

Systematic Review: Effects Of Exposure To Mercury (Hg) As A Cause Of Autism Spectrum Disorders (Asd) In Children

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ABSTRACT

Introduction: The prevalence of autistics in the world currently reaches 15-20 cases per 10,000 children or ranges from 0.15-0.20%. Autistic is a very complex developmental disorder in children, starting to appear before the age of 3 years. Mercury has an influence on events. Mercury has an influence in the onset of Autism Spectrum Disorders (ASD) disorder in children. **Purpose:** The purpose of writing a literature review is to determine the effects of mercury exposure as the cause of Autism spectrum disorders (ASD) in children. **Methods:** The inclusion criteria used are the population of children and pregnant women, exposure to the effects of mercury on Autism Spectrum Disorders (ASD), research articles, articles published in 2012-2022 and English language. While the exclusion criteria used are abstract, research article, and type of quantitative research. Data sources from Pubmed and Scopus started from 2012 to 2022. **Results:** total data based on searches using keywords A,B (n=13,084), focus on mercury and autism incidence (n=6), methods used (n=46), full abstract article type (n=6), inclusion criteria (n=6), 2012-2022 (n=6). **Discussion :** There is a weak relationship between mercury and the incidence of Autism spectrum disorders (ASD). However, the literature review has limitations so it is necessary to re-research the negative impact of the brand on Autism spectrum disorders (ASD) **Conclusion:** There is a significant

weak relationship between mercury exposure and the incidence of Autism Spectrum Disorders (ASD). However, there is literature that states that exposure to mercury can cause developmental disorders in children, especially nerves.

Keywords : Mercury, Autism, Children, secure work

INTRODUCTION

The prevalence of autistics in the world currently reaches 15-20 cases per 10,000 children or ranges from 0.15-0.20%. Autism was first described by Kanner (1943) who was written in his report of 11 children who had similar habitual tendencies. Autism Spectrum Disorders (ASD) belongs to a group of multifactorial neurodevelopmental disorders characterized by impaired social communication, social interaction, and repetitive behavior. ASD affects 1 in 59 children, and is about 4 times more common in boys than girls. A strong genetic component, along with environmental factors in the early stages of development, contributes to the pathogenesis of ASD (Guang, 2018).

Autistic is a very complex developmental disorder in children, starting to appear before the age of 3 years. This condition causes them to be unable to communicate or express their desires,

resulting in impaired behavior and relationships with other people. Autistic disorder (ASD) is a neurodevelopmental syndrome with onset before the age of 36 months. The diagnostic criteria consist of disorders in sociality and communication plus repetitive behaviors and stereotypes (Bernard et al., 2001, Blaurock-Busch et al., 2011).

Autism spectrum disorder (ASD), as a general term refers to a group of complex neurodevelopmental disorders that exist from early childhood. This disorder is characterized, in varying degrees, by difficulties in social interaction, verbal and non-verbal communication, and repetitive behavior. This happens not only in developed countries but also in developing countries such as Indonesia. Some of the possible causes of being autistic are sourced from heavy metal poisoning including chemical products, fertilizers, industrial paints, building materials, fish that are high in

mercury, silver tooth fillings, mercury-containing preservatives (thiomersal) in vaccines, nasal sprays, and more. Lead can be found on the ground near roads, leaded gasoline and can still be found in paints from old houses.

Children who accidentally eat paint flakes or those who have pica can develop toxic lead levels (Blaurock-Busch et al., 2011). Most of the children get lead poisoning from living or living in old houses that have lead paint. Many homes built before 1978 have lead paint on the inside and outside of the building. When the old paint cracks and peels off, it creates lead dust.

Mercury is an element that has an atomic number (NA = 80) and has a relative molecular mass (MR = 200.59). According to A Wiguna (2016), Mercury is a metallic element that is often used in the use of technology given the chemical symbol Hg with an indication of its meaning as a silver liquid. Mercury is a very rare element in the Earth's crust, and is relatively concentrated in some volcanic regions and sea mineral deposits of lead-heavy metals. Mercury is widely used in production activities such as dental amalgam, fungicides, batteries, etc.

