Environmental Toxicology and Pharmacology

Volume 74, February 2020, 103312

Review or Mini-review

Examining the evidence that ethylmercury crosses the blood-brain barrier

Janet K. Kern [a b c], David A. Geier [a b], Kristin G. Homme [d], Mark R. Geier [a b]

https://doi.org/10.1016/j.etap.2019.103312

Abstract

Scientific research can provide us with factual, repeatable, measurable, and determinable results. As such, scientific research can provide information that can be used in the decision-making process in the care of patients and in public policy. Although it has been suggested that ethylmercury ($C_2H_5Hg^+$)-containing compounds do not cross the blood-brain barrier (BBB), this review examines the literature that addresses the question as to whether ethylmercury-containing compounds cross the BBB. The review will begin with cellular studies that provide evidence for the passive and active transport of mercury species across the BBB. Then, animal and clinical studies will be presented that specifically examine whether mercury accumulates in the brain after exposure to ethylmercury-containing compounds or Thimerosal (an ethylmercury-containing compound used as a preservative in vaccines and other drugs that metabolizes or degrades to ethylmercury-containing compounds and thiosalicylate). The results indicate that ethylmercury-containing compounds are actively transported across membranes by the L (leucine-preferring)-amino acid transport (LAT) system, the same as methylmercury-containing compounds. Further, 22 studies from 1971 to 2019 show that exposure to ethylmercury-containing compounds (intravenously, intraperitoneally, topically, subcutaneously, intramuscularly, or intranasally administered) results in accumulation of mercury in the brain. In total, these studies indicate that ethylmercury-containing compounds and Thimerosal readily cross the BBB, convert, for the most part, to highly toxic inorganic mercury-containing compounds, which significantly and persistently bind to tissues in the brain, even in the absence of concurrent detectable blood mercury levels.

Introduction

Scientific research can provide us with factual, repeatable, measurable, and determinable results. As such, scientific research can provide information that can be used in the decision-making process in the care of patients and in public policy.

In 2018, Boom et al. published a review in the *Journal of Family Strengths* stating that, "*Ethyl mercury does not cross the blood-brain barrier and is structurally different from methyl mercury…*" This statement by Boom et al. (2018) was in the context of describing ethylmercury as being safer than methylmercury.

Factual truth in science is part of the role of science and adherence to the evidence is critical. The evidence indicates that ethylmercury ($C_2H_5Hg^+$) -containing compounds do cross the blood-brain barrier (BBB). In this current review, the evidence supporting the notion that ethylmercury-containing compounds cross the BBB will be presented and discussed. The review will begin with a summary of cellular studies showing the passive and active transport of mercury species across the BBB. Then, animal and clinical studies that specifically examine whether mercury accumulates in the brain after exposure to ethylmercury-containing compounds or Thimerosal (an ethylmercury-containing compound used as a preservative that metabolizes or degrades to ethylmercury-containing compounds and thiosalicylate) will be presented from a historical perspective.

Section snippets

Cellular studies – showing passive and active transport across the BBB

Some mercury species, such inorganic mercury-containing compounds, do not readily cross the BBB. However, organic mercury is fat soluble and has a high affinity for thiol groups and as such, it can easily penetrate the BBB (Dewi et al., 2014). It has been accepted for decades that methylmercury-containing compounds, an organic form of mercury, cross the BBB (Kerper et al., 1992). First, methylmercury-containing compounds can passively cross the BBB because, as mentioned, they are fat soluble…

Clinical studies-– showing accumulation in the brain after exposure to ethylmercury-containing compounds

Clinical studies were found that show accumulation of mercury in the brain after exposure to ethylmercury-containing compounds. Mal'tsev (1972) commented that, upon autopsy of children who died of ethylmercury-containing compound exposure, degenerative, inflammatory, and necrotic alterations were seen, as well as hemorrhages in the central nervous system, kidney, liver, heart, and intestines.

Between 1969 and 1975 there were 13 cases of exomphalos treated with topically applied Thimerosal (Fagan …

Current use of Thimerosal

Although Thimerosal has been removed from some childhood vaccines in the United

States (US), Thimerosal is still used in many childhood vaccines in the developing world. In the US, Thimerosal is still used in the meningococcal vaccine which is recommended for young adults going to college. Thimerosal was also in the tetanus-toxoid vaccine until a few years ago and it is given to individuals of all ages (Johns Hopkins Bloomberg School of Public Health, 2019). Further, in the US, over half of…

Current opinion on the safety of Thimerosal

Whether Thimerosal exposure has any impact on children's development is a controversial issue. As stated by DeSoto and Hitlan (2010) in their review of the controversy, *"This particular controversy does have truly high stakes for many reasons."* There are claims that Thimerosal is safe for use in children (Boom et al., 2018) and there are claims that it is not (Geier et al., 2017), and there is research to support both claims. To add to the confusion, the US CDC claims that Thimerosal is safe (…

Conclusion

As mentioned, scientific research can provide us with factual, repeatable, measurable, and determinable results. It can provide researchers and clinicians with evidenced-based information by asking important questions in healthcare, such as, do ethylmercury-containing compounds cross the BBB, particularly Thimerosal, which is used as a preservative in some medical products such as in vaccines and allergy testing. The aforementioned studies address this question and their research provides an…

