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Trace Contaminants in Drinking Water and Neurological Health

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Abstract

Maintaining drinking-water quality is a regulatory priority in the United States to protect public health. Nonetheless, existing regulatory frameworks may not adequately address risks posed by emerging contaminants or by chronic, low dose exposures. The emergence of novel chemical entities with incompletely characterized toxicological profiles, together with limited epidemiological evidence regarding long term, low level exposures, likely contributes to regulatory gaps. Following an overview of common sources of water contamination, this review evaluates selected neurotoxicants documented to affect the central and peripheral nervous systems. It also provides a concise discussion of mixture effects, including additive, synergistic, and antagonistic interactions, and examines mechanistic pathways through which these contaminants may induce neurological dysfunction. The primary objective is to underscore the importance of considering neurotoxicity at trace contaminant concentrations in drinking water. Although a comprehensive assessment of chronic low level exposures is beyond the scope of this brief review, this analysis highlights the paucity of longitudinal and mechanistic studies necessary to determine the health consequences of sustained exposure to trace contaminants and supports the need for targeted toxicological investigations.

Keywords: Nervous systems, Drinking water, Epidemiological evidence, Toxicological investigations, Neurotoxicants.

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Introduction

The entire community consumes drinking water, making its cleanliness a crucial foundation for general public health considerations. Impurities are present in trace amounts even though strict rules are in place to guarantee that drinking water is free of dangerous contaminants. The source and purification methods employed affect the drinking water's overall quality. Water supply contamination typically results in a slow and steady decline in health rather than immediate symptoms of poisoning. This effect is brought on by long-term low-dose exposure, which causes water-soluble, amphiphilic environmental pollutants to bioaccumulate and concentrate in lipid deposits. Cellular malfunction may occur after a threshold concentration is reached. Therefore, there may be a chance that exposure to trace levels of water pollutants will raise the prevalence of slow-moving illnesses that are typically linked to aging or stunted growth. The central nervous system (CNS), which is particularly vulnerable to harm during development and then accelerates neurodegenerative processes as people age, is involved in many of these illnesses.

The harmful effects of environmental pollutants found in drinking water depend on the stage at which the organism is developing. For example, inadequate energy generation may result from in utero stressors that disrupt mitochondrial activity. This disturbance

of normal cellular function may disrupt the correct growth of the central nervous system. Anomalies in the controlled gene expression required for proper development could be another early effect of exposure to pollutants. Early CNS development can also result in genetic imprinting that does not immediately show functional alterations. However, the combination of aging processes and these early genetic changes may increase a person's susceptibility to disease later in life. Exposure later in life may intensify age-related declines in central nervous system function. Senescence, for instance, triggers an increase in inflammation and oxidative stress. According to this article's review, a number of drinking water contaminants raise one or both of these processes, which are believed to be major causes of neurodegenerative diseases. Instead of focusing on direct alterations to the prenatal central nervous system, this review primarily examines negative effects on the adult brain.

Potential Industrial Waste Contamination Sources for Potable Water

Residential water sources may become contaminated by the runoff from numerous industrial processes that consume enormous amounts of water. This is how chemicals, including both organic and inorganic salts, end up in water systems. The quality of water leaving the sites of hydraulic fracturing (fracking), a technique used to produce shale gas, has recently been significantly impacted. Hydrocarbons, including methane, ethane, and propane, have the potential to escape and contaminate shallow groundwater during drilling. The injected hydraulic fracturing fluid, which contains a range of chemicals such as acids, surfactants, acrylic polymers, and borate compounds, among other things, can also contaminate surface water [1]. Since the far higher concentrations of neurotoxic acrylamide present in cooked meals and coffee [2] typically overshadow the presence of this chemical in water sources owing to the breakdown of polyacrylamide grouting agents, it is not covered here.