In addition, mercury is used in the manufacture of medical devices such as blood pressure gauges, thermometers, and pacemakers. The presence of exposure to

mercury will lead to the occurrence of cases of poisoning. There were several cases of poisoning caused by mercury, namely the first case in Minamata Japan in 1953. Methylmercury is known to interfere with fetal development, resulting in birth defects in fetuses that are exposed to mercury. Not only that,

Usually mercury is still found in many children's electric toys and chemical equipment. The buildup of Hg triggers oxidative stress and inflammatory reactions in the brain and also increases the number of auto-antibodies necessary for the onset of autism and other neurodevelopmental disorders.

Based on research conducted by Vincent, et al (2014), it is stated that there is a significant correlation between maternal serum and the baby's blood mercury levels. Lead and mercury are considered one of the main causes of autism. Environmental exposure as well as defects in heavy metal metabolism are responsible for high levels of heavy metals. Detoxification by chelating agents has a big role in the improvement of such children (Yassa, 2014). Based on the results of the research above, the amount is not enough to describe the effect of mercury exposure on autistic events for children.

It is necessary to search the library through literature review so that a library with sufficient quantity and quality is obtained to analyze the effects of mercury exposure and autistic events and find out the strength of the relationship between mercury and autistic events. This literature review examines the effects of mercury exposure on the incidence of Autism Spectrum Disorders (ASD) and how mercury relates to this disease. The purpose of writing a literature review is to study and find out the relationship between mercury and Autism Spectrum Disorders (ASD).

METHOD

A systematic review through a review of several mercury scientific articles to identify the effects of mercury that can result in autistic events on children. The inclusion criteria used in this article review are the effects of mercury which can result in autistic events in children, while the exclusion criteria are articles that are abstract, articles that do not use English and articles that are not displayed in full text. The search for articles with English that can be accessed is limited from internet searches through databases namely: PubMed and Scienccedirect.

With the keywords effect mercury and autism. Articles that already meet the inclusion criteria are then systematically collected and reviewed. Search for articles

that meet the criteria for incubation and published from the last 5 years, namely 2018-2022. The search process obtained 14 articles that met the requirements of inclusion and exclusion. Articles that qualify for exclusion use PICOS.

RESULTS

Using the search method PubMed and Scienccedirect obtained 6 articles. Below is shown the prisma flowchart of the results of searching for data with the PICOS method and its explanation.

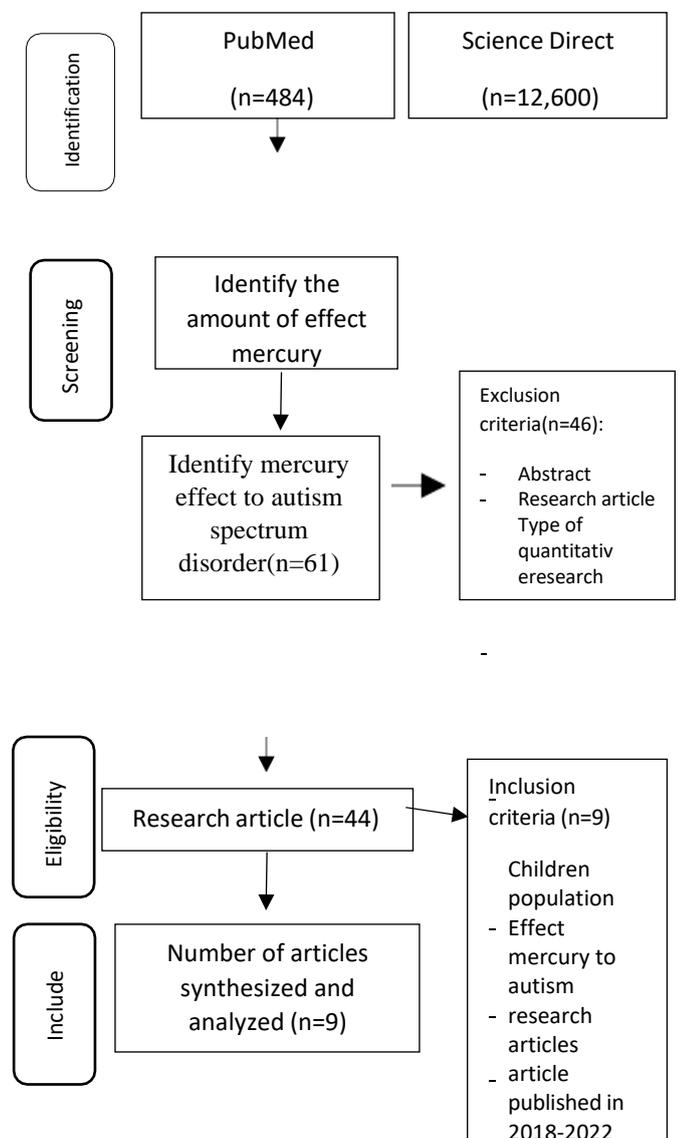


Figure 1 Diagram of the process of finding data on exposure to the effects of mercury on the occurrence of Autism Spectrum Disorders (ASD) disorders in children.

