Current Opinions in Neurological Science
ISSN: 2575-5447

Research Article Volume 6 Issue 1 • 2021

On Potentially Reversible Forms of Dementia

Alain L. Fymat*

Professor, International Institute of Medicine & Science, California, U.S.A.

***Corresponding Author:** Alain L Fymat, Professor, International Institute of Medicine & Science, California, U.S.A.

Received : October 20, 2021
Published : November 08, 2021

Abstract

We are barely emerging from the COVID-19 pandemic that we are concerned with the coming of the dementia pandemic. Prompted by economic development and increasing lifespan, dementia in its several types and forms has surfaced as a major global public health concern that may devastate world's economies and health care systems. However, dementia is not an emerging problem as it has been with us since Antiquity. While the causal etiology of many types of dementia, including Alzheimer's disease, still remains unclear, I had posited earlier that they are but autoimmune diseases that have gone rogue. After characterizing dementias according to the affected brain area(s), their progressiveness and irreversibility, their derivability from another disorder (primary or secondary), and their reversibility, I set forth their main contributors and why it is difficult to arrive at an early accurate diagnosis. I also analyze those potentially reversible dementias, particularly those resulting from exposure to toxicants and their bioaccumulation in the brain. I further list the multiple elemental exposures potentially associated with neurodegenerative diseases including dementia and briefly outline a successful detoxification therapy

Abbreviations: AD: Alexandre's disease; ADD: Alzheimer's disease dementia; BD: Behcet's disease; CBD: Corticobasal degeneration; CJD: Creutzfeldt-Jacobs disease; CTD: Cerebro-tendinous xanthomatosis; DDE: Dichlorodiphenylchloroethylene; DDT: Dichlorodiphenyltrichloroethane; DPA: Dentatorubal pallidoluysian atrophy; FFI: Fatal familial insomnia; FTDD: Frontotemporal disorders dementia; KD: Krabbe's disease; LBD: Lewy body dementias; MD: Mixed dementia; MS: Multiple sclerosis; MSUD: Maple syrup urine disease; NCL: Neuronal ceroid lipofuscinosis; NPD: Nieman-Pick disease; PCB: Polychlorinated biphenils; PCE: Perchloroethylene; PDD: Parkinson's disease dementia; PFOA: Perfluoroctanoic acid; PFOS: Perfluorooctanesulfonic acid; PMD: Pelizaeus-Merzbacher disease; PSP: Progressive supranuclear palsy; SD: Sjogren's disease; SeD: Senilitic dementia; SLE: Systemic lupus errhythematosus; SyP: Syphilitic dementia; VDD: Vascular disease dementia.

Introduction

Dementia is an umbrella term for several brain diseases that manifest themselves by a group of symptoms affecting memory, other cognitive abilities, and behavior. Pictorially, that umbrella includes the following types of dementia: Alzheimer's (accounting for 50%-75% of cases or one in every nine people aged 65 and over), vascular (20%-30%), Lewy body (10%-25%), frontotemporal (10%-15%), and others. According to Global Health Estimates, in 2016, dementia was the fifth global cause of death, climbing up in rank since then.

Nonetheless, dementia is not an emerging disease. It has been with us since Antiquity. It was uncommon in pre-industrial times and relatively rare before the 20th century (for a historical account, see for example my book bearing the same title). During the 19th century until the first half of the 20th century, doctors came to believe that dementia in the elderly was the result of cerebral atherosclerosis (either blockages of the major arteries supplying the brain or small strokes within the vessels of the cerebral cortex). Until the end of the 19th century, dementia was a much broader clinical concept that encompassed mental illness and any type of psychosocial incapacity. In 1907, Alzheimer's disease was described and associated with particular microscopic changes in the brain. It was seen as a rare disease

