	Drug	Manufacturer	Mechanism of action	Stage of development	Side effects
New drugs	3APS (Alzhemed)	Neurochem, Inc.	inhibits amyloid-beta aggregates, binds and reduces soluble amyloid-beta	Phase 3	Nausea, vomiting
	MPC-7869 (Flurizan)	Myriad Pharmaceuticals	NSAID derivative; inhibits amyloid-beta aggregates and reduces their levels of amyloid-beta with little or no anti-inflammatory effect	Phase 3	None disclosed
	AAB-001	Elan Pharmaceuticals	monoclonal antibody binds to and clears amyloid-beta, is designed to directly deliver antibodies to amyloid-beta	Phase 2	None disclosed
	Neramexane	Forest Laboratories	NMDA receptor antagonist: blocks the effects of excessive glutamate at the receptor	Phase 3	None disclosed
Drugs for other conditions	Simvastatin (Zocor)	Merck	Statin; reduces cholesterol-carrying protein that promotes amyloid-beta aggregation	Phase 3	None disclosed for the trial, but Zocor has been known to cause nausea, diarrhea, abdominal pain and muscle cramps
	VP4896	Voyager Pharmaceutical	Hormone drug leuprolide acetate; decreases amount of luteinizing hormone in body, might prevent brain cell death	Phase 3	None disclosed
	Valproate	Manufacturer not disclosed	Anticonvulsant drug; neuroprotective properties may delay clinical progression of Alzheimer disease	Phase 3	None disclosed
Dietary supplements	Gingko biloba		Antioxidants neutralize free radicals and may reduce or prevent the damage they cause in brain cells	Phase 3	Headache, upset stomach, allergic reactions
	Vitamin E Selenium		Antioxidants neutralize free radicals and may reduce or prevent the damage they cause in brain cells	Phase 3	None disclosed

Target practice: Most candidates being tested for Alzheimer disease are based on the amyloid hypothesis.

people do is for reviewers of grants and papers and conference organizers to broaden their perspective and shift emphasis."

But with conference presentations and publications devoted primarily to the amyloid hypothesis, even those entering the field are exposed mainly to this view of the disease.

This result is particularly insidious, says Keith Crutcher, a neuroscientist at the University of Cincinnati. "Newer people coming into the field get the impression that the case has already been solved," Crutcher says. "It has the subtle effect of dissuading other people from entering the field."

In the past few years, the US National Institutes of Health has begun initiatives to encourage young researchers and more peripheral or risky projects. For example, the R03 grant offers young scientists up to $50,000 for two years to help gather data for larger grants, and the R21 grant offers $275,000 for two years.

Steve Snyder, program director for the etiology of Alzheimer disease at the US National Institute of Aging, says he has also on occasion made a special effort to pick up grants that refute the amyloid hypothesis.

Of the $75 million Snyder allocates in grants, fully half goes to research related to the amyloid hypothesis and the other half to work on the remaining topics such as learning and memory, tau, genetics, glial cells and apolipoprotein E.

Although none of the researchers are really biased, "there are people on the panels whose own research interests mesh quite nicely with amyloid-beta," Snyder says. "When those people are making decisions, that outlook can have a bearing on what happens next. I don't know how to get around that."

Lone target

If amyloid gets so much attention from the scientists, it's because there's almost overwhelming evidence that it's correct fundamentally, says Harvard neurologist Selkoe.

An eye on...

If there is a holy grail of genetic mysteries, Alzheimer disease certainly qualifies—with **Richard Mayeux** hot on its trail. Mayeux has spent the past 18 years trying to tease out the complex genetic causes of late-onset Alzheimer disease.

Mayeux, co-director of Columbia University's Taub Institute for Research on Alzheimer's disease and the Aging Brain, appears to be on the brink of nailing a culprit, nearly 13 years after the discovery of *APOE*, the only gene known in its mutated form to be associated with the common, late-onset form of the disease. Mayeux has painstakingly built a database of clinical histories and cell lines from about 500 Dominican families prone to the late-onset form of the disease. He won't reveal more about the candidate he and his collaborators are pursuing because the findings are unpublished.

The mere mention of a new Alzheimer gene is sure to stoke the ongoing debate about genetic testing. Like many scientists, Mayeux supports genetic tests for individuals from families that carry mutations for the early-onset disease, especially for those considering having children. But for the late-onset disease, which comprises more than 98% of cases, Mayeux is vocally opposed to testing.

"If there were a treatment or a cure, then by all means it would be important to have genetic testing," says Mayeux. "Until that happens, I really think it's inappropriate."

Meredith Wadman, Washington, D.C.