

Chapter 6

Environmental Toxins as Causes of Brain Degeneration in Sub-Saharan Africa

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Abstract Brain degeneration, especially Dementia is a complex human disease. The Alzheimer's Association estimates that one in 10 persons over 65 and nearly half of those over 85 have Alzheimer's disease. There is paucity of data on the prevalence of dementia in Sub-Saharan Africa. Available data suggests a general prevalence of dementia at 6.4 % in Tanzania and HIV related dementia at 31 % in Uganda. Despite the growing burden of dementia in low-income countries, there are few previous data on the prevalence, causes and risk factors of dementia in sub-Saharan Africa.

Therefore, it is important to identify protective and risk factors for dementia to prevent this disease at an early stage. Several factors are related to dementia, e.g. age, ethnicity, sex, genetic factors, physical activity, smoking, drug use, education level, alcohol consumption, body mass index, co-morbidity, and environmental factors. Due to paucity of Sub-Saharan African data, this review looks at studies done elsewhere to evaluate the association between environmental toxins and risk of dementia, especially Alzheimer's and Parkinson's diseases. We have examined whether evidence from previous studies on association between toxin environmental exposures and dementia is of sufficient strength to warrant specific recommendations for behavioral, lifestyle, or pharmaceutical interventions/modifications targeted to these endpoints. We also suggest future research directions for researchers in dementia-related fields in Sub-Saharan Africa.

Keywords Dementia • Alzheimer's disease • Environmental toxins • Sub-Saharan Africa

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What Is Dementia?

Dementia is an acquired complex of intellectual deterioration which affects at least two areas of cognitive function. Decline must affect ability to function normally. It is a syndrome, not a diagnosis. The executive functions which are affected include: making a plan and carrying it out, weighing information and making good decisions, initiating activities, appropriate social behavior as well as changes in personality. Personality characteristics and denial of memory problems are also associated with executive dysfunction. In addition, the cognitive impairments must be severe enough to cause impairment in social and occupational functioning. Importantly, the decline must represent a decline from a previously higher level of functioning. The cognitive deficits occurring exclusively during the course of delirium, usually short-term, should not be diagnosed as dementia. The Alzheimer's Association estimates that one in 10 persons over 65 years and nearly half of those over 85 years have Alzheimer's disease (<http://health.usnews.com/health-conditions/brain-health/alzheimers-disease>, 30/10/12).

Types and Causes of Dementia

Some of the major disorders causing dementia are;

- Degenerative diseases e.g. Alzheimer's disease, Pick's disease etc.;
- Vascular dementia e.g. multi-infarct dementia;
- Anoxic dementia e.g. secondary to cardiac arrest);
- Traumatic dementia e.g. dementia pugilistica [boxer's dementia];
- Infectious dementia e.g. Creutzfeldt-Jakob Disease, HIV-associated dementia etc.
- Toxic dementia e.g. alcoholic dementia.

There are many different types of dementia (Table 6.1). It is however still unknown how some diseases may be linked to dementia.

Risk Factors

Many factors can eventually lead to dementia. Some can't be changed while other can be addressed to reduce the risk.

Table 6.1 Types of dementia

Type of dementia	Percentage of all dementia types (approximate) (%)	Causes
Alzheimer's disease	60	Degenerative disease causing "plaques and tangles" to build up in the brain tissues that kill and shrinks the brain
Lewy body dementia	15	Degenerative disease associated with an accumulation of "Lewy Bodies" in the brain causing impairment in cognitive function
Mixed dementia	10	Combination of degenerative disease and other type of dementia
Vascular dementia (multi-infarct or mini-strokes)	5	Circulatory disease of heart and blood vessels resulting in stroke or mini-stroke that damage areas of the brain
Other dementias	10	
1. Frontal lobe dementia and Picks disease		1. Affects frontal lobe, behavior problems
2. Creutzfeldt-Jakob disease		2. Viral disease
3. Multiple sclerosis, Parkinson's disease, Huntington's chorea		3. Diseases of the nervous system
4. Brain damage alcohol abuse, toxins		4. Brain trauma, damage may improve if toxins are removed