The total search for mercury effect-based data (n= 13,084) data was focused on the incidence of Autism Spectrum Disorders (ASD) (n=61), then searched by type of research article (n=44) then from 44 types of research articles, a selection of articles analyzed based on PICOS inclusion (Population, Intervention, Comparison, Results, Study Design, Year of Publication, and language) as follows:

- 1) Population of children and pregnant women.
- 2) Exposure to the effects of mercury on Autism Spectrum Disorders (ASD).
- 3) Research articles.
- 4) Article published in 2012-2022 and
- 5) English.

Each article is studied and analyzed according to the inclusion criteria. There are many articles that are eliminated because they do not meet the criteria,

including: not a research article, a non-child population, in the results section it does not expose the desired variables, and the study is not published in 2012-2022.

Article analysis is obtained after carrying out the stages of identification, screening, setting criteria for up to 9 articles

analyzed. A total of 9 international articles met the criteria and were sampled for synthesis and analysis. The inclusion criteria of "outcomes" were determined according to the purpose of writing the literature review, variables were included in the PICOS method so that they could be broadly explored, and it was clear the effect of mercury exposure on the occurrence of Autism Spectrum Disorders (ASD) in children. There are articles that meet the criteria. The article is analyzed and synthesized and displayed in table 1 below:

No	Heading	Design, sample and measurement	Analytical Techniques	Result
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1.	Prenatal mercury exposure and features of autism: a prospective population study. Molecular autism,	This article uses three strategies, namely direct comparison, score comparison, and indirect measurement. Using test interactions between Risk and fish breeds and non-fish eaters	The analysis consists of two sets of analyses using logistic regression	There were no suspected side effects of total prenatal blood Hg levels in diagnosed autism (AOR 0.89; 95% CI 0.65, 1.22) per SD Hg (P = 0.485). The only indication of side effects was related to the poor measure of social cognition when the mother did not eat fish, where the AOR was 1.63 [95% CI 1.02, 2.62] per SD Hg (P = 0.041), differing significantly from the relationship between fish-eating breeds (AOR = 0.74 [95% CI 0.41, 1.35])
2.	Metal and essential element concentrations during pregnancy and associations with autism spectrum disorder and attention deficit/hyperactivity disorder in children	The method in this study uses a limited cubic spline model and uses a quantile-based g-computational approach.	The study included 397 ASD cases identified through associations with norwegian patient registry	The results of this study show some relationship between the level of metals and trace elements during pregnancy and ASD and ADHD in children. The most famous one of them involves mercury .Our results suggest that even the population level of this compound may have a negative impact on neurodevelopment.

3.	Interaction between a mixture of heavy metals (lead, mercury, arsenic, cadmium, manganese, aluminum) and GSTP1, GSTT1, and GSTM1 in relation to autism spectrum disorder	Using the regression method of negative and positive quartile counts to assess the relationship between metal variables and ASD.	Using regression analysis techniques.	Based on the gWQS model, the study found that there was an inverse relationship of the overall mixed score with ASD [MOR (95% CI) = 0.70 (0.49, 0.99); $P < 0.05$] and [MOR (95% CI) = 0.46 (0.25, 0.84); $P = 0.01$], respectively. In the unrealized negative gWQS model, we found a slightly significant interaction between GSTP1 and a mixture of three metals (Pb, Hg, and Mn) ($P = 0.07$) while the association was no longer significant after adjustment for the same covariate ($P = 0.24$)
4.	A form of lead and mercury toxicity	Blood and hair samples were obtained from 45 children from Upper Egypt with autism between the ages of 2 and 10 and 45 children served as controls in the same age range	Samples were randomly analyzed for lead and mercury using atomic uptake and ICP-MS. Data from the two groups were compared, then followed up of autistic children after	The results obtained showed significant differences between the two groups, there were high levels of mercury and lead in autistic children. Lead and mercury are considered one of the main causes of autism. Environmental exposure as well as defects in heavy metal metabolism are responsible for high levels of heavy metals. Detoxification by chelating agents has a huge role in the