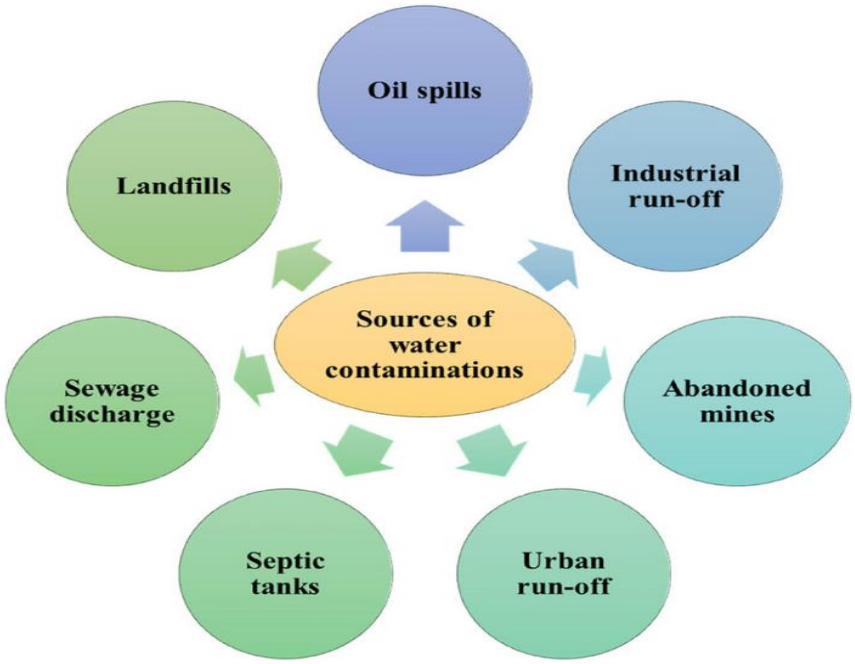

Figure-1 sources of water contaminations

Fertilized Dumps

Among the substances commonly discovered in water sources as runoff from agricultural fields are pesticide and fertilizer residues. Irrigation with tainted water containing various agrochemicals is one of the primary sources of metals and organic compounds in agricultural soils [3, 4]. Additionally, the raising of cattle may contaminate field water effluent with bacteria and animal waste. Lastly, the water's toxic burden may be increased by garden chemical runoff. Nitrate, a form of agricultural pollution, is frequently found in water sources. Due to the extensive usage of nitrogen fertilizers, nitrate is often found [5]. Neural tube abnormalities were shown to be four times more common in offspring of women whose public water supply contained nitrate above the US maximum contamination level [6].

Neurotoxic effects are present in several pesticides [7]. These frequently occur together with unidentified antagonistic or synergistic effects. Many pesticides have regulatory guideline levels (RGVs) and maximum water concentration values (MCVs) that differ by several orders of magnitude. Furthermore, to allow for uncertainty, these values frequently surpass the highest values determined for the risk to human health. A large number of indicated dosage limits exceed acceptable daily ingestion levels. The existing global drinking water regulation procedures do not yet provide safe standards in a way that protects public health, even while international authorities are working to control pesticide levels in water and other sources. Clearly, this area requires significant work [8, 9].

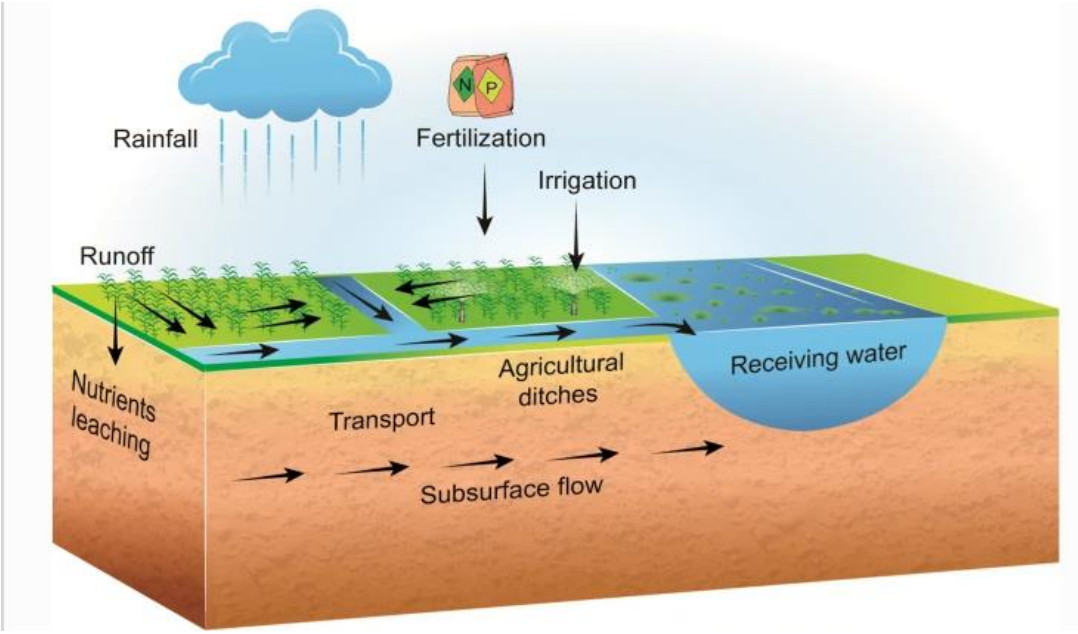

Figure-2 Existing global drinking water regulation procedures

Water Purification

Ironically, processes meant to make water more drinkable pose a threat to the quality of water storage facilities. The formation of a biofilm in drinking water distribution systems enables microbial growth [10]. One method of disinfection involves the use of chlorine and its compounds. Stable and potentially hazardous chlorinated organics can arise when these agents interact with traces of organic molecules in water. It has been demonstrated that chlorinated wastewater is cytotoxic to mammalian cells [11]. Copper piping erodes when chlorine and ammonia are used to disinfect water, which could raise the amount of the metal in drinking water. Chlorine has a pH-dependent effect on corroding copper pipes [12]. Alumina is another potentially hazardous substance that is added to water to coagulate particle pollutants and precipitate organic materials, which clarifies the water. Water's aluminum content may rise as a result [13]. Acid rain's growing frequency causes aluminum to seep from rocks, which can increase the amount of aluminum in water supplies. Aluminum levels in drinking water are linked to the prevalence of Alzheimer's disease (AD), according to epidemiological data [14]. Laboratory studies from experimental animals exposed to drinking water containing aluminum at levels comparable to those in some home supplies [15, 16] support this. Nonetheless, there is ongoing debate over the potential causal link between the presence of aluminum in water and the development of AD [17]. A recent study assessed the relationship between the child's negative neurodevelopmental outcomes and exposure to disinfection byproducts present in tap water during pregnancy. For girls, exposure to disinfection by-products was positively correlated with mental score at one year of age; however, this difference did not hold true when the evaluation was done at four or five years of age [18]. Therefore, additional research is required to determine whether and how minute concentrations of disinfectants in tap water could have neurodevelopmental or neurodegenerative effects.