Source: Modified from "Definition of Dementia," (Compiled by Wisconsin Bureau of Aging & Long Term Care Resources, Department of Health and Family Services 4/2403 rev. <http://www.dhs.wisconsin.gov/aging/dementia.htm>, downloaded on 30/10/12)

Non-modifiable Risk Factors

- **Age.** The risk of Alzheimer's disease, vascular dementia and several other dementias increases significantly with age [1]. However, dementia isn't a normal part of aging.
- **Family history.** People with a family history of dementia are at greater risk of developing it. However, many people with a family history never develop symptoms, and many people without a family history do. If they have specific genetic mutations, they are at significantly greater risk of developing certain types of dementia [2].
- **Down syndrome.** By the time they reach middle age, most people with Down syndrome develop the plaques and tangles characteristic of Alzheimer's disease, according to studies [3]. Many, but not all, also develop dementia.

Modifiable Risk Factors

The following factors can be controlled to reduce the risk of dementia:

- **Alcohol use.** Alcohol consumption is one possible risk factor for Alzheimer's Dementia, AD. Alcoholism is associated with extensive cognitive problems [4], including alcoholic dementia [5]. The effects of alcohol on cognition, brain disorders, and brain chemistry are somewhat similar to AD's effects on these three areas, it is possible that alcohol use might increase the risk of developing AD [6].
- **Atherosclerosis.** This buildup of plaques is a significant risk factor for vascular dementia as it may lead to stroke. Studies have also shown a possible link between atherosclerosis and Alzheimer's disease [7].
- **Blood pressure.** Uncontrolled hypertension is a risk of developing Alzheimer's disease and vascular dementia. Cumulative evidence implicates hypertension in the pathogenesis of AD [8, 9].
- **Cholesterol.** High levels of low-density lipoprotein (LDL) cholesterol can significantly increase the risk of developing vascular dementia [10]. Some research has also linked high cholesterol levels in middle age each increase the risk of going on to develop AD in later life [11].
- **Depression.** Late-life depression, especially in men, may be an early indication for the development of Alzheimer's-related dementia [12].
- **Diabetes.** People with Type 2 diabetes have an increased risk of developing both Alzheimer's disease and vascular dementia [13].
- **High estrogen levels.** High levels of total estrogen in women have been associated with greater risk of developing dementia [14–16].
- **Homocysteine blood levels.** Elevated blood levels of homocysteine – a type of amino acid produced in the body – may increase the risk of developing Alzheimer's disease and vascular dementia [17].
- **Smoking.** It likely increases the risk of developing dementia because it's a risk factor for atherosclerosis and other types of vascular disease. Recent prospective studies on cohorts without dementia suggest that smokers have a significantly increased risk of dementia, including AD [18, 19].

Environmental Toxins and Dementia

Dementia may originate from environmental toxic substances, namely exposure to heavy metals such as lead, mercury and aluminum; as well as to carbon monoxide, solvents, pesticides and electromagnetic fields [20]. This tends to affect exposed individuals at a relatively young age and the optimal preventative strategies include avoidance of the toxic substances.

Toxic encephalopathy is a general term used to describe any sort of cerebral damage that comes from the use of or exposure to toxic compounds, chemicals or

