

An epidemiological analysis of the ‘autism as mercury poisoning’ hypothesis

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Abstract. Where direct experimental research into a causal hypothesis of a disease is impossible due to ethical and practical considerations, epidemiological inference is the accepted route to establishing cause. Therefore, to examine the *autism as mercury poisoning* hypothesis, this paper reviews the existing scientific literature within the context of established epidemiological criteria and finds that the evidence for a causal relationship is compelling. Exposure to mercury (via vaccines and maternal dental amalgam) *in utero* and during infant years is confirmed; mercury poisoning is known to cause symptoms consistent with autism; animal modeling supports the link and, critically, mercury levels are higher in both the urine and blood of autistic children than in non-autistic peers. Analogous to epidemiological evidence of the smoking–lung cancer relationship, a mercury–autism relationship is confirmed. The *precautionary principle* demands that health professionals not take an action if there is suspicion that the action may cause severe or lifelong health effects: it does not require certainty. Therefore, given the severity, devastating lifelong impact and extremely high prevalence of autism, it would be negligent to continue to expose pregnant and nursing mothers and infant children to any amount of avoidable mercury.

Keywords: Autism, mercury, epidemiology, precautionary principle, pink disease

1. Introduction

Autism is a neurodevelopmental disorder presenting in childhood that affects up to 1 in 150 children in the United States [8]. The condition is characterised by severe impairments in socialisation, communication and behaviour. Children with autism may display a range of problem behaviours such as hyperactivity, poor attention, impulsivity, aggression, self-injury and tantrums. Furthermore, these children often display unusual responding to sensory stimuli such as hypersensitivities to light or certain sounds, colours, smells or touch and have a high threshold of pain [1]. The prevalence of autism is increasing at epidemic rates [47] that are not accounted for by changing diagnostic criteria or improved diagnostic systems [5,12].

Autism was first proposed as a new disorder in 1943 by Kanner [26]. Since that time, the search for a causal agent has remained elusive. One dominant theory relates to genetic susceptibility [14]. The search for a genetic basis for autism has, so far, proven unsuccessful despite extensive research work [2,7,35,48]. Furthermore, it is difficult to reconcile a genetic cause with autism epidemiology given that autism was unknown prior to 1940 and the prevalence of the condition has increased exponentially since that time. These factors suggest that a purely genetic cause is unlikely.

The other dominant theory is that autism is caused by *in utero* and/or early infant exposure to mercury [4,28]. The primary source of exposure to mercury amongst infants is via vaccines (both maternal

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and pediatric) and dental amalgam (maternal). The hypothesis has been acknowledged as biologically plausible by the Centers for Disease Control in the United States [39], and it is thus imperative that consideration of the hypothesis in the context of an epidemiological examination be conducted.

An epidemiological review is essential as we can never conduct a study that proves (or disproves) mercury causes autism because we cannot, ethically or practically, conduct an experimental randomised controlled trial in which some children are allocated to be exposed to a known neurotoxin (mercury) and others not. The situation is analogous to that of research into smoking and lung cancer. We do not have (and cannot get) direct experimental evidence that smoking causes lung cancer, but we can approach it epidemiologically (as we indeed have), and the smoking–lung cancer relationship is now well established as a causal one [32].

Just as with the smoking–lung cancer relationship, all we are able to do with the autism and mercury relationship is measure the association between the two variables and, if certain criteria are met, determine whether one likely causes the other. Although an association between two phenomena is not indicative of causation, one can apply criteria to gauge the strength of the association, and if it is strong, infer that one phenomenon causes the other. This is the foundation of the epidemiological approach to cause–effect [44]. Historically, there are five criteria used in epidemiology to establish cause–effect relationships [38]. These are:

- (1) high relative risk,
- (2) consistency,
- (3) graded response to a graded dose,
- (4) temporal relationship,
- (5) plausible mechanism.

Therefore, to establish that mercury causes autism, we would need a series of studies examining the relationship between the two variables in various ways that address these criteria. This paper aims to review the existing scientific literature on mercury and autism within this epidemiological framework.