of middle age because the first person diagnosed with it was a 46-year-old woman (Frau Auguste Dieter, a patient of Alois Alzheimer). By the 1960s, the link between neurodegenerative diseases and age-related cognitive decline was established. By the 1970s, the medical community maintained that Alzheimer 's disease was the cause of the vast majority of mental impairments rather than vascular disease, which is rarer than previously thought. In 1976, neurologist Robert Katzmann suggested a link between senile dementia and Alzheimer's disease dementia. By the end of the 20th century, the medical community believed that dementia is a mixture of both Alzheimer's disease dementia and vascular disease dementia. In the beginning of the 21st century, on the basis of pathological examination of brain tissues, by symptomatology, and by different patterns of brain metabolic activity, a number of other types of dementia have been differentiated from Alzheimer's disease dementia and vascular disease dementia. However, the causal etiology of many types of dementia, including Alzheimer's disease, remains unclear and many hypotheses (theories) have been advanced, but these are largely based on risk factors. In 2017, I posited that the *root cause* (not a risk factor) of Alzheimer's and other neurodegenerative diseases is an autoimmune disease having gone rogue (Fymat, 2017-2020).

The Coming of Age of the "Dementia Pandemic"

We are barely emerging from the COVID-19 pandemic that we are concerned with the coming of the dementia pandemic. Indeed, because of economic development and increasing lifespan, dementia in its several types and forms has surfaced as a major global public health concern that may devastate world's economies and health care systems (see Table 1):

YEAR	NUMBER OF CASES (in millions)	INCREASE FROM 2010
2010	35.6	--
2015	46	26%
2017	50	40%
2030	82	130%
2050	152	326%

Source: World Health Organization

Table 1: *Worldwide statistics of dementia and predictions*

The numbers of cases increases significantly with age and the more so for people living in low- and middle-income countries (nearly 60% of people affected), where the sharpest increases in numbers are predicted. In 2013, the number of deaths was about 1.7 million (up from 0.8 million in 1990), but they are increasing significantly with age. While smaller than the number of deaths reported for the COVID-19 pandemic, they are steadily increasing and may unfortunately approach (if not exceed) them (Fymat 2018d, e; 2019a, d, e; 2020f, g, i).

What is the Situation Today?

The causal etiology of many types of dementia, including Alzheimer's disease, still remains unclear. Whereas much is known about dementia and its underlying and contributing factors, and much has been published on the subject, we still do not understand the deep biology of the disease. Lacking this understanding, we have so far failed to find a cure and continue to be limited to symptomatic treatments that have limited or no effect. To be sure, many hypotheses have been advanced but these are largely based on risk factors, correlations or associations. But, risk factors, correlations, associations, and the like ... are not causation! Likewise, risk management and symptomatic treatments... are not cure, only palliation! What is going on? Have we got the cause of dementia all wrong? I believe so for rather than remaining focused on the primary endpoint of a cure, we have meandered around and shifted the emphasis to surrogate endpoints even though the latter had not been clinically demonstrated to correlate well with the disease. In brief, we lost the proverbial forest for the trees! Yet, hundreds of clinical trials have been undertaken and billions of dollars have been spent each year in rising healthcare costs relating to dementia, in addition to the financial and emotional burdens on families, friends, and care partners/givers. Irrespective of geographical location, racial/ethnic background, and cross-cultural and socioeconomic divides, one can die

prematurely of dementia because there still are no cures or effective long-term treatments.

Since 2017, I have posited that neurodegenerative diseases including dementia in many of its forms are but autoimmune diseases that have gone rogue. For example, the generally accepted amyloid-beta protein deposits (or plaques) including interactions between them and neurofibrillary tangles may only be the signs of a brain homeostasis that had broken down under an avalanche of brain insults (cytokine or/and chemokine storms).

Categorization of the Different Types of Dementia

Dementias can be categorized according to (1) the affected brain area(s), (2) their progressiveness and irreversibility, (3) their derivability from another disorder (primary or secondary), and (4) their reversibility, as summarized below in Table 2:

CATEGORY	CHARACTERISTIC	SYMPTOMS	DISEASE EXAMPLES
1. AFFECTED BRAIN AREA	Cortical (outer cortex)	o Memory o Thinking (thought, perception) o Language o Social behavior	o Alzheimer's disease dementia o Creutzfeldt-Jakob disease dementia
	Subcortical (below the cortex)	o Memory (speed of thinking) o Emotions o Movement (ability to start activities)	o Parkinson's disease dementia o Huntington's disease dementia o HIV-associated dementia
	Corticobasal	o Many different types of neurological problems	o Alzheimer's disease dementia o Parkinson's disease dementia o Parkinsonism o Creutzfeldt-Jakob disease dementia
	Hippocampus	o Memory	o Alzheimer's disease dementia
	Midbrain and *substantia nigra*	o Movement	o Parkinson's disease dementia
	Brain stem	o Speed o Alertness o Autonomic dysfunction	o Parkinson's disease dementia
	Hypothalamus	o Autonomic dysfunction	o Parkinson's disease dementia
	Olfactory cortex	o Smell	o Alzheimer's disease dementia
2. PROGRESSIVENESS/ IRREVERSIBILITY	Becomes worse over time	Interference with more and more cognitive abilities	o Alzheimer's disease dementia o Lewy body dementias o Vascular disease (25%) dementia o Multi-infarct dementia o Frontotemporal dementia o Mixed dementia
3. DERIVABLE FROM ANOTHER PRIMARY OR SECONDARY DISORDER	Primary (does not result from any disease)	Dementia	o Alzheimer's disease dementia
	Secondary (peripheral to a pre-existing mental illness or condition, or injury)	o Brain infection o Multiple sclerosis: some degree of paralysis, tremor, nystagmus, and disturbances of speech. The various symptoms depend upon the seats of the lesions o Progressive supranuclear palsy: heterogeneous degeneration with nuchal dystonia and dementia	o Brain infections o Progressive supranuclear palsy o Multiple sclerosis
4. REVERSIBLE	See below	See below	See below

Table 2: *Categorization of dementia types*

As seen from Table 2, many symptoms are associated with different diseases, rendering the diagnosis difficult to attain.

Main Contributors to Dementia

No less than 24 disorders are contributing to dementia, some of which being confounding factors that have precluded so far the identification of the root cause of dementia and hindered its diagnosis. These are summarized in Table 3:

ADD	VDD	LBD	OTHER	IMMUNO-MEDIATED	INHERITED	SYNDROME
50%-70%	25%	15%	o PDD o FTDD o MD o SeD o SyD o PSP o CBD o Encephalopathy o CJD	o BD o MS o Sarcoidosis o SD o Celiac & non-Celiac	o AD o KD o NPD o MSUD o PMD	o Fragile X-associated tremor/ ataxia o San Filipo B o Epilepsy o CTD o DPA o FFI o Glutaric aciduria type1 o NCL o Neuro-acanthocytosis o Organic acidemias o Pino-cerebellar ataxia type 2 o Urea cycle

Table 3: *Main contributors to dementia*

Risk Factors

While each form of dementia has its own risk factors, most forms have several risk factors in common. These are: age (the strongest known risk factor) although dementia is not a normal part of aging, family history, lifestyle, and pre-existing conditions (such as high blood pressure, diabetes). It is not known how treatment for these problems influences the risk of developing dementia. In addition, more than one type of dementia may exist in the same person. Further, it seems as though people who remain physically active, socially connected, and mentally engaged may be less likely to fall prey to dementia (or develop dementia later than others).

Signs and Symptoms

Dementia evolves in three consecutive phases (early, middle, and late phase) ending up in near total dependence and inactivity, serious memory disturbances, and more obvious physical signs and symptoms. Its signs and symptoms vary across types and stages and also with the individual. They are slow and progressive.

Common symptoms are: impairment of memory, other cognitive abilities, behavioral and emotional problems, language difficulties, and decreased motivation. However, memory loss by itself does not mean having dementia; rather, it is an indication of the need for professional treatment.

It should be noted that behavioral and psychological symptoms occur almost always in all types of dementia and may manifest as: agitation/aggression, anxiety, apathy, appetite changes, behavioral changes, delusions/hallucinations, depression, disinhibition, impulsivity, irritability, mood elations, motor abnormalities, psychosis, and sleep disturbances.

Lastly, long-term and often gradual decrease in the ability to think and remember may be great enough to interfere significantly with a person's ability to maintain activities of daily living.