			<p>treatment with chelating agents</p>	<p>improvement of such children.</p>
<p>5.</p>	<p>The Association Between Maternal Prenatal Fish Intake and Child Autism-Related Traits in the EARLI and HOME Studies</p>	<p>Cd causes non-chromatography methods for blood Hg speciation based on selective determination of inorganic and total Hg by CV-AAS with their difference accounting for organic Hg</p>	<p>inductively coupled plasma mass spectrometry (ICP-MS) due to its unique advantages of high sensitivity, wide dynamic range, and multi-isotope analysis capabilities. ICP-MS can be used to analyze blood with less sample preparation especially those involving the dissolution of the matrix with acidic or alkaline solutions, which can be</p>	<p>This study examined the relationship between prenatal fish intake and children's autism-related traits according to the Social Responsive Scale (SRS) and cognitive development scores in two U.S. prospective pregnancy cohorts. In an adjusted linear regression analysis, higher maternal fish intake in the second half of pregnancy was associated with an increase in the child's autism trait (higher raw SRS score; = 5.60.95% CI 1.76, 12.97).</p>

			accelerated by microwave irradiation	
6.	A meta-analysis of the evidence on the impact of prenatal and early infancy exposures to mercury on autism and attention deficit / hyperactivity disorder in the childhood. Neurotoxicology, 44, 121-131.	This study used Case-control studies or prospective / retrospective cohort studies qualified if the hazard ratio (HR) or odds ratio (OR), as well as the 95% confidence interval (CI) regarding mercury exposure during the perinatal and early infancy periods and ASD or ADHD, were calculated in the study.	In some studies, various periods and doses of mercury exposure were adopted, and the corresponding HR or OR was calculated to confirm the relationship between mercury and neurodevelopmental disorders in some detailed patterns. The data were processed using meta-analysis.	95% CI for summary OR clinical mercury exposure for ASD and for ADHD includes a value of zero 1 and only slightly above that value. These results suggest that exposure to prenatal mercury or early infancy through vaccination has no serious side effects on the increased risk of ASD or ADHD, while exposure to environmental mercury caused by air pollution or maternal fish consumption may increase the incidence of ASD and ADHD, respectively

7.	A Correlation Analysis of Attitude, Subjective Norm and Behavioral Control Toward the Intention of Safety Behavior	This study is an observational study with a cross sectional design.	This study was conducted in March-April 2017, with a population of 37 people and obtained a sample of 34 through a simple random sampling calculation formula. Data collected using questionnaires	Based on the results of the study, there is no relationship between attitudes towards safety behavior in plate cutting workers of the commercial ship division at PT. SAHABAT Indonesia (Persero) and there is no correlation between subjective norms and the behavior of workers' workers Cutting Plate Commercial Ship Division PT. FRIEND Indonesia (Persero) and there is a correlation of behavioral control to the intent of Workers' safety conduct Cutting Plate Commercial Ship Division PT. FRIEND Indonesia (Persero)
8.	Heavy metals in drilling-waste leachates from East Java, Indonesia	This study used the toxicity method characteristic of leaching procedure (TCLP). Ten heavy metal elements As, Ba, Cd, Cr, Cu, Pb, Se, Ag, Zn and Hg were investigated.	Heavy metals leached from drilling waste were assessed using TCLP. The sample is crushed into particles with a diameter of less than 9.5 mm. The crushed sample was extracted with acetic acid (pH 2.88), 20 times the	The results showed that the concentration of all metals studied was below the Indonesian Regulatory Standards No. 18 and 85 (1999). Although all heavy metal drilling waste is below the maximum permissible level, field monitoring should be carried out to provide an ongoing assessment of the fate and effect of heavy metals in the disposal of drilling waste.