Water Conduits

Water delivery through metal-lined conduits can be another factor that can impair the quality of the final product emerging from household taps. While the use of lead piping has been greatly curtailed in recent years, lead soldering is still a popular means of annealing piping. The evidence that even low levels of lead is a developmental hazard to human populations is unambiguous [19]. In addition, the use of copper tubing is currently widespread. Newly emerging data involving both epidemiological reports and studies on experimental animals are increasingly indicating that water-borne copper can also be a source of neurotoxicity [20–23].

Consumer Products

The aquatic ecosystem and ultimately drinking water can get contaminated by pharmaceutical substances [24, 25]. 48.7% of people use at least one prescription medication every 30 days, and some of these compounds progressively find their way into water supplies, according to the Centers for Disease Control and Prevention (CDC). On Cape Cod, high concentrations of the antibiotic sulfamethoxazole, the anticonvulsant phenytoin, and the surfactant perfluoro octane sulfonate were commonly found in water from public drinking water supply wells [26].

Pharmacological substances may have negative consequences in aquatic environments. Fish behavior can be affected by environmental dosages of the anxiolytic medication oxazepam [27]. Pharmacological compounds in water sources can therefore have a negative impact on aquatic life and ultimately human health. When lead-containing batteries and brake pads—which are high in zinc and copper—are improperly disposed of, metals may find their way into the water system. Several metals found in tires and brakes, including copper, zinc, lead, and cadmium, can also affect stormwater runoff from roads [28].
Consideration of Neurotoxic Potential of Individual Contaminants in Metals

Lead (Pb)

Lead seepage into drinking water from industrial waste is a long-standing issue. This situation is made worse by the fact that some waters, particularly those from low-lying areas, contain considerable levels of lead [4, 29]. The neurotoxicity of extremely low amounts of lead that can affect vast populations has been generally acknowledged for the past 20 years, although lead poisoning was formerly thought to affect only a limited population of industrially exposed workers. This negative impact is most noticeable in the developing brains of fetuses and newborns. Cognitive and behavioral deficits have been linked to low-dose lead exposure [30].

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Aluminum (Al)

Al concentrations in drinking water vary widely [40]. As a coagulant of organic materials, the metal is frequently added to water, and any leftover amounts that are unintentionally dissolved are regarded as harmless. Nonetheless, a growing body of research from laboratory and epidemiological investigations indicates that the amount of aluminum present in some drinking water may be hazardous. In experimental animals, prolonged exposure to such levels can result in oxidative stress and neuroinflammation [15, 21]. Exposure to aluminum may accelerate the development of neurological diseases like Alzheimer's. Results demonstrating increased Al in postmortem AD brain tissue [41–43] support this. The presence of aluminum in AD patients' cerebral arteries [44] raises the possibility that the metal may interfere with the blood-brain barrier [45]. This link between Al consumption and neurodegenerative disease has been reinforced by epidemiological research. In regions with high levels of Al in the drinking water supply, the prevalence of AD rose dose-dependently [46]. Increased Al concentrations were linked to poorer cognitive function in a meta-analysis of nine investigations [47]. Evidence from human and animal research suggesting the concurrent presence of silicic acid appears to be protective against Al toxicity, possibly due to the creation of an inert aluminosilicate, complicates the assessment of the effects of Al in drinking water [48, 49]. Since AD is a pleiotropic disease with several origins, it is challenging to attribute a single encounter to the condition. Recent studies have assessed and compiled the data, both positive and negative, that Al plays a role in AD [50]

Copper

Negative neurological consequences may also be linked to low levels of copper salts in water that was previously thought to be innocuous. Cu is a trace element that plays a biological role as a cofactor in numerous enzymes, in contrast to lead and aluminum. However, there are numerous processes in place to keep the metal bound to proteins since the free forms of copper are hazardous. Menkes' and Wilson's diseases, two genetic conditions that interfere with Cu homeostasis, provide examples of Cu's neurotoxic