Diagnosis

Because symptoms are very similar in all types of dementia, they cannot by themselves help in reaching the correct diagnosis of dementia type(s). A diagnosis requires a change from a person's usual mental functioning and a greater decline than one would expect due to aging. As shown in Tables 2 and 3 above, beyond the main contributors (Alzheimer's disease, vascular disease, Lewy body), the diagnosis may become more elusive when some of the many contributors to dementia enter.

Potentially Reversible Conditions

All people with memory difficulty should at least be checked for:

- Hypothyroidism,
- Vitamin B_{12} deficiency,
- Lyme disease,
- Neurosyphilis, and importantly
- Toxicants exposure and bioaccumulation.

This latter factor, in particular, has been the subject of numerous studies (see References). Table 4 lists those elemental exposures that may be potentially associated with neurodegenerative diseases including dementia.

Category	Toxicants	Neurological effects
Metals	Aluminum Arsenic Copper Lead Manganese Mercury Tin Zinc	Neurotoxic effects, Cognitive decline
Pesticides	Aldrin Chlordane Dichlorodiphenylchloroethylene (DDE), Dichlorodiphenyltrichloroethane (DDT) Dieldrin Heptachlor Maneb Methyl parathion Organophosphates Paraquat Pyrethroids Rotenone	Alzheimer's disease and neurotoxic effects
Flame retardants (brominated, chlorinated)	2,2', 4.4'-tetrachlorobiphenyl 6-Hydroxy-2.2', 4.4'-tetrabromodiphenyl ether Decabromodiphenyl Hexabromocyclododecane Pesticides (others) Perfluorinated compounds Polychlorinated biphenyls (PCB) Solvents Tetrabromobisphenol Trichloroethylene	Neurotoxic effects and Dementia
Solvents	Carbon disulfide Perchloroethylene (PCE) Toluene	
Pharmaceuticals	Anesthetic agents Benzodiazepine	Alzheimer's disease
Air pollution	Carbon monoxide Nitrogen dioxide Ozone Particulate matter Second hand smoke (Nicotine, Cadmium) Methanol	Dementia Parkinson's disease Multiple sclerosis Amyotrophic lateral sclerosis Neurodegeneration

Plasticizers	Bisphenol Phthalate esters	
Food ingredients (see current list in fda.gov)	Artificial food constituents Dyes and lakes Food and color additives Ingredients (acidulants, anti-caking agents, binders, color additives, dough strengthening & conditioners, emulsifiers, fat replacers, firming agents, flavor enhancers, humectants, leavening agents, stabilizers, thickeners, texturizers, yeast nutrients, etc.)	
Others	Acrylamide Dioxins Formaldehyde Methanol Mycotoxins Organic compounds Petrochemicals Perfluorooctanesulfonic acid (PFOS) Perfluoroctanoic acid (PFOA) Synthetic chemical agents	Dementia

Source: Augmented from Genuis & Kelln (2015)

Table 4: *Elemental exposures potentially associated with neurodegenerative diseases including dementia*

The escalating health threats posed by exposure to the above tabulated toxicants has not been sufficiently recognized because it was believed that they are readily eliminated by the body. Yet, the continuous exposure to them, their increasing concentrations, and their long half-lives cause their bioaccumulation in various organs, resulting in various pathologies. Genius and Kelln have identified the following harm mechanisms: "mitochondrial damage, oxidative stress, cell death, neurotransmitter dysregulation, endocrine disruption, and epigenetic modification". These authors have also pointed out potential treatments based on the elimination of these toxicants. They have further discussed a case report study of a single patient who presented with a significant burden of lead owing to his past occupational exposure. Tests performed to assess the levels of toxicants revealed elevated values of ferritin, immunoglobulin E, C-reactive protein, and creatinine. They also revealed positive antinuclear antibody and decreased glomerular filtration rate. Through interventions to excrete the excessive lead (skin depuration, oral DMSA, and EDTA) and nutritional supplementation (to prevent mineral deficiency), the patient reportedly recovered his good health within one year and progressively resumed a normal life with good quality after six years of therapy.

