

Alzheimer-Plus

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There is always hope—even now that immunization with beta-amyloid has not busted international psychogeriatrics; now that a term once so popular in European neuropsychiatry—"Parkinson plus"—has been de-constructed with the tools of a smart modern neurology (and that dementia with Lewy bodies has been reinvented); now that molecular biology has left some temporary responsibility for clinicians dealing with demented patients themselves, would it not be thrilling to attempt a fundamental reconsideration of some basic concepts of great—albeit temporary—practical relevance?

Let us reconsider two questions: First, why did Alois Alzheimer hesitate to accept Kraepelin's complimentary "Alzheimersche Erkrankung" (the name by Kraepelin of "Alzheimer's disease")? Alzheimer, Lewy, and many other true neuroscientists had seen so many plaques and—after 1903—so many neurofibrillary tangles in the brains of elderly patients, demented or nondemented, that they had great doubt regarding the pathological significance of this histological finding in old age. It took a long time until Martin Roth's arguments regarding a statistical relationship between the severity of brain changes and cognitive impairment sank into the critical minds of clinicians and neuropathologists, leading to some modest operational refinement of the clinical and neuropathological diagnosis of so-called Alzheimer's disease.

Second, the Emperor's New Clothes effect. Why is everyone jumping at "Alzheimer's disease" today, most without ever having seen their patients' plaques and tangles? This diagnosis appears to betray the great diagnostic and therapeutic authority of well-informed clinicians and researchers pushing the frontiers of science. I really enjoy such puns as "dementia of the Alzheimer's type" (the double genitive indicating maximum expertise regarding a most complex matter and really deep thought) or statements such as "Alzheimer's disease is the most prevalent cause of dementia (72%)," etc. If everybody keeps talking and writing about it, Alzheimer's disease *must* be there; this is the first apparent proof for the existence of Alzheimer's disease, or rather the usefulness of the Alzheimer's disease concept. The concept gains further credibility by the apparent nonexistence of Alzheimer's disease in at least a subgroup of elderly individuals, some of whom appear to have other forms of dementia (e.g., "vascular dementia"), others who have no cognitive impairment at all (at least as long as the exquisite club of successfully aged individuals is not examined with rigorous neuropsychological methods—no offense intended).

Do we need another example of the Emperor's New Clothes effect? Consider "dementia with Lewy bodies" (but

probably not without plaques and neurofibrillary tangles), which has also popped up and fails to be falsified. Before we lose our faith in nihilism and, as time does not pass without leaving more beta-amyloid and tau-traces in all our brains, let us face it, there is

- no pure Alzheimer's disease in old age (almost),
- but there are also no elderly demented patients without plaques or neurofibrillary tangles (almost).
- Consequently there are (almost) no elderly patients over age 50 with pure vascular dementia, pure Lewy body dementia, or other forms of dementia without Alzheimer pathology.

Does this sound as if I were advertising "ye olde waffly organic brain syndrome" again, after the most celebrated advance of our subject over the last 20 years has been the epidemic adoption of the Alzheimer's disease concept, and after so many Alzheimer's societies have been founded? It only sounds like it and one should certainly admire this brilliant intellectual quantum jump, quite naturally claimed by US-American contemporaries, by British intelligence operating 50 years ago, and by classical German neuroscience (we really knew it all before).

No, I do not so advocate, but I admit to a lingering fear that scientific brilliance may blind clinicians and obscure a vast number of rather obvious and important processes contributing to dementia, usually over several decades of an individual's lifetime. Therefore we are dealing with "Alzheimer-plus" on two levels:

1. An elderly individual's large number of treatable risk factors (from hypertension and hypotension, cholesterol, hyperglycemia and hypoglycemia, hyperhomocysteinemia, etc., to social isolation with lonely TV-dinners as an example of

a restricted cognitive diet), *and* they can be identified early on in every individual patient *and* in patients with manifest dementia, *and* we need to tackle them, *and* we cannot wait until there is even more pressing scientific evidence.

2. An individual mixture of plaque, tangle, vascular, Lewy body, lobar atrophy type, and other brain pathology reflected by clinical symptoms, by neuroimaging, and by neurochemical findings.

These findings call for a customized and sophisticated cocktail of psychosocial and medical interventions.

The clinical diagnosis of probable Alzheimer's disease in an elderly demented individual is no intellectual achievement at all. It is as trivial and unsatisfactory as the prescription of memantine, cholinesterase inhibitors, or EGb761. It is beyond question whether an elderly demented patient has plaques and neurofibrillary tangles in the brain with consecutive cholinergic deficits, problems with glutamatergic neurotransmission, etc., and that the patient will benefit from treatment with efficacy proven for rather pure Alzheimer's disease. The only challenge is to detect other factors that may contribute to the pathophysiology and symptoms of our patients, factors that are accessible to further specific interventions. Our responsibility is growing. Psychogeriatrics is no longer a subject for lazy colleagues. Alzheimer's disease is for the simple-minded, "Alzheimer-plus" is not.

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