potential [51]. It has been demonstrated that the levels of Cu in drinking water are more harmful than those found in food at comparable concentrations [52]. The pH and the kinds of conduits that are utilized control the metal levels in drinking water. Cu concentrations are higher in homes with plumbing systems that use Cu tubing because of the metal's slow corrosion. However, letting the water run before using it significantly reduces the levels of copper in the water [53]. Regulations pertaining to the amount of copper in residential water established a maximum level of 1.3 parts per million [54]. Standing water in corroding copper pipes can lead to levels as high as 7.8 mg/L [55].Gastrointestinal symptoms may be linked to increased consumption of copper through drinking water [56]. There are worries that the metal might also be a contributing factor in neurodegenerative conditions like Parkinson's disease (PD) and Alzheimer's disease. These worries stem from the discovery that the non-ceruloplasmin-bound component of copper is elevated in the cerebral fluid of PD patients [58] and the serum of AD patients [57]. A transgenic mouse model of AD has demonstrated that long-term exposure to copper speeds up disease-associated pathology [22,23], and occupational exposure to copper has been connected to a higher risk of Parkinson's disease [59]. Free Cu has been linked to cognitive deterioration [60], which supports its possible involvement in AD [61].Specific Cu-binding sites are present on the amyloid precursor protein [62] as well as the amyloid peptide [63] where the metal attaches [64]. Upon binding, Cu undergoes redox cycling which leads to formation of reactive oxygen intermediates [65,66]. Low-dose exposure to Cu in the drinking water significantly increased markers of oxidative stress in the brain of exposed animals [21] and increased activation of the transcription factor, AP-1 [67]. Since AP-1 is activated by redox status, the mechanism by which Cu modulates the transcription factor is likely related to its stimulation of oxidative processes.Inability of microglia to sequester Cu bound to amyloid plaques may enhance inflammatory events known to be exacerbated in AD [68]. Most recently, levels of Cu as low as 2 µM (a level only 10% of maximal levels of Cu recommended by the EPA) in the drinking water of aged mice, have been found to inhibit the actions of low-density lipoprotein receptor-related protein 1 (LRP1), which is involved in the transport of β-amyloid out of cells. This leads to accumulation of β-amyloid and neuroinflammation within the brain [69]. Overall, this concordance of laboratory and studies of human populations suggests a major, largely unacknowledged hazard. Thus, Cu in drinking water may have the ability to cause adverse neurological effects through several separate but intertwined mechanisms.

Arsenic and Cadmium

The presence of inorganic arsenic or cadmium in drinking water can present a serious hazard. Chronic arsenic poisoning is found in large parts of Bangladesh and adjoining parts of India, where ground water is severely contaminated with heavy metals [70]. One study of nearly a million subjects in a part of West Bengal reported a prevalence rate of arsenicosis in over 15% of the inhabitants. The highest level of arsenic found in drinking water was over 1300 µg/L and values of over 100 µg/L were common. Peripheral neuropathy was present in 16% of cases [71]. Arsenic exposure has also been linked to neurodevelopmental abnormalities. For example, in a case control study conducted in Bangladesh, mothers with higher arsenic exposure and folate deficiency were found to be at a higher risk of giving birth to an infant with neural tube defects. This was associated with histone modifications, which were taken to imply epigenetic effects [72]. Furthermore, cognitive [73,74] and motor [75] function is lower in children that consume arsenic contaminated water for a prolonged period. This metal may also enhance biological processes associated with neurodegenerative disorders. For example, arsenic promotes accumulation of α-synuclein, a neuronal protein that plays an important role in Parkinson’s disease [76]. An epidemiological relation between arsenic exposure and a higher incidence of neurodegenerative disorders has been reported [77]. This may be attributable to the ability of arsenic to promote oxidative stress and inflammation, both of which are associated with neurodegeneration [78]. The hazards of arsenic in drinking water are not confined to third world countries. Some parts of the US, notably Texas and the Great Lakes Basin, have arsenic levels of over 50 µg/L in groundwater [79].

While the neurotoxic aspects of arsenic are overshadowed by its potential as a carcinogen, damage to the developing nervous system poses a grave long-term risk. Similarly, while cadmium exposure is associated with nephrotoxicity, low doses of cadmium in drinking water can promote excess free radical related oxidative events. The brain appears to be more sensitive to such changes than other organs [80]. It is likely that exposure to neonates is more harmful compared to adults [81]. Cadmium levels in drinking water have been found to exceed the permissible limits of the World Health Organization in both Egypt and Iran [82,83]. The hazard posed by seemingly low-level exposures to several heavy metals, such as cadmium, mercury and lead is exacerbated by the tendency of these metals to accumulate in tissues over time.

Organic Materials

Halogenated Residues

Organochlorine pesticides owe their effectiveness to their stability rather than to their reactivity. This durability allows prolonged allosteric interaction with key receptor sites and ion channels. Their non-reactiveness is the same quality that can permit their persistence in aqueous media. Another class of stable organ halogen compounds that has diffused into the environment, includes polychlorinated biphenyls (used as electrical insulators) and polybrominated biphenyls (used as fire retardants). The inadvertently produced dioxins are also in this group. Due to their exceptionally low reactivity, trace amounts of these materials can persist for extended periods in water supplies. Despite their inertness, such compounds can selectively target specific biological sites and impede their function for long periods by allosteric means. Their neurotoxicity is well established [84]. A further presence of organohalogens

in drinking water comes from the use of chlorine, bromine or their derivatives such as chloramines and chlorine dioxide as a means of water disinfection. Water sterilization byproducts include trihalomethanes, halo acetic acids, halo acetaldehydes, haloacetonitriles, halo amines, nitrosamines, and halo benzoquinones [85]. While most of these have not been extensively studied, the neurotoxicity of several disinfection byproducts, including dibromacetic acid found in water stocks, has been described [86]. An association between extended exposure to trichloroethylene (TCE) and Parkinson's disease has been reported: the exposure of animals to TCE can lead to striatal degeneration and the onset of parkinsonian characteristics. This has been attributed to mitochondrial dysfunction perhaps due to the formation of chloral from TCE and the subsequent synthesis of 1-trichloromethyl-1,2,3,4-tetrahydro-beta-carboline (TaClo) a specific dopaminergic neurotoxin [87].