2. Mercury is known to be able to cause neurodevelopmental disorders in young children (high relative risk, plausible mechanism)

Mercury has long been known to be a potent neurotoxin and, in fact, the brain is the primary target tissue of mercury, with the fetal and newborn brain being more susceptible to mercury damage than the adult brain [10]. Unsurprisingly, then, mercury poisoning in infants is known to produce symptoms including mental retardation, loss of coordination in speech, writing, and gait, stupor, and irritability and bad temper progressing to mania [39]. Beyond single case reports of relatively rare infant mercury poisoning incidents [3] we have a well-documented large-scale international infantile mercury poisoning epidemic that clearly illustrates how mercury can (and does) produce neurodevelopmental disorders in children [13].

Pink Disease is a medical condition that strikes infants aged 0–6 years and is typified by abnormal behavioural and psychological manifestations including psychosis, loss of speech, and social withdrawal [33]. The Pink Disease epidemic of 1900–1956 was ultimately found to be caused by mercury (mercurous chloride) contained in common teething and worming treatments of the day. Only a very small sub-population of children were effected, thus suggesting that individual susceptibility to mercury’s effects was highly variable and was therefore an independent risk factor for Pink Disease beyond mercury exposure alone.

This example from medical history helped advance toxicologists’ understanding of the effects of mercury beyond the basic principle of “the dose makes the poison” [31]. More recent conceptualizations of toxicology acknowledge the role of both dose and individual susceptibilities to the toxic agent of interest [19]. This modern conceptualization is entirely consistent with the recorded history of Pink Disease and provides a model for how one might view the autism as mercury poisoning hypothesis as concurrently implicating individual susceptibility to mercury’s effects [21]. In this sense, the autism as mercury poisoning hypothesis is consistent with the diathesis-stress model of disease [49], whereby the causal mechanism is conceptualised as an interplay between a predisposing physiological susceptibility (e.g., sensitivity to mercury) *in conjunction with* an environmental stressor (e.g., mercury).

3. Symptoms of autism are consistent with those of mercury poisoning (consistency, plausible mechanism, high relative risk)

With regard to the historical analogy of autism to Pink Disease, it is critical to remain cognizant of the following:

- (1) The forms of mercury thought to cause autism (ethyl mercury from vaccines and mercury vapour from maternal dental amalgam) are different forms of mercury than that which caused Pink Disease (mercurous chloride).
- (2) The mode of exposure also differs. In Pink Disease exposure was primarily via oral ingestion, whereas in modern times, the major exposure is intra-venous (direct to infant vaccination) or via the placenta and/or breast milk in the case of maternal amalgams and vaccines.
- (3) It is well established that mercury poisoning presents as differing syndromes dependent on form of mercury, route of exposure and individual difference variables like age of individual and idiosyncratic biochemical conditions [19].

So, one must accept that it would be unlikely to discover identical syndromes to autism in medical history literature as the hypothesised phenomenon of mercury poisoning via vaccinal mercury (ethyl mercury) and amalgam mercury (mercury vapour) has not, to date, been documented. Nevertheless, several researchers have commented on the similarities between infantile mercurialism and autism [4, 16,28]. In fact, mercury can cause immune, sensory, neurological, motor and behavioral dysfunctions similar to traits defining or associated with ASDs [17]. Symptoms common to both infantile mercurialism and autism include mental retardation, loss of speech, social withdrawal, sensory disturbances and unusual behaviours [4,17,33,43].

4. The biochemical abnormalities found in autism are consistent with mercury poisoning (consistency, plausible mechanism)

Beyond the directly observable behavioural consistencies between autism and infantile mercurialism, it is important to consider the specific pathologies of the two syndromes. Biological findings in autism that are consistent with mercury poisoning include elevated oxidative stress [27], depleted levels of glutathione [25], neurochemical irregularities [9], gastro-intestinal distress [23], immune dysregulation [11] and generalized and neural inflammation [40]. All of these are also well documented effects of mercury poisoning and, specifically, mercury poisoning in infants [4]. These findings should also be viewed in light of the direct toxicological findings that autistic children have higher measurable mercury burden than their non-autistic peers (see Section 9).

