Pfizer's Neurontin (gabapentin). A Louisiana doctor said, "Pregabalin is a me-too drug. Gabapentin has a broader indication; pregabalin is more in the class with other anti-convulsants." A Utah doctor said, "There is no excitement about pregabalin, but it is another bullet in our armamentarium"

SANOFI'S Gabitril (tiagabine)

A poster supported further development of this anti-convulsant for diabetic polyneuropathy.

PARKINSON'S DISEASE (PD)

Second line Parkinson's drugs -- Pfizer's Mirapex (pramipexole), Pfizer's Cabaser/Dostinex (cabergoline), etc. – are dopamine-sparing, but they can cause sudden sleepiness. If that happens, sources said, they cut the dose or switch patients to another agent. An Illinois doctor said, "All these agents can cause daytime sleepiness."

Many PD patients suffer from hallucinations. These are mostly nocturnal visualizations of people or animals in vivid color, but generally they are not auditory, tactile or frightening to patients – though they can be more difficult for caregivers. A speaker identified three key risk factors for PD hallucinations: (1) co-existence of cognitive problems, (2) depression, and (3) sleep problems. The use, dose or initiation of levodopa is *not* a risk factor.

BERTEK'S apomorphine

TAP Pharmaceuticals has the rights to sell apomorphine in the U.S. for erectile dysfunction, but Bertek has the rights in Parkinson's Disease. Apomorphine helps eliminate "off" time, and Bertek has developed a subcutaneous pen injector system that patients or caregivers can use to quickly terminate an unexpected "off" episode. Apomorphine can cause significant nausea, but a source said the nausea can be relieved by pre-treatment with tiagabine for the first month (and then discontinuing the tiagabine). The idea would be for patients to use the apomorphine from once to three times a day, on a PRN basis. A doctor questioned whether insurance companies will be willing to pay for this, "Coverage will be an issue. If initiation in a doctor's office is required with titration over two hours, that will severely limit use."

CEPHALON'S CEP-1347

CEP-1347 is currently in a two-year Phase II/III trial in patients with very early disease who don't need medication at the time of diagnosis to see if the drug can prevent progression. Enrollment should finish in the first quarter of 2004, and it is a two year study, so the first patients will not complete until January 2005. A researcher said, "CEP-1347 is being studied in new onset patients for neuroprotection, not for treatment of symptoms. It has promise in preventing apoptosis."

Atypical antipsychotics

The effect of atypical antipsychotics in PD patients is extremely variable; experts insisted there is not as much class effect in PD as there is in schizophrenia. Novartis's Clozaril (clozapine) appears to be the most effective, having been shown in double-blind, randomized trials to abate hallucinations.

A 12-week, double-blind study at Baylor University of 200 mg quetiapine (**AstraZeneca's Seroquel**) in 31 patients with PD psychosis found the drug did not improve psychosis compared to placebo, though it was well-tolerated and did not worsen PD motor signs. About half the patients went on to Clozaril, about a third improved to the point where they stopped taking any medication, and about one-sixth remained on quetiapine. The investigator said, "We did the same study with olanzapine (**Lill Zyprexa**), and it significantly worsened gait and other things. It had a more robust effect (on psychosis), but that was more than countered by a worsening of PD."

Another study found that Seroquel causes diabetes in PD patients treated with it. However, the researcher said her preference is still to use Seroquel for the psychosis of PD because it is the most effective atypical antipsychotic. She said, "The atypicals are not the same in PD. Risperidone (**Johnson & Johnson's Risperdal**) looked good at first, but then it was found to worsen PD symptoms. Zyprexa doesn't work well in PD. It is too early to be sure about aripiprazole (Bristol-Myers Squibb's Abilify), but the results appear mixed so far. You cannot assume how an atypical works in schizophrenia is how it will work in PD."

TEVA'S rasagiline

Rasagiline is a novel, potent, second-generation, selective, irreversible monoamine oxidase type-B (MAO-B) inhibitor that blocks the breakdown of dopamine. Results were presented from the 26-week PRESTO study of 472 patients who were experiencing motor fluctuations despite optimized

PRESTO Results

Measurement	0.5 mg/day rasagiline n=164	1.0 mg/day rasagiline n=149	Placebo n=159
Primary endpoint: Change in daily "off" time from baseline	-1.41 hours (p<.02 vs. placebo)	-1.85 hours (p<.0001 vs. placebo)	-0.91 hours
Change from baseline in mean total daily "on" time *without* troublesome dyskinesias	1.01 hours	1.28 hours	0.49 hours
Change from baseline in mean total daily "on" time ***with*** troublesome dyskinesias	0.21 hours (nss vs. placebo)	0.62 hours (p<.05 vs. placebo)	0.26 hours
Global improvement by examiner	-.039 (p=.0027)	-0.68 (p<.001 vs. placebo)	N/A
Adverse events	86.8%	90.9%	94.6%
Serious adverse events	57.2%	66.5%	60.4%
Termination	11.9%	13.4%	11.4%

dosages of levodopa. The trial showed that either 0.5 mg or 1.0 mg QD rasagiline, added to levodopa therapy, significantly reduced total "off" time (when Parkinson's symptoms were not adequately controlled) and improved motor function. An expert said, "This is exciting. It is a new and improved selegiline with fewer side effects."