Acrylamide

In addition to being a grouting agent, polyacrylamide works well as a flocculant to clear water. It is helpful for lining canals, wells, and pipes to minimize water loss by leaking. Additionally, pesticide mixtures contain polyacrylamide to boost viscosity. Water supplies may be toxically contaminated when polyacrylamide breaks down into the monomeric form, acrylamide. Poisoning instances have been reported after drinking water from wells or pipes that have recently been grouted. Ataxia, hallucinations, and memory problems are among the serious neurotoxic consequences that have resulted from these [88]. Acrylamide contamination is typically not a significant problem for a number of reasons. Acrylamide does not bioaccumulate and is biodegraded in water with a half-life of around two days. Furthermore, the consumption of acrylamide from regularly consumed foods is orders of magnitude higher than what is predicted from water [89].

Bisphenol A

Bisphenol A (BPA) is a significant chemical that is used in huge quantities to make a variety of polymers, such as epoxy resins and polycarbonates. Epoxy resins are utilized to line water supply pipes in addition to being employed in the production of bottles and the lining of cans that carry food items. Bisphenol A is a carcinogen and developmental toxin that acts on estrogen receptors. Through processes unrelated to the estrogen receptor, it also results in metabolic and behavioral alterations as well as neuronal death [90]. Since another study (backed by the polycarbonate industry) did not show evidence of neurotoxicity, the neurotoxicity of BPA is debatable [91]. Although the amount of BPA in bottled water is a serious worry, this chemical has also been detected in tap water in a number of nations, including the US, at concentrations that may be higher than those in bottled water [92].

Additional Organic Pollutants with an Anthropogenic Origin

The perfume business makes extensive use of harmless substances like synthetic musks (like 1,3,4,6,7,8-hexahydro-4,6,6,7,8,8-hexamethylcyclopenta[γ]-2-benzopyran). China's water supplies have reportedly been contaminated by them. It is necessary to carefully assess the potential hazard of these compounds because they are highly stable, have extremely low biodegradability, and can bioaccumulate [93, 94]. Surfactants like 4-nonylphenol are among the other substances that are frequently used in personal care products. Urban stream water also contains these [94]. 4-nonylphenol is known to activate retinoid receptors and cause neurotoxicity [95].

Mixtures of Contaminants

Mixtures of pollutants can pose a serious risk to public health, even when different agents may be within the safety limits established by regulatory bodies. It is difficult to forecast the health effects of such multi-component elements because of all the possible interactions between toxicants. Tap water, for instance, has been connected to neural tube abnormalities in mouse embryos. Since no single pollutant was found to be responsible for the result, the authors speculate that a mixture of low-dose contaminants may be to blame [96]. Because of their long-lasting effects on the brain, concurrent exposure to a variety of hazardous heavy metals, including lead, cadmium, arsenic, and methylmercury, is a significant cause for concern. Although the precise toxicological processes triggered by exposure to these mixes are still unknown, they have an impact on numerous common metabolic pathways linked to cognitive impairment [97]. The likelihood of additive, synergistic, or antagonistic interactions amongst water pollutants is another effect of several agents present in the water on related processes. An investigation of four hazardous metals in a solitary cell system demonstrates the intricacy of this problem. Effects were additive at first, then synergistic, and eventually antagonistic as the concentration of metal increased [98]. It is noteworthy that effects were additive or synergistic at the lower dosages examined, which are most likely to represent the actual situation. When intact animals are exposed to amounts of lead, cadmium, and arsenic that correspond to the Lowest seen Effect amounts (LOELs) of each element, similar additive or synergistic interactions have been seen [99]. Neurodevelopmental research conducted in Bangladesh has shown that manganese, lead, and arsenic can increase each other's toxicity. Lead and manganese seem to interact in human populations in a way that is not additively synergistic [100]. In a more specific animal model system, synergistic neurotoxic interactions between metals at concentrations similar to those in some Indian groundwaters have also been documented [101].

Because the water content of a single element cannot be taken into consideration in isolation, the question of whether the regulatory limits for individual compounds are actually sufficient for the real-world scenario emerges. Although this is undoubtedly a complicated

and challenging problem to solve, it is pertinent to water sources, which are rarely impacted by a single contaminant.