5. There is a positive relationship between mercury exposure and autism prevalence (graded response to a graded dose, high relative risk)

Although the old toxicology adage, “the dose makes the poison” [31] is established as only a partial explanation for the phenomena of poisoning, it remains a useful heuristic for determining relative risk of specific levels of exposure to toxic agents. Therefore, within the context of an epidemiological investigation, one would expect there to be at least some dose–response relationship between mercury and autism if the relationship is indeed real and of a causal nature.

Higher levels of exposure to mercury have been observed among children with autism compared to controls in one unpublished [41] and one published study [18], with the former study finding a relative risk of autism of 2.48 in infants receiving 62.5 µg or more of ethyl-mercury (via vaccines) by three months of age. Additionally, in an ecological study by Palmer et al. [30] it was found that “the association between environmentally released mercury and special education rates were fully mediated by increased autism rates” (p. 203). This means that one may reasonably infer a direct relationship between degree or level of mercury exposure and autism. Taken together, these datasets represent direct epidemiological evidence for the dose–response relationship between mercury and autism.

6. Children are being exposed to mercury (temporal relationship, high relative risk, plausible mechanism)

A fundamental component of an etiological examination of autism and mercury demand that there be demonstrated evidence of mercury exposure in the first place. Of this, we can be certain. In fact, the World Health Organisation has acknowledged that dental amalgam is not only the major source of mercury exposure in adults, but also infants as this mercury easily passes to fetuses via the placenta or to infants via breastmilk [46]. There is also confirmed exposure via mercury in vaccinations. For example, Stajich et al. [37] found that “comparison of pre- and post-vaccination mercury levels showed a significant increase in both preterm and term infants after vaccination” (p. 679).

Several papers have demonstrated that children have been exposed to increasing levels of mercury over the several decades since the first cases of autism were reported [4]. In fact, in the late 1990s and early 2000s, infants in the US were being exposed to mercury at levels often several times higher than federal safety guidelines [28]. This is fundamental to understanding the mercury–autism relationship. The mercury that millions of children are exposed to is possibly chronic (via maternal mercury amalgam), but also acute from bolus exposures occurring from time to time as part of the standard vaccination schedule (e.g., day of birth, 6 months, 12 months, 2 years and 4 years).

7. The emergence of autism in the 1930s and the subsequent rise in prevalence rates coincide with increasing exposure of mothers, fetuses, neonates and infants to mercury (temporal relationship)

Autism is a modern disease. It was first identified in the late 1930s and reported in 1943 by Kanner [26]. It is important to place the arrival and subsequent epidemic growth of autism into the historical context of environmental exposure to mercury. Therefore, it is important to acknowledge that the commencement of widely available vaccinations (containing mercury) commenced in the 1930s. Additionally, the early 1900s saw the increasing availability and popularity of dental care where mercury

amalgam fillings were the dominant restorative material [36]. It is also of interest to note that vaccinations and dental care were not yet freely available under a public health program, but were more commonly adopted only by the middle and higher socio-economic classes. This historical context is also consistent with the mercury–autism hypothesis as it was a noteworthy feature of many of the early reports of autism that the condition was strongly identified as being associated with the upper-middle and higher classes [26,34].

8. Animal studies show that mercury can cause autistic-like behaviours (plausible mechanism, consistency)

Where direct experimental studies of a hypothesised disease process cannot be conducted (on ethical grounds) it is accepted that animal models represent a reasonable alternative. With regard to the mercury–autism hypothesis, this has several unique challenges. First, it is not accepted that non-human animals can “have” autism. Even if they could, we do not have any established criteria for how that might be assessed and diagnosed. Additionally, different species respond to mercury in differing ways. Nevertheless, rats are regarded as providing a broadly equivalent biochemistry for the purposes of most human-analogue trials. They have the further advantage of being relatively intelligent with relatively well understood social conventions broadly analogous to human social behaviour [45].