Conclusions

As we are entering a dementia pandemic that may devastate world's economies and health care systems, it behooves us to focus on the causal etiology of dementia and other neurodegenerative diseases. I have posited earlier that they are the consequence of an autoimmune disease in overdrive. While that theory is under critical review with the hope that it may provide the needed ultimate treatment, we should also dedicate efforts to eliminating those potentially reversible dementia forms that are due to continual exposure to toxicants and their bioaccumulation. Detoxification therapies exist, have been proven in a variety of cases, and need to be made more widely known and available.

References

1. Baltazar MT., et al. "Pesticides exposure as etiological factors of Parkinson's disease and other neurodegenerative diseases--a mechanistic approach". *Toxicology Letters* 230.2 (2014): 85-103.
2. Barnham KJ and Bush AI. "Biological metals and metal-targeting compounds in major neurodegenerative diseases". *Chemical Society Reviews* 43.19 (2014): 6727-6749.
3. Billioti de Gage S., et al. "Benzodiazepine use and risk of dementia: prospective population based study". *British Medical Journal* 345 (2014): e6231.

4. Bleecker ML., et al. "Differential effects of lead exposure on components of verbal memory". *Occupational and Environmental Medicine* 62.3 (2005): 181-187.
5. Block ML., et al. "The outdoor air pollution and brain health workshop". *NeuroToxicology* 33.5 (2012): 972-984.
6. Bondy SC. "Prolonged exposure to low levels of aluminum leads to changes associated with brain aging and neurodegeneration". *Toxicology* 315.1 (2014): 1-7.
7. Bradberry S., *et al*. "Use of oral dimercaptosuccinic acid (succimer) in adult patients with inorganic lead poisoning". *QJM: An International Journal of Medicine* 102.10 (2009): 721-732.
8. Bredesen DE. "Reversal of cognitive decline: a novel therapeutic program". *Aging* 6.9 (2014): 707-717.
9. Brewer GJ. "Alzheimer's disease causation by copper toxicity and treatment with zinc". *Frontiers in Aging Neuroscience* 6 (2014): 92.
10. Cannon JR and Greenamyre JT. "The role of environmental exposures in neurodegeneration and neurodegenerative diseases". *Toxicological Sciences* 124.2 (2011): 225-250.
11. (U.S.) Centers for Disease Control and Prevention: Department of Health and Human Services: "Fourth National Report on Human Exposure to Environmental Chemicals: Updated Tables". (2013).
12. Exley C and Vickers T. "Elevated brain aluminium and early onset Alzheimer's disease in an individual occupationally exposed to aluminium: a case report". *Journal of Medical Case Reports* 8.1 (2014): 41.
13. Fymat AL. "Epilepsy: A Review". *Journal of Current Opinions in Neurological Science* 1.5 (2017): 240-254.
14. Fymat AL. "Parkinson's Disease and Other Movement Disorders: A Review". *Journal of Current Opinions in Neurological Science* 2.1 (2017): 316-343.
15. Fymat AL. "Alzheimer's Disease: A Review". *Journal of Current Opinions in Neurological Science* 2.2 (2018): 415-436.
16. Fymat AL. "Alzheimer's Disease: Prevention, Delay, Minimization and Reversal". *Journal of Clinical Research in Neurology* 1.1 (2018): 1-16.
17. Fymat AL. "Alzhei … Who? Demystifying the Disease and What You Can Do About it". *Tellwell Talent Publishers* (2018): 236.
18. Fymat AL. "Dementia Treatment: Where Do We Stand?" *Journal of Current Opinions in Neurological Science* 3.1 (2018): 599-603.
19. Fymat AL. "On Dementia and Other Cognitive Disorders". *Journal of Clinical Research in Neurology* 2.1 (2018): 1-14.
20. Fymat AL. "Is Alzheimer a Runaway Autoimmune Disease? And How to Cure It?" *Proceedings of the European Union Academy of Sciences* (2018): 379-83.
21. Fymat AL. "Dementia: A Review". *Journal of Clinical Psychiatry and Neuroscience* 1.3 (2019): 27-34.
22. Fymat AL. "The Pathogenic Brain". *Journal of Current Opinions in Neurological Science* 3.2 (2019): 669-671.
23. Fymat AL. "On the Pathogenic Hypothesis of Neurodegenerative Diseases". *Journal of Clinical Research in Neurology* 2.1 (2019): 1-7.
24. Fymat AL. "Dementia with Lewy Bodies: A Review". *Journal of Current Opinions in Neurological Science* 4.1 (2019): 15-32.
25. Fymat AL. "What do we Know about Lewy Body Dementias?" *Journal of Psychiatry and Psychotherapy* 2.1 (2019): 1-4.
26. Fymat AL. "Viruses in the Brain...? Any Connections to Parkinson's and other Neurodegenerative Diseases?" *Proceedings of the European Union Academy of Sciences* (2019): 249-52.
27. Fymat AL. "Recent Research Developments in Parkinson's Disease". *Current Opinions in Neurological Science* 5.1 (2020): 12-30.
28. Fymat AL. "Is Alzheimer's an Autoimmune Disease Gone Rogue? The Role of Brain Immunotherapy". *Journal of Clinical Research in Neurology* 3.2 (2020): 1-3.
29. Fymat AL. "Alzheimer's: What do we Know about the Disease and What Can Be Done About It?" *EC Journal of Psychology & Psychiatry* 9.11 (2020): 69-74.
30. Fymat AL. "Alzheimer's: Will there ever be a Cure?" *Journal of Clinical Psychiatry and Neuroscience* 3.4 (2020): 1-5.
31. Fymat AL. "Parkinson's: What is Known about the Disease and What Can Be Done About It?" *Journal of Clinical Research in Neurology* 3.2 (2020): 1-12.
32. Fymat AL. "Dementia: Should we Reorient our Approach to Treatment?" *EC Journal of Psychology & Psychiatry* 9.12 (2020): 1-3.
33. Fymat AL. "Dementia – What is its Causal Etiology?" *International Journal of Neuropsychology and Behavioral Sciences* 1.1 (2020): 19-22.
34. Fymat AL. "Parkin... ss..oo..nn: Elucidating the Disease... and What You Can Do About it". *Tellwell Talent Publishers* (2020): 258.