STROKE

After numerous stroke drug failures over the past 10 years, doctors are wary of new agents. Nothing on the horizon is generating much excitement. The exception is **AstraZeneca's Exanta** (ximelagatran). Doctors questioned about new agents all mentioned Exanta, and they predicted it will do very well as a replacement for warfarin – if the liver enzyme issue doesn't worsen. One commented, "Liver monitoring is easier and less costly than warfarin monitoring."

Several reasons were cited for drugs failing in human clinical trials that looked promising in animal studies:

1. Study noise – scale problems, bad luck, the heterogeneity of human stroke, etc.
2. Clinical requirement for a lasting benefit.
3. Serious design flaws in many studies due to: treatment delay, inadequate dosing, limited power, etc.
4. Biological differences between animals and humans.
   a. The human brain is bigger and diffusion is less effective.
   b. The human brain has more white matter (33%), which likely dies by a different mechanism than gray matter does.
   c. Human stroke has greater variability in ischemic onset and magnitude.

The lessons identified for future stroke studies:

- Pick models with a robust effect – e.g., cats or primates, not just rats.
- Control temperature.
- Test multiple agents – though this is unlikely soon.
- Initially a drug can do better in either white or gray matter, but eventually it will need to have an effect in both.
- Design the study well, with particular attention to patient selection and power.

ASTRAZENECA/RENOVIS'S NXY-059 is in a Phase IIb/III study to assess its efficacy and safety with intravenous administration in acute ischemic stroke. The trial is a double blind, randomized, placebo controlled, parallel group, multicenter study. One expert said, "I think the data looks great so far." But another expert said, "I don't think NXY-059 works."

BARR LABORATORIES' BRL-52537

Early animal studies have encouraged researchers about this kappa-opioid receptor agonist, but they said Barr is not interested in pursuing this agent in stroke. One said, "Barr is leery of the neuroprotection area."

THE MEDICINE COMPANY'S clevidipine

This ultra short-acting dihydropyridine calcium channel antagonist, licensed from AstraZeneca, is being investigated as a treatment for stroke. Clevidipine, an IV agent, acts by selectively relaxing smooth muscle cells that line small arteries, resulting in widening of the arterial lumen and reduction of blood pressure. The potential advantages of clevidipine are:

- Ease of use.
- Short-half life.
- Demonstrated safety.
- May minimize reflex tachycardia.
- Metabolized by enzymes in blood plasma, independently of the liver and kidney.
- May be cardiac- and renal-protective during ischemic events.
- Fast control of blood pressure.

Phase III trials are supposed to start by the end of 2003, but sources were not optimistic. One said, "I can't get excited after all the stroke drugs that have failed. I'll wait and see what happens with it."

MISCELLANEOUS

Botulinum toxic

- A double-blind study of 14 patients found that 5,000 U of botulinum toxin B, given in one injection, did not significantly improve freezing of gait in Parkinson's Disease.
- An expert predicted that Allergan's Botox would get approved for migraine but commented, "I wish we could tell who will respond."
- A Mayo Clinic study found that Inamed's Dysport (botulinum toxin A) can be diluted with 2% lidocaine just as Elan's Myobloc (botulinum toxin B) – but the study found no difference in perception of pain with or without the lidocaine.

FUJISAWA'S Prograf (tacrolimus, FK-506)

A mouse study suggested this may have utility in MS. Researchers noted: "Pharmacologic agents that can protect against axonal loss or promote axonal regeneration may be useful for preventing the deteriorating course of MS (and the conversion from relapsing remitting to chronic progressive MS." The study compared FK-506 to cyclosporine (CsA) and an FK-506 derivative. The study found: "FK-506 reduced clinical severity of the initial phase of EAE and completely

prevented relapse and dramatically lowered (by 90%) the degree of damage in the spinal cord…CsA reduced severity in the initial phase of EAE but did not prevent relapse and reduced spinal cord damage by 30%…The FK-506 derivative (FR-131706) did not alter the course of EAE but reduced the degree of spinal cord damage by 50%."

IDEC Pharmaceuticals' Rituxan (rituximab)

A small (10 patient), open-label, Phase II study of Rituxan as add-on therapy in MS found that 25 ft. walk remained stable or improved in 6 of 7 patients and CSF IgG decreased by 32%. Researchers concluded, "Rituxan is safe in relapsing MS patients as add-on therapy. Peripheral blood B cells were virtually depleted in all patients. Serum and CSF antibodies to rMOG were not changed at five months post-treatment, and CSF-B cells were decreased but not eliminated in all patients." A Genentech official, asked if the company was considering a larger trial, said it is under consideration, but indicated the company was waiting for the MRI data before making a final decision. An MS expert said, "I think the monoclonal antibodies deserve to be studied in MS." Another expert said, "This could be an interesting story."