Funding

This research was funded by the non-profit organizations, CoMeD, Inc. and Institute of Chronic Illnesses, Inc.…

Declaration of Competing Interest

This work has not been published previously. It is not under consideration for publication elsewhere. It is approved by all authors and tacitly or explicitly by the responsible authorities where the work was carried out, and that, if accepted, it will not be published elsewhere in the same form, in English or in any other language, including electronically without the written consent of the copyright-holder.…

References (48)

A.M.J.N. Blair *et al.*
Tissue concentrations of mercury after chronic dosing of squirrel monkeys with thiomersal
Toxicol. (1975)

J.G. Dórea
Low-dose Thimerosal (ethyl-mercury) is still used in infants` vaccines: should we be concerned with this form of exposure?
J. Trace Elem. Med. Biol. (2018)

G.J. Harry *et al.*
Mercury concentrations in brain and kidney following ethylmercury, methylmercury and Thimerosal administration to neonatal mice
Toxicol. Lett. (2004)

J.K. Kern *et al.*
The relationship between mercury and autism: a comprehensive review and discussion
J. Trace Elem. Med. Biol. (2016)

D. Mrozek-Budzyn *et al.*
Neonatal exposure to Thimerosal from vaccines and child development in the first 3 years of life
Neurotoxicol. Teratol. (2012)

M. Olczak *et al.*
Neonatal administration of a vaccine preservative, thimerosal, produces lasting impairment of nociception and apparent activation of opioid system in rats
Brain Res. (2009)

L.T. Zimmermann *et al.*
Comparative study on methyl- and ethylmercury-induced toxicity in C6 glioma cells and the potential role of LAT-1 in mediating mercurial-thiol complexes uptake
Neurotoxicology (2013)

K. Afsordeh *et al.*
Alterations of neuroimmune cell density and pro-inflammatory cytokines in response to thimerosal in prefrontal lobe of male rats
Drug Chem. Toxicol. (2019)

M. Aschner *et al.*
Mercury 203 distribution in pregnant and nonpregnant rats following systemic infusions with thiol-containing amino acids
Teratology. (1987)

J.P. Barile *et al.*
Thimerosal exposure in early life and neuropsychological outcomes 7-10 years later
J. Pediatr. Psychol. (2012)

View more references

Cited by (12)

Mercury in the brain (tumor tissues) and in markers (hair and blood) of

exposure in Western Amazonia patients

2022, Journal of Trace Elements in Medicine and Biology

Citation Excerpt :

...The most widespread form of environmental Hg contamination is MeHg found in consumed fish and seafood. However, other forms of organic Hg are well absorbed and distributed to all body tissues, easily crossing the blood-brain barrier to reach the brain - its main target tissue [18,19]. Indeed, an extremely high level of Hg (1974 ng.g−1) was reported in the left occipital cortex of an individual poisoned by organic mercury [20]....

Show abstract

Short exposure to ethyl and methylmercury prompts similar toxic responses in Drosophila melanogaster

2022, Comparative Biochemistry and Physiology Part - C: Toxicology and Pharmacology

Citation Excerpt :

...Concerning molecular mechanisms underlying to EtHg-induced cytotoxicity, oxidative stress also has received a special mention in various studies. Events as inhibition of thioredoxin system, GSH depletion, RS overproduction, and mitochondrial dysfunctions have already been evidenced in different cell lines after exposure to EtHg (Choi et al., 2016; Branco et al., 2017; Kern et al., 2020). In vitro experiments comparing the toxicities of respective organomercurials have revealed critical mechanistic approaches to the effects of compounds....

Show abstract

Maternal gestational mercury exposure in relation to cord blood T cell alterations and placental gene expression signatures

2021, Environmental Research

Citation Excerpt :

...Silver-mercury dental amalgams may also expose the developing fetus to elemental mercury (Watson et al., 2012). Mercury is well known to biomagnify across the placenta (Straka et al., 2016) and cross the blood-brain barrier (Kern et al., 2019) and to have detrimental effects on the development of the nervous system (Kim et al., 2020). But there is a lack of information on its effects on the developing human immune system....

Show abstract

Neurotoxic effects of combined exposures to aluminum and mercury in early life (infancy)

2020, Environmental Research

Citation Excerpt :

...Indeed, comparing TCV-Hg between neonates and 6-month-old infants, it appears that in the latter blood Hg clears faster mainly because of higher stool excretion than in neonates (Dórea, 2013). Thus, Thimerosal use in pediatric vaccines should heed the risks associated with EtHg crossing the BBB of young babies (Kern et al., 2020). The concentrations of Al and Hg in infants' tissues vary and may reflect the elements' half-lives in body....

Show abstract

Biometals in Autism Spectrum Disorders

2020, Biometals in Autism Spectrum Disorders

Analytical Methods, Occurrence, Fate, and Toxicity of Ethylmercury in the Environment: Review and Outlook

2023, Reviews of Environmental Contamination and Toxicology

View all citing articles on Scopus

View full text