35. Fymat AL. "Dementia: Fending off the Menacing Disease... and What You Can Do About it". *Tellwell Talent Publishers* (2020).
36. Fymat AL. "Paradigm for Pandemic Prediction and Prevention," Proc. European Union Academy of Sciences Pandemics, *Universal Journal of Mathematics & Computation* 9 (2021): 27-42.
37. Fymat AL. "The Human Brain – Wonders and Disorders". *Tellwell Talent Publishers* 29 (2021).
38. Fymat AL. "Pandemics: Prescription for Prediction and Prevention". *Tellwell Talent Publishers* 23 September (2021).
39. Gatto NM., *et al.* "Components of air pollution and cognitive function in middle-aged and older adults in Los Angeles". *Neuro Toxicology* 40 (2014): 1-7.
40. Genuis SJ. "Toxic causes of mental illness are overlooked". *NeuroToxicology* 29.6 (2008): 1147-1149.
41. Genuis SJ. "Elimination of persistent toxicants from the human body". *Human and Experimental Toxicology* 30.1 (2011): 3-18.
42. Genuis SJ. "What's out there making us sick?" *Journal of Environmental and Public Health* (2012): 605137.
43. Genuis SJ., *et al.* "Toxic element contamination of natural health products and pharmaceutical preparations". *PLoS ONE* 7.11 (2012): e49676.
44. Genuis SJ., *et al*. "Clinical detoxification: elimination of persistent toxicants from the human body". *The Scientific World Journal* (2013): 238347.
45. Genuis SJ and Kelln KL. "Toxicant exposure and bioaccumulation: a common and potentially reversible cause of cognitive dysfunction and dementia". *Behavioral Neurology volume* (2015): 620143.
46. Goldman M., *et al*. "Solvent exposures and Parkinson disease risk in twins". *Annals of Neurology* 71.6 (2012): 776-784.
47. Health Canada. "Second report on human biomonitoring of environmental chemicals in Canada". (2013) 2ndHumanBiomonitoringReport.pdf
48. Jin CF., *et al*. "Industrial solvents and psychological effects". *Clinics in Occupational and Environmental Medicine* 4.4 (2004): 597-620.
49. Kanthasamy A., *et al*. "Emerging neurotoxic mechanisms in environmental factors-induced neurodegeneration". *NeuroToxicology* 33.4 (2012): 833-837.
50. Kilburn KH. "Why is chemical brain injury ignored? Pondering causes and risks". *Archives of Environmental Health* 58.3 (2003): 132-134.
51. Liu KS., *et al*. "Neurotoxicity and biomarkers of lead exposure: a review". *Chinese Medical Sciences Journal* 28.3 (2013): 178-188.
52. Lucchini R and Zimmerman N. "Lifetime cumulative exposure as a threat for neurodegeneration: need for prevention strategies on a global scale". *NeuroToxicology* 30.6 (2009): 1144-1148.
53. Mah L., *et al*. "Ambient lead exposure is associated with greater risk of conversion to Alzheimer's disease and hippocampal atrophy in individuals with amnestic mild cognitive impairment". *The American Journal of Geriatric Psychiatry* 22.3 (2014): S117-S118.
54. Patterson C., *et al*. "Diagnosis and treatment of dementia: 1. Risk assessment and primary prevention of Alzheimer's disease". *Canadian Medical Association Journal* 178.5 (2008): 548-556.
55. Porru S and Alessio L. "The use of chelating agents in occupational lead poisoning". *Occupational Medicine* 46.1 (1996): 41-48.
56. Rappaport SM and Smith MT. "Environment and Disease Risks". *Science* 330.6003 (2010): 460-461.
57. Reis J and Román GC. "Environmental neurology: a promising new field of practice and research". *Journal of the Neurological Sciences* 262.1-2 (2007): 3-6.
58. Rhodes D., et al. "Relationship of bone and blood lead levels to psychiatric symptoms: the normative aging study". *Journal of Occupational and Environmental Medicine* 45.11 (2003): 1144-1151.
59. Richardson J., *et al*. "Elevated serum pesticide levels and risk for Alzheimer disease". *Journal of American Medical Association Neurology* 71.3 (2014): 284-90.
60. Rother HA. "Communicating pesticide neurotoxicity research findings and risks to decision-makers and the public". *Neuro Toxicology* 45 (2014): 327-337.
61. Sabbath EL., *et al*. "Time may not fully attenuate solvent-associated cognitive deficits in highly exposed workers". *Neurology* 82.19 (2014): 1716-1723.
62. Schofield P. "Dementia associated with toxic causes and autoimmune disease". *International Psychogeriatrics* 17.1 (2005): S129-147.