Table 6.2 Effects of environmental toxins on human health

Metal	Organic diseases	Neurologic and psychiatric effects [23]
Aluminum	Joint pain, bone calcium loss anaemia [24]	Dementia, Alzheimers, Parkinsons, Encephalopathy with loss of memory, concentration and mobility
Arsenic	Type 2 diabetes [25]	Damage to the nervous system leading to weakness, deafness, paresthesia, organic psychosis with drowsiness, agitation, stupor, delirium, schizophrenia
Cadmium	Damage to kidney and lungs, fragile bones, anaemia, increased risk of cancer if inhaled [26]	No reference found at this stage
Mercury	Brain damage, Autoimmune diseases e.g. Rheumatoid Arthritis [27], Cardiovascular diseases [28], liver cancer	Diminished intelligence, speech disorders, restlessness, aggressiveness, visual and hearing disorders, polyneuropathy, myasthenia gravis, Alzheimers
Nickel	Allergies, dermatitis, Eczema [29]	Headache, dizziness, lack of sleep
Lead	Hematological and Cardiovascular effects e.g. hypertension MLEWE [55], kidney damage [30]	Depression that may lead to suicide, lack of attention, damage to visual intelligence and motor function, memory disorder, learning difficulties, fatigue, agitation, aggressiveness, psychoses, hallucinations, peripheral polyneuropathy, encephalopathy, saturnism (lead poisoning)
Organic zinc	Stomach cramps, nausea, vomiting, anaemia, damage to the pancreas	Cerebral edema with nausea, vomiting, dizziness, visual disorder, cramps, forgetfulness, fatigue, lack of interest, headaches, sleeping difficulties

Source: Social, Health and Family Affairs Committee, Parliamentary Assembly of the Council of Europe. Health hazards of heavy metals. Doc. 12613, 12 May 2011. <http://assembly.coe.int/ASP/Doc/XrefViewPDF.asp?FileID=12818&Language=EN>

metals [21]. This damage is sometimes repairable, but in cases in which the damage persists, the risk for development of degenerative dementia increases.

Exposure to any kind of toxic substance with a negative effect on the brain can cause toxic encephalopathy, and ultimately, the onset of dementia. Some of the most common environmental toxic substances that can cause this damage are:

- **Heavy metals:** Mercury, lead, aluminum, arsenic, lead, toluene and lithium, even in small doses, can have a long-term damaging effect on the brain [22] leading to both encephalopathy and dementia (Table 6.2).
- **Pesticides:** Many families of pesticides are known to contain neurotoxic properties [31] that cause serious central nervous system damage e.g., carbamates, organophosphates, organochlorines, and bipyridyles [32]. Evidence consistently suggests that a higher risk of Parkinson's Dementia (PD) is associated with pesticides and that a higher risk of AD is associated with pesticides [33].

- **Solvents:** It is recognized that exposure to solvents can be neurotoxic [34]. However, an association between solvent exposure and neuro-degeneration, particularly AD, has yet to be established. Some studies have demonstrated a moderate-to-strong association between solvent exposure and AD, with a greater effect in men and more years of exposure [35].
- **Electromagnetic fields:** Although no documented causal relationship between occupational electromagnetic field (EMF) exposure and AD has been found, a link between occupations involving exposure to electric and magnetic fields and the subsequent development of AD has been hypothesized. Some research findings [36] suggest that EMF exposure may contribute to an increased production of b-amyloid in the brain, which might eventually result in AD.
- **Carbon Monoxide:** In patients with acute poisoning, 30 % or more may experience delayed onset of neuropsychiatric symptoms [37]. Symptoms include cognitive and personality changes, dementia, psychosis, Parkinsonism, amnesia, depression, and incontinence

Even small amounts of these toxic materials, especially over a long period of time, can cause gradual mental deterioration.

Association Between Toxic Environmental Exposures and Dementia

This section examines whether evidence from previous studies on association between toxin environmental exposures and dementia is of sufficient strength to warrant specific recommendations for behavioral, lifestyle, or pharmaceutical interventions/modifications targeted to these endpoints.

Williams et al. [38] identified a systematic review by Santibanez et al. [39], that examined occupational risk factors for Alzheimer's disease (AD), focusing on the associations between AD and pesticides, solvents, electromagnetic fields, lead, and aluminum in the workplace. The review included 21 case-control studies and three cohort studies published between 1984 and 2003. Some studies examined multiple factors, and number of studies and subject counts are included for each exposure. Therefore, the study count in Table 6.3 exceeds the 22 studies identified. Case control studies were included in spite of the inherent weakness for establishing causality, due to paucity of data from cohort studies. Further, exposures to specific toxic substances are relatively uncommon and would require very large sample sizes to have sufficient power to detect an effect in general community samples.