Mechanisms of Neurotoxicity

While each of the above-discussed compounds that have the potential to contaminate water supplies has a unique neurotoxicity profile, many substances share some effects. It should come as no surprise that these occurrences often indicate a diseased cell with less-than-ideal metabolic activity. One of these procedures is an improvement on inflammatory mechanisms that follow innate immune response activation. The presence of excessive pro-oxidant activity is another common phenomenon. Neurodegenerative illnesses are linked to both of these common pathways. The methods by which drinking water quality might be lowered and thus affect brain function are outlined in figure-3.

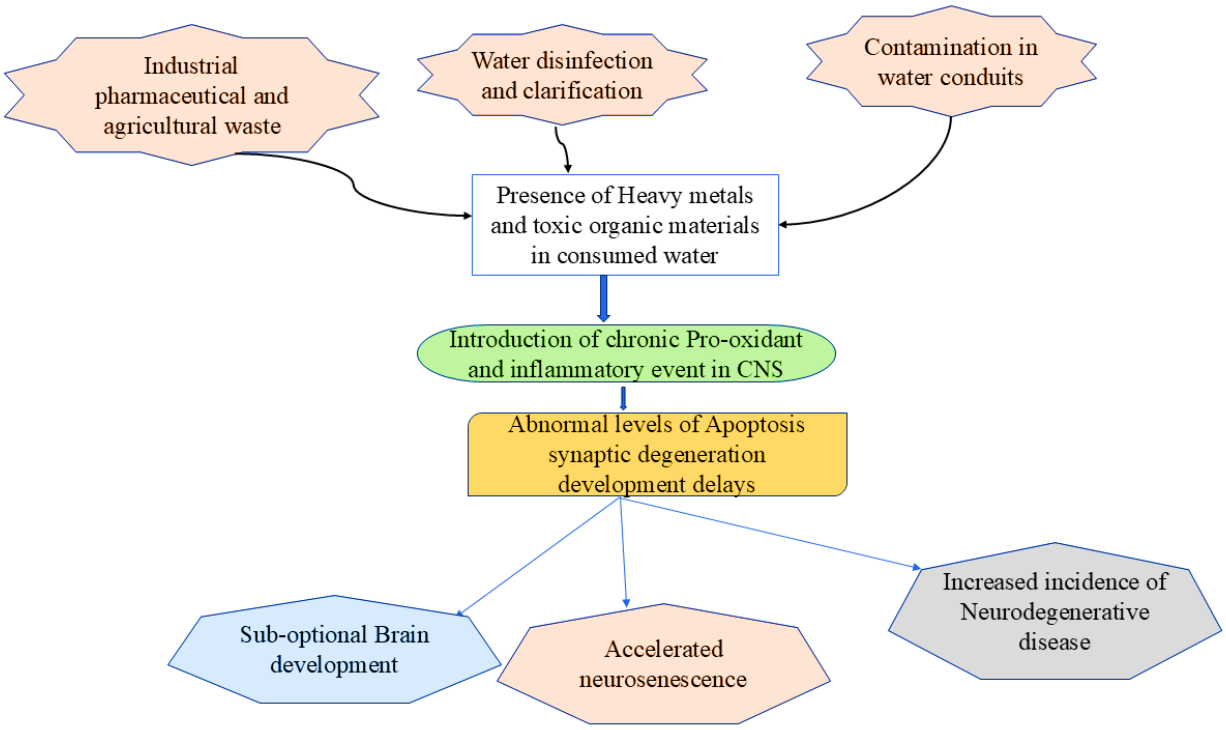

Figure -3 Sources of neurotoxic agents in drinking water and their potent consequences

Neuroinflammation

The cellular and molecular mediators that make up the immune system coordinate resistance to a variety of assaults, including defense against potentially harmful substances. The inflammatory response serves as the initial line of defense for innate immunity, which quickly recruits cells to protect against potentially harmful chemicals. Cytokines and chemokines are important players in inflammation and cooperate to provide protection [102]. It was once believed that the central nervous system (CNS) was immunologically privileged because the blood-brain barrier protected the brain. It has been demonstrated, therefore, that this barrier does not grant the brain immunological privilege and that the central nervous system actively interacts with peripheral immune cells [103]. In addition, after environmental assaults, the brain can activate the innate immune system [15]. Neurodegeneration can result from prolonged immune activity after a brief toxic exposure, even while acute immune responses in the brain that eventually subside are beneficial [104]. Chronic neuroinflammation is thought to be one of the main mechanisms of disease pathology in AD and is exacerbated as the illness progresses [105, 106]. The brains of AD patients have higher amounts of the two most significant inflammatory cytokines, interleukins 1 and 6 (IL-1, IL-6) and tumor necrosis factor alpha (TNF-α) [107]. The blood-brain barrier may be compromised by inflammatory cytokines, allowing environmental toxins to enter the brain parenchyma [108].

Oxidative Stress

Immune cells use the respiratory burst as a strategy to eliminate infections, and reactive oxygen species play a physiological function [102]. On the other hand, excessive or long-term concentrations of these oxidant species may be harmful. Once accumulated, contaminants like redox-active metals can promote the creation of free radicals, which can lead to neurotoxicity. Maintaining the health of the central nervous system requires efficient mitochondrial functioning. In order to actively transport nutrients into the brain and export environmental neurotoxins that may have unintentionally entered the brain, this organelle needs energy. Defensive antioxidant systems may eventually be exhausted by drinking water pollutants that impair mitochondrial function or increase the

formation of reactive oxygen species. A rise in oxidative stress that follows may result in aberrant brain activity. In fact, patients with neurodegenerative diseases like Alzheimer's disease frequently exhibit oxidative stress and mitochondrial malfunction [109–112].