63. Sears ME. "Chelation: harnessing and enhancing heavy metal detoxification--a review". *The Scientific World Journal* (2013): 219840.
64. Squitti R. "Copper subtype of Alzheimer's disease (AD): meta-analyses, genetic studies and predictive value of non-ceruloplasmim copper in mild cognitive impairment conversion to full AD". *Journal of Trace Elements in Medicine and Biology* 28.4 (2014): 482-485.
65. Squitti R. "Low-copper diet as a preventive strategy for Alzheimer's disease". *Neurobiology of Aging* 35.2 (2014): S40-S50.
66. Stewart WF and Schwartz BS. "Effects of lead on the adult brain: a 15-year exploration". *The American Journal of Industrial Medicine* 50.10 (2007): 729-739.
67. Tilson HA and Kodavanti S. "The neurotoxicity of polychlorinated biphenyls". *NeuroToxicology* 19.4-5 (1998): 517-525.
68. Edwin van Wijngaarden., et al. "Bone lead levels are associated with measures of memory impairment in older adults". *Neuro Toxicology* 30.4 (2009): 572-580.
69. Visvanathan R. "Is it truly dementia?" *The Lancet* 357.9257 (2001): 684.
70. Walker B Jr. "Neurotoxicity in human beings". *Journal of Laboratory and Clinical Medicine* 136.3 (2000): 168-180.
71. Yang M., et al. "Alzheimer's disease and methanol toxicity (part 1): chronic methanol feeding led to memory impairments and tau hyperphosphorylation in mice". *Journal of Alzheimer's disease* 41.4 (2014): 1117-1129.