One study has examined the effects of the mercury–autism hypothesis as directly as possible by mirroring mercury form (ethyl mercury), dose (weight adjusted as per the standard US vaccine schedule) and administration mode (intra-venous injection) to the standard vaccination schedule of the USA [22]. The researchers demonstrated that the toxic effect of the ethyl mercury compound found in many vaccines was dependent on the mouse-strain used. Specifically, toxic effects (resembling autistic symptoms) were noted more commonly amongst specific breeds of mice. This study demonstrated not only that dose-adjusted exposure to mercury equivalent to human exposure could produce autistic-like behaviours, but that the factor of individual susceptibility was an adjunct in the process – exactly as the mercury–autism hypothesis predicts when understood as a diathesis–stress model.

9. Mercury levels are higher in autistic than non-autistic children (plausible mechanism, graded dose–response relationship, temporal relationship, consistency, high relative risk)

Perhaps the most compelling toxicological evidence available, short of experimental evidence, is the finding that the level of the hypothesised causal agent is significantly higher in the proposed affected population. Specifically, the mercury–autism hypothesis would suggest that mercury should be measurably higher in autistic than non-autistic children. A review of the literature in this area finds that this is, indeed, the case. Significant elevations in measurable mercury in urine [6] and blood [15] have been reported, as well as elevations in specific biomarkers of mercury [16,29]. An advantage of simple 2 group blood-work studies like that reported by DeSoto and Hitlan [15] is that they are not open to multiple or complex interpretation. For example, when considered in light of the previously described epidemiological evidence for the autism as mercury poisoning hypothesis, the fact that blood levels of mercury are indeed higher in autistic children than non-autistic children can only be interpreted as suggestive that either (1) mercury causes autism, or (2) autism causes mercury. The second notion is patently nonsensical

and unsupported by any scientific literature, and the idea that it may be neither (1) nor (2) is not valid as the statistical methodology largely rules out the possibility of coincidence.

It is interesting to reflect on the fact that the proponents of the *Pink Disease as mercury poisoning* hypothesis had only basic urinary mercury studies to guide them whereby some (but not all) studies showed that urinary mercury was often higher in Pink Disease children than non-affected peers. Despite the limited scientific evidence, this proved enough in the 1950s to prompt the widespread application of the *precautionary principle* which resulted in the removal of mercury containing teething and worming treatments from the market, and the subsequent eradication of the disease. This provides us with a strong and telling lesson of the importance of applying the precautionary principle on suspicion of harm rather than awaiting certainty of it.

10. The precautionary principle

The most fundamental principle accepted across all disciplines of health care is the *precautionary principle* (“First, do no harm”). It does not demand certainty that an action causes an adverse health effect in order to establish that one should not take the action – it merely requires suspicion of harm [20]. The science behind the autism as mercury poisoning hypothesis meets all epidemiological criteria across too many independent studies to be dismissed as coincidence. So, the hypothesis that mercury likely causes autism is confirmed epidemiologically.

11. Absence of evidence and evidence of absence

In reviewing the literature, one finds several studies that fail to find a relationship between autism and mercury (e.g., [24,41]). Nevertheless, these papers merely reported *failing* to find evidence that supports the mercury–autism relationship. It is important to remember that *absence of evidence* is not synonymous with *evidence of absence*. Very often, studies fail to find relationships when the effect size is small, and/or the sample size is small or of an ungeneralisable nature. In these cases the researchers merely report absence of evidence of the relationship, and not evidence of absence of that relationship. Therefore, these studies do not represent an inconsistency in the literature on the mercury–autism relationship. This pattern frequently occurs in research across nearly all disciplines. The precautionary principle demands that we take the reports of positive associations between mercury and autism seriously and consider them preferentially to null findings in order to meet *duty of care* obligations enshrined in the precautionary principle.

12. Conclusion

The existing scientific literature provides grounds for strong suspicion that mercury plays a causal role in the development of autism. Given this suspicion, and the severe nature, devastating lifelong impact and extremely high prevalence of autism, it would be negligent to continue to expose pregnant and nursing mothers and infant children to any amount of avoidable mercury. Health authorities worldwide should move without hesitation to ban and remove all mercury in all medical products at the earliest possible date.

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