			weight of the sample. The extraction vessel was continuously stirred in an end-to-end manner at 30 rpm for 18 hours.	
9.	Control of Hazardous Chemical as an Effort for Compliance Criteria of OHS Management System: A Cross Sectional Study at PT.X Surabaya, Indonesia	The survey method was a cross-sectional study. Primary data obtained from observations of validation and direct interviews with HSE officers in compliance with the standard of OHSMS. Secondary data was obtained from company documentation, including company policies, commitments, and standard operating procedures	The results meet the third item with the monitoring principle and the performance rating 46 criteria in, and one criterion fails the minor result category, namely criteria 9.3.5, and criteria. Was shown to be the performance calculation. The level was 97.87%	The conclusion of this study is that the company's Hazardous Chemicals Management does not yet meet the standards of the Occupational Safety and Health Management System, but the category rating of was satisfactory. It was a thing.
10.	Factors analysis affecting nurse efficacy in implementing resuscitation in cardiac arrest patients	The design used was observational analytics with cross-sectional studies in May-July 2016. The variables identified are independent variables, namely Mastery of	The data analysis used in this study includes univariate tests, bivariate tests and multivariate tests	The results showed that ada relationship between the experience of Mastery, verbal persuasion and the self-efficacy of the nurse in performing resuscitation in patients with cardiac arrest in the emergency room at dr. R. Koesma Tuban General

		<p>Experience Factors, Experience or Representative Modeling factors, Verbal factors and Physiological persuasive factors and Affective States to dependent variables, namely nurse self-efficacy</p>	<p>Hospital and . There is nothing to do with vicarious tween or Modeling and Physiological and Affective States with self-efficacy nurses inperforming resuscitationin patients with cardiac arrest at Dr. R General Hospital. Koesma Tuban</p>
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Based on the results of the literature review, the relationship of mercury exposurefactors to the incidence of Autism spectrum disorders (ASD) shows that there is a relationship between mercury exposureand the occurrence of sutis. This is in accordancewith the research carried out by Heba (2014),the results show that timbal and mercury are considered one of the maincauses of autism. Environmental exposure as well as defects inmetabolism are affectedby exposure to heavy metals. The presenceof mercury pollution can also increase the potential for Autism Spectrum Disorders(ASD) disorders.Asd conditions can cause children to be unable to communicate or express their desires, resulting in impaired behavior and relationships with other people.

A similar study was conducted by Skogheim et al (2021) which showed that mercury exposure may have a negative

impact on nerves. Mercury belongs to heavy metals that can cause health problems. Pregnant women have a fairly high risk when there is mercury pollution in their environment. This is because, all the food consumed by the mother will have an impact on the future of the child. If there is mercury chemical pollution, it will cause health problems for pregnant women and the fetus in the womb. Pollution of mercury exposure in the environment can be caused by air pollution or consuming fish that has been contaminated with mercury can increase the incidence of Autism Spectrum Disorders (ASD) in children (Yoshimas et al, 2014).

This is supported by Rahbar's research (2020) which states that mercury levels with the incidence of Autism Spectrum Disorders (ASD) in children have significant interactions that are lacking. This is in contrast to research conducted by

Golding et al (2018) which showed that there were no suspected side effects of total Hg levels of prenatal blood in autism diagnosed. The existence of this difference of opinion is due to limitations in research. Therefore, it is necessary to conduct more research on the relationship of mercury (Hg) with the incidence of Autism Spectrum Disorders (ASD).

DUSCUSSIONS

Mercury (Hg) is found innately in the environment and becomes more abundant by human activities such as mining which causes a 1.5% increase in Hg in the atmosphere. There are activities that increase its availability in the atmosphere such as the extraction of Hg, and its use in certain products (electronic devices, paints) and industrial use as catalysts. Hg is mostly transferred into biological systems through contaminated food, such as plants or fish. Hg exists in organic and inorganic form. The most available form of organic Hg is methylmercury (MeHg) while inorganic Hg is available in the form of mercury or mercury with an average half-life of forty days.

Maternal hair collected at birth provided unspecified prenatal exposure to methylmercury (MeHg) in 1237 mother-child pairs from populations with high fish consumption and MeHg exposure [17].