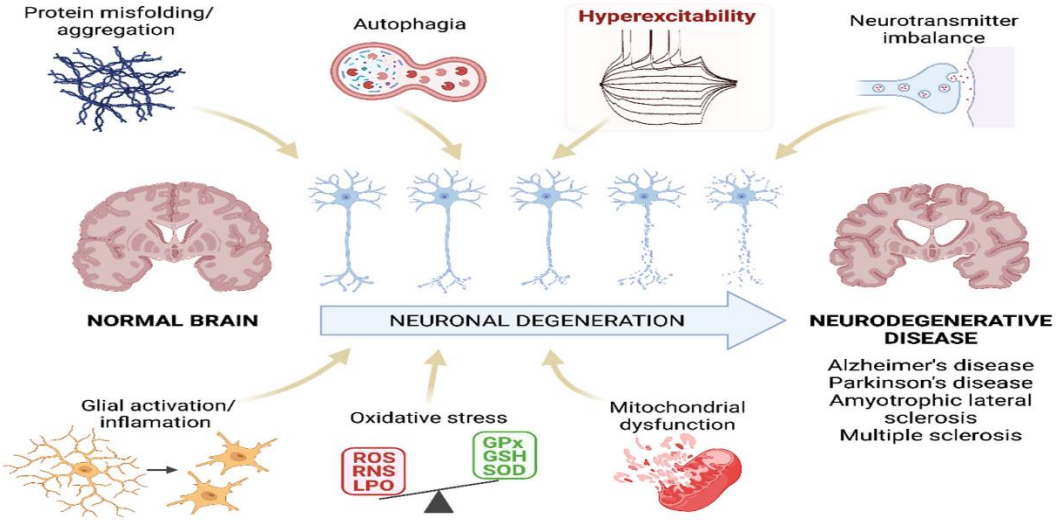

Figure-4 Oxidative stress developed neurotoxicity

Conclusions

The quality of the water supplies used in homes has significantly improved. Still, there is a great deal of variation among communities, partly because of disparate norms. Every US state has its own criteria in addition to those set by the federal government and the World Health Organization. Global health would be effectively protected by a single set of drinking water regulations that are supported by both economic viability and scientific proof. Using green chemistry techniques is one way to lessen the negative effects of pollutants in drinking water. The green pharmacy movement, for example, is a program that aims to improve wastewater treatment by methods like ozonation, which can further break down pharmaceutical substances, or to design medications that are more biodegradable [24, 113, 114]. Improving planning and technology is another suggested strategy. An illustration of this strategy would be the source separation of wastewater, which would separate "blackwater" from the toilet from "greywater" from showers or washing machines. More effective treatment of the separated wastewater is thus possible [115]. Such worldwide technological advancements would reduce contamination and guarantee that there will be enough clean water to support a world population that is expanding quickly.

Future Perspectives

Advances in analytical chemistry, high-throughput toxicology, and computational modeling create opportunities to close critical knowledge gaps regarding trace contaminants in drinking water and neurological health. Priority areas include development of standardized, ultra-sensitive monitoring frameworks for emerging chemicals and their transformation products; longitudinal epidemiological cohorts with rigorous exposure assessment across the life course; and mechanistic studies that integrate in vivo, in vitro, and in silico approaches to identify pathways of neurodevelopmental and neurodegenerative toxicity at low doses. Research on mixture effects should move beyond single-compound paradigms, employing mixture-based risk assessment, exposome profiling, and systems-biology methods to detect additive and synergistic interactions. Identification and validation of early biomarkers of exposure and effect will facilitate causal inference and clinical translation. Vulnerable populations—infants, pregnant persons, older adults, and socioeconomically disadvantaged communities—must be prioritized. Policymakers should adopt adaptive regulatory frameworks that account for cumulative exposures and incorporate new scientific evidence rapidly. Finally, interdisciplinary partnerships among chemists, toxicologists, epidemiologists, clinicians, and community stakeholders will be essential to translate findings into preventive strategies, remedial technologies, and equitable policy measures that protect neurological health from trace water contaminants. Investments in capacity-building, data sharing, and community-engaged research will accelerate translation and ensure interventions are context-appropriate and health-protective outcomes rapidly.

References

1. Kumari, M., Dubey, A., Ghosh, N.S., Sen, S., (2025). Zebrafish as an Innovative Experimental Model: A Strong Framework for Medical Research in Preclinical Screening. Egyptian Journal of Aquatic Biology and Fisheries, 29(4), 2519-2551. doi: 10.21608/ejabf.2025.446041
2. Pérez, H.L.; Osterman-Golkar, S. A sensitive gas chromatographic-tandem mass spectrometric method for detection of alkylating agents in water: Application to acrylamide in drinking water, coffee and snuff. Analyst 2003, 128, 1033–1036.