Poetic Genetics

This small, private company (www.poetgene.com) was formed by Stanford genetics researcher Michele Calos, PhD, to research integrase-mediated gene therapy. At the ANA meeting, scientists reported on a mouse study in which they successfully inserted genes into muscle cells using rings of genetic material called plasmids. The key ingredient that allowed the genes in the plasmid to be integrated into the host muscle cell's genetic materials was a protein called integrase. Plasmids normally don't integrate genes as efficiently into the host cell's genome, but the use of integrase assists this process. The therapy holds promise for treating muscular dystrophy.

Takeda's Ramelteon (TAK-375)

This novel indenofuran derivative, a selective ML1 receptor agonist, is in Phase III trials to treat insomnia. Cat data was presented at this meeting indicating TAK-375 does not cause the adverse effects normally associated with benzodiazepines, such as learning and memory impairment, motor dysfunction or drug dependence.

Transkaryotic Therapies's Replagal

Genzyme's Fabrazyme gained FDA approval (and orphan drug status) this year, and TKT's Replagal did not, but both drugs continue to battle it out in Europe. A U.K. study presented at the ANA meeting found that Replagal reversed hearing deteriorating and showed a gradual improvement in patients, suggesting, researchers concluded, a need for long-term treatment.

UCB Pharma's levetiracetam

A poster reported on a four week, open-label, 10-patient, pilot study which found that levetiracetam showed "no significant improvement in efficacy" for essential tremor. Researchers concluded, "Our results do not support controlled trials at these doses (500 mg BID or 1500 mg BID)."

Another study of levetiracetam in myoclonus was equally pessimistic. Researchers said, "Only two of eight patients showed an improvement, but, in view of the early anecdotal reports of dramatic outcomes, it may be considered as add-on therapy in patients with intractable myoclonus on conventional treatment."

Free Radicals a Major Suspect in ALS

Evidence is mounting that free radicals play a major role in the death of nerve cells in amyotrophic lateral sclerosis. Research has suggested that the motor neurons in these patients are dying, at least in part, because they are being overburdened with glutamate. Researchers from the University of California, Irvine, presented evidence of a vicious feed-forward loop in which free radicals prevent the destruction of glutamate. As glutamate levels rise, cells respond by producing yet more free radicals, further interfering with the clearance of glutamate.

Possible Free Radical Assay to Identify Alzheimer's

Doctors and patients would love to have an accurate and simple way to diagnose and then track the progression of Alzheimer's disease, but so far blood tests and spinal taps have not been found to accurately reflect brain levels of beta-amyloid, the toxic protein that is the prime suspect in the disease. A researcher from the Farber Institute of Neurosciences in Philadelphia reported that F2-isoprostanes – by products of free radical processes in the brain – increase in parallel as beta-amyloid levels rise in the brains of aging mice.

Limbic Encephalitis Treatable

Many patients suffering from limbic encephalitis – a rare but debilitating dementia-like neurological disorder typically blamed on an immune response to a tumor – may instead have a different immune system syndrome that is treatable with existing therapies. However, in many cases of limbic encephalitis, no evidence of a tumor is found. British researchers reported that potassium channel antibodies in the circulation of unexplained limbic encephalitis responded to treatment with immunological therapies such as plasma exchange, intravenous immunoglobulin, and steroids.

Stems Cells Aid Nerve Regeneration

Even months after an injury, stem cells can help rescue damaged nerve fibers, a rat study found. Johns Hopkins Researchers reported that stem cells supply key nutritive

molecules and protect against harmful ones, allowing nerves to regenerate as much as six months after the injury. This is the first demonstration of regeneration in chronically denervated nerves, researchers claimed. They attached a freshly cut nerve to one that had been cut six moths before and allowed to deteriorate. They then transplanted stem cells from the nervous systems of mice – stem cells that were genetically engineered to make the growth factor GDNF – into the nerve repair area. In addition to the physical nerve regeneration, there was a return of about 25% of the muscle function in the muscles controlled by the nerve.

Autoimmune Autonomic Neuropathy Due to Antibodies

AAN is thought to be a close relative of myasthenia gravis, an autoimmune disorder where antibodies mistakenly attack the otherwise healthy junctions where nerves meet the muscles that they control. In AAN, the same sort of antibodies appear to attack the autonomic nervous system. Mayo Clinic researchers reported that they have successfully transferred an experimental version of this disorder from one animal to another via a transfusion of antibodies isolated from blood plasma. An investigator said this means that treatments which are efficient for antibody disorders, including plasma exchange, intravenous immunoglobulin and immuno-suppressants, can be appropriately offered to these patients.

Common Origins of Episodic Disorders

It appears that episodic diseases such as epilepsy, migraine, periodic paralysis, etc., share common causes – mutations in proteins that help conduct ions into and out of cells.

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