Two cohort studies reported higher adjusted relative risks for AD with exposure to defoliants and fumigants (RR 4.35; 95 % CI 1.05–17.90) and pesticides in men [RR 2.39, 1.02–5.63] [40]. The single cohort study evaluating solvent exposure [41] did not find an association with AD (RR 0.88; 95 % CI 0.31–2.50). Studies of lead exposure were all case-control design and assessed as low quality; none showed a statistically significant association with AD. One study of aluminum exposure was

Table 6.3 Toxic environmental factors and risk of developing AD – characteristics of studies reviewed by Santibanez et al. [39]

Risk factor	Studies ^a	Subjects ^a	Countries
Solvents	10 case control	3,748	North America (6), Western Europe (2), Asia (2), Canada
	1 cohort	694	
Electromagnetic fields	6 case control	6,205	U.S.A (4), Western Europe (2), U.S.A
	1 cohort	20,068	
Pesticides	4 case control	1,471	Canada (2), U.S.A (1), Australia (1), Canada (1), France (1)
	2 cohort	2,201	
Lead	6 case control	2,182	U.S.A (4), U.K (1), Australia (1)
Aluminium	3 case control	1,056	U.S.A (1), U.K (1), Australia (1)

Source: Williams et al. [38] (Evidence Reports/Technology Assessments, No. 193.) Available from: <http://www.ncbi.nlm.nih.gov/books/NBK47456>

^aSome studies examined multiple factors, and number of studies and subject counts are included for each exposure. Therefore, the study count in this table exceeds the 22 studies identified

case-control study and found no association with AD [RR 0.95; 95 % CI 0.5–1.9] [42]. Similarly, the two other case-control studies [43, 44] did not find any association between aluminum and AD. Rondeau et al. [45] in cohort study observed that the risk of AD was increased for aluminum intake ≥ 0.1 mg/day (RR 1.34; 95 % CI 1.09–1.65) and there was no dose response relationship.

Using a subgroup from the Canadian Study of Health and Aging (15 % of the cohort), Kroger et al. [46] used a nested case-control design to evaluate the association between blood mercury levels and AD. After a median of 4.9 years, individuals in the 3rd (OR 0.41; 95 % CI 0.23–0.74) and 4th quartiles of exposure (OR 0.56, 0.32–0.99) were at lower risk for AD. However, the relatively low participation rate may have introduced significant selection bias. Kamel et al. [47] observed that exposure to certain pesticides may increase risk of Parkinson disease (PD), a cause of dementia. Lee et al. [48] also found that traumatic brain injury and paraquat exposure each increased the risk of PD moderately, with exposure to both factors almost tripled PD risk. These environmental factors seem to act together to increase PD risk in a more than additive manner.

Conclusions and Recommendations

In systematic review, few cohort studies examined the association between toxic-environmental exposures and risk of dementia. Most case-control studies had important methodological limitations that may have biased the results. Among the exposures considered, only pesticides showed a consistent association with AD and PD. Hence, there is justification for specific recommendations for behavioral, lifestyle and pharmaceutical interventions/modifications to reduce exposure to pesticides.

Despite the growing burden of dementia in low-income countries, there are few previous data on the prevalence, causes and risk factors of dementia in sub-Saharan Africa. The prevalence of dementia of 6.4 % (95 % CI 4.9–7.9), in this rural Tanzanian population is similar to that reported in high-income countries [49]. In a Ugandan study 31 % of the HIV-positive patients were found have HIV-Associated Dementia and these were frequently patients of advanced disease stage and decreased CD4 count [50–52]. There is need for further research to determine the general prevalence of dementia in Sub-Saharan Africa as well the measure of association between dementia and potential environmental toxins.

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