The increase in IQR in MeHg was nominally associated with a 0.05-point decrease in the Social Communication Questionnaire (SCQ) score. Box 1) at the age of 7 years. The authors hypothesized that the neurodevelopmental benefits of fish consumption associated with polyunsaturated fatty acids outweighed the negative effects of MeHg, and the evidence of the interaction was suggestion (Prenatal exposure to metals and autism spectrum disorder: Current status and future directions)

Based on previous studies cited by Golding, et al (2018) states that blood Hg levels increase if women eat fish during pregnancy and with the number of amalgam patches in the mouth. Golding, et al (2018) stated that, of the 177 pregnancies that resulted in a child being diagnosed with autism, 45 had total blood Hg levels. The average blood level of Hg in this group [2.15(SD 0.95) g/L] was similar to the level in the 3840 remaining pregnancies [2.08 (SD 1.09)g/L, P = 0.655]. The correlation between an increase in maternal mercury levels and an increase in the level of autistic traits shows that there is nothing statistically significant. There is no evidence of an increase in prevalence to one of the extreme levels of autistic traits with an increase in Hg in prenatal blood.

The only association of adjusted

statistical significance at a rate of 0.05 had to do with the relationship between Hg and poor social cognition among the offspring of women who did not eat fish; this relationship is significantly different from women who eat fish, suggesting that nutritional benefits in fish counteract possible adverse cognitive and behavioral differences that may be caused by exposure to Hg. This is in line with the research conducted by Vegard et al (2021), Non-linear mercury with an increased risk of ASD among lower mercury concentrations and no clear risk at higher concentrations. The level of mercury in the blood is associated with the total intake of fish and seafood, as well as several sub-categories (Brantsæter et al., 2010).

However, this is different from previous studies conducted by Grandjean & Ladrigan (2006), which stated that exposure to mindfulness, especially in childhood, has been shown to affect nerves in children although there are some inconsistencies in the findings due to the impact of the role of seafood intake. Based on other studies, the use of henna during pregnancy, and the type of water used during pregnancy had significant values when compared to the control group (Yassa, 2014). Lead and mercury were measured in total blood and hair as well as values before treatment and after treatment

and ADHD and environmental exposure. Since ethylmercury decomposes much faster than methylmercury, the risk of brain damage from it is considered to be smaller than that derived from methylmercury (Aschner and Ceccatelli, 2010).

Although a slightly significant association was observed between environmental mercury exposure and ADHD in current meta-analyses, further replicated findings are needed with adjustments to fish consumption as in Sagiv et al. (2012), since the detrimental effects of methylmercury on child neurodevelopment may be reduced with beneficial effects of seafood. On the other hand, exposure to environmental perinatal mercury is significantly associated with an increased risk of developmental disorders.

with DMSA. According to the results of a study conducted by Yassa (2014), there are significant results in the measurement of heavy metals with autism causes.

It can be concluded that there is a significant relationship between these two heavy metals and the emergence of autism. In their study of the autism spectrum, Windham et al. (2006) suggested that there is a potential link between autism and metal concentrations. Lyall et al. (2014), Rossignol et al. (2014), Blaurock-Busch et al. (2011), and Blaurock-Busch et al. (2012), all indicate that heavy metals are common environmental factors, which cause autism. This study revealed that exposure to lead and/or mercury in both the prenatal and postnatal periods had a positive correlation with the presence of autistic children in the family (Yassa, 2014). Blanchard et al. (2011) reported that increased autism HR correlates with higher mercury concentrations in a series of area-based ecological studies, consistent with current findings.

A similar study conducted by Yoshimashi et al (2014) using meta-analysis, showed that the calculated OR summary did not provide a significant relationship in any of the analyses regarding thimerosal exposure (ethylmercury), while a significant positive relationship was observed between ASD

CONCLUSIONS

The conclusions of the literature review from several studies stated that there was a significant weak relationship between mercury exposure and the incidence of Autism Spectrum Disorders (ASD). However, there is literature that states that exposure to mercury can cause developmental disorders in children, especially nerves. This difference is due to limited evidence, so research needs to be carried out to prove the relationship between mercury exposure and Autism

Spectrum Disorders (ASD) in children. It is necessary to conduct further studies regarding the negative impact of mercury on the occurrence of autism disorders for children.

In addition, it is necessary to test more deeply related to the consumption of marine fish on pregnant women which can cause autism

disorders for children. The results of this literature review are important to assist the government in controlling exposure to mercury chemicals both in the land and sea environment. If there is equipment that uses mercury material above the threshold value (NAV), the government must make sanctions against the company.

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