International Psychogeriatrics, Vol. 13, No. 1, 2001, pp. 3-4

Guest Editorial

The Vanishing Plaque

Recently articles have appeared suggesting that in transgenic mice, vaccination with small parts of beta-amyloid can produce antibodies that prevent formation of amyloid plaques in the young and banishment in older mice. (Mice do not have tangles.) Because vaccines have eliminated or mitigated the effect of smallpox, polio, tuberculosis, and other dread diseases, such news is electrifying. However, disbelief is not long suspended when certain facts are presented. First, the role of plaques and tangles is moot. Second, there are reckoned to be at least 55 kinds of dementia, with Alzheimer's disease (AD) having a major but decreasing proportion as new types are recognized. (Thus some would argue that Lewy body disease constitutes as much as 20% of all dementias.) Third, AD is not well diagnosed in life, being a postmortem diagnosis. Finally, we now recognize that there is a considerable overlap between AD and vascular dementia in terms of etiology and presentation. So just what are we vaccinating against? Beyond that of course is the mixed bag of variables involved in AD. Think of age, gender, race, intelligence, education, aluminum, oxidants, cholinesterase, and vascular risk factors. These are but a few.

For a witty further comment, we asked Professor Hans Förstl to advise us.

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AN-1792: A Frank Revolution?

Will AN-1792, the "vaccine against Alzheimer's," gain the same significance for the aging human brain as the year 1792 for history? Recent reports look promising. Will old-age psychiatrists and geriatricians, whose pharmacotherapeutic activities against dementia were traditionally compared to using aspirin against brain tumors, now have to downsize their business? This may well happen. Will society have to cope with costly cohorts of the wise very old, who will then be able to enjoy intellectually rich lives and cunningly claim their rights? An answer would go beyond the available evidence.

There is no need to review very basic issues in a specialist journal, for example, the general importance of AD; the nature of AD beta-amyloid plaques and neurofibrillary tangles, which are usually found in great numbers in the brains of the majority of elderly patients with dementia; current disappointment with symptomatic treatment; modest hope regarding preventive strategies with lipid-lowering statins and radical scavenging vitamins, estrogens, etc.

The experienced old-age psychiatrist leaning dangerously towards the Type II error, whose immature enthusiasm about vain new theories has long withered away with the permanent exposure to his elderly patients' relentless deterioration, would have told you that this vaccine idea could not possibly work at all, because:

- immunizing against the beta-amyloid will inevitably lead to autoimmune phenomena;
- a vaccine with beta-amyloid in its beta-pleated sheet form would never lead to the production of specific antibodies acting on the other side of the blood-brain barrier;
- even if there were antibodies against beta-amyloid in the brain, what sort of positive effect should they achieve extraneuronally where amyloid is deposited but not generated;
- if the vaccine—against all odds—should exert effects on the other side, they would certainly come too late as a cure for a damage that has already been done, or be so extremely dramatic as to play havoc on all levels of brain function;
- extraneuronal beta-amyloid plaques represent just one of many epiphenomena in which the relationship between the clinical deficits and behavior and cognitive performance remains to be determined;
- it is a long way from transgenic mice to men.

The last point is very well taken; mice are much smaller and—demented or not—do not fare well in paper-and-pencil tests. But all the other concerns seem to disappear in view of hot new results.

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