3. Zhang, L.; Mo, Z.; Qin, J.; Li, Q.; Wei, Y.; Ma, S.; Xiong, Y.; Liang, G.; Qing, L.; Chen, Z.; et al. Change of water sources reduces health risks from heavy metals via ingestion of water, soil, and rice in a riverine area, South China. Sci. Total Environ. 2015, 530–531, 163–170.
4. Islam, M.A.; Romic´, D.; Akber, M.A.; Romic´, M. Trace metals accumulation in soil irrigated with polluted water and assessment of human health risk from vegetable consumption in Bangladesh. Environ. Geochem. Health 2017.
5. Brender, J.D.; Weyer, P.J. Agricultural compounds in water and birth defects. Curr. Environ. Health Rep. 2016,3, 144–152.
6. Croen, L.A.; Todoroff, K.; Shaw, G.M. Maternal exposure to nitrate from drinking water and diet and risk for neural tube defects. Am. J. Epidemol. 2001, 153, 325–331.
7. Costa, L.G.; Giordano, G.; Guizzetti, M.; Vitalone, A. Neurotoxicity of pesticides: A brief review. Front. Biosci.2008, 13, 1240–1249.
8. Li, Z.; Jennings, A. Worldwide regulations of standard values of pesticides for human health risk control: A review. Int. J. Environ. Res. Public Health 2017, 14, 826.
9. Li, Z.; Jennings, A.A. Implied maximum dose analysis of standard values of 25 pesticides based on major human exposure pathways. AIMS Public Health 2017, 4, 383–396.
10. Liu, S.; Gunawan, C.; Barraud, N.; Rice, S.A.; Harry, E.J.; Amal, R. Understanding, monitoring, and controlling biofilm growth in drinking water distribution systems. Environ. Sci. Technol. 2016, 50, 8954–8976.
11. Du, Y.; Wu, Q.Y.; Lu, Y.; Hu, H.Y.; Yang, Y.; Liu, R.; Liu, F. Increase of cytotoxicity during wastewater chlorination: Impact factors and surrogates. J. Hazard. Mater. 2017, 324, 681–690.
12. Lytle, D.A.; Liggett, J. Impact of water quality on chlorine demand of corroding copper. Water Res. 2016,
13. 92, 11–21.
14. Gopal, K.; Srivastava, S.B.; Shukla, S.; Bersillon, J.L. Contaminants in drinking water and its mitigation using suitable adsorbents: An overview. J. Environ. Biol. 2004, 25, 469–475.
15. Rondeau, V.; Jacqmin-Gadda, H.; Commenges, D.; Helmer, C.; Dartigues, J.F. Aluminum and silica in drinking water and the risk of Alzheimer's disease or cognitive decline: Findings from 15-year follow-up of the PAQUID cohort. Am. J. Epidemiol. 2009, 169, 489–496.
16. Dubey A, Shahi S, Singh SK, Kumari M, Dwivedi S. Containers on the micro- and nanoscale for neurodegenerative diseases: nose-to-brain drug transportation. Research Journal of Biotechnology.20 (8)264-272(2025). https://doi.org/10.25303/208rjbt2640272
17. Bondy, S.C. Low levels of aluminum can lead to behavioral and morphological changes associated with Alzheimer's disease and age-related neurodegeneration. Neurotoxicology 2016, 52, 222–229.
18. Santibáñez, M.; Bolumar, F.; García, A.M. Occupational risk factors in Alzheimer's disease: A review assessing the quality of published epidemiological studies. Occup. Environ. Med. 2007, 64, 723–732.
19. Villanueva, C.M.; Gracia-Lavedan, E.; Julvez, J.; Santa-Marina, L.; Lertxundi, N.; Ibarluzea, J.; Llop, S.; Ballester, F.; Fernández-Somoano, A.; Tardón, A.; et al. Drinking water disinfection by-products during pregnancy and child neuropsychological development in the INMA Spanish cohort study. Environ. Int. 2018, 110, 113–122.
20. Liu, J.; Gao, D.; Chen, Y.; Jing, J.; Hu, Q.; Chen, Y. Lead exposure at each stage of pregnancy and neurobehavioral development of neonates. Neurotoxicology 2014, 44, 1–7.
21. Sparks, D.L.; Schreurs, B. Trace amounts of copper in water induce beta-amyloid plaques and learning deficits in a rabbit model of Alzheimer's disease. Proc. Natl. Acad. Sci. USA 2003, 100, 11065–11069.
22. Becaria, A.; Lahiri, D.K.; Bondy, S.C.; Chen, D.; Hamadeh, A.; Li, H.; Taylor, R.; Campbell, A. Aluminum and copper in drinking water enhance inflammatory or oxidative events specifically in the brain. J. Neuroimmunol. 2006, 176, 16–23.
23. Kitazawa, M.; Cheng, D.; Laferla, F.M. Chronic copper exposure exacerbates both amyloid and tau pathology and selectively dysregulates cdk5 in a mouse model of AD. J. Neurochem. 2009, 108, 1550–1560.