The Supposed Vaccines-Autism Relationship As Mother-Child Attachment’s Trauma

Alketa H. Bakiri1,2,#, Anxhela Gurakuqi-Qirko3,4,#, Dorela Luku5, Doris Ç. Mingomataj2, Odilija Rudzeviciene6, and Ervin Ç. Mingomataj5,*

1 American Hospital of Tirana, Outpatients Service, Tirana, Albania; 
2 Albanian University, Faculty of Medical Sciences, Tirana, Albania; 
3 Dept. of Biomedical and Experimental Sciences, University of Medicine, Tirana, Albania; 
4 Division of Internal Medicine & Respiratory Function Lab, “Shefqet Ndroqi” University Hospital, Tirana, Albania; 
5 “Mother Theresa” School of Medicine, Dept. of Allergology & Clinical Immunology, Tirana, Albania; 
6 Vilnius University, Faculty of Medicine, Clinic of Children Diseases, Vilnius, Lithuania.

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ABSTRACT

Vaccines are the safest and most effective tools for preventing infectious diseases, but in certain populations, the attitude of autism fear towards the vaccinations is expanding, as was the case for the measles, mumps, and rubella (MMR). The autism spectrum disorder (ASD) includes a range of neurodevelopmental pathologies, characterized by deficits in social communication and interactions, with onset in early development. Although the detailed ASD mechanisms remain unclear, the most largely-reported potential causative factors are genetics and environmental ones. This work suggests that the relationship between MMR (or other vaccines administrated in the parenteral route during the second half-year of life) and the subsequent development of the ASD could be a surrogate of disturbances on the mother-child attachment. Being in the situation of limbic hyperexcitability and the state of hyperactive hypervigilance, the one-year-old autistic child has formed its specific attachment to its mother, which represents the symbol of security, comfort, and protection against the strangers. The lack of expected maternal protection against the painful vaccine injection may lead to an “apocalypse” concerning to mother-child attachment, as well as to child disappointment and frustration. In other words, the parenteral vaccination in the presence of the mother and the violation of child by the strangers can serve only as an apparent trigger that makes autism behavior distinguishable and expressive for the parents and caregivers. Consequently, the association of parenteral vaccination with ASD occurrence among genetically-predisposed children can be considered an attachment-related trauma and maybe the decisive traumatic experience related to clinical development of autism.

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Corresponding Author: Ervin Ç. Mingomataj, “Mother Theresa” School of Medicine, Dept. of Allergology & Clinical Immunology, Tirana, Albania.
INTRODUCTION:
Vaccines are the safest and most effective tools for preventing infectious diseases and their success in achieving relevant public health outcomes, such as the drastic reduction or eradication of many seriously debilitating or life-threatening conditions, is well-established.\(^1,2\) In populations, who are no more aware of the risk of these infections, the attitude of suspicion and fear towards the vaccinations is expanding and in some cases reaches a worldwide media coverage as was the case for the measles, mumps, and rubella (MMR) vaccine.\(^1,2\)

In 1998, a British doctor, Andrew Wakefield, and co-authors, reported the association between MMR vaccine and the occurrence of autism, which is explained as a possible cause of the inflammatory process.\(^2\) A limited number of recent publications have explained the occurrence of autism after the application of certain vaccines with exposure to Hg-containing thimerosal or gut microbiota alterations.\(^3-5\) Development of autism spectrum disorders (ASD) is associated with neuroimmune inflammatory dysregulations, including the increase of interleukins (IL)-1\(\beta\), IL-6, IL-17, and tumor necrosis factor-alpha.\(^6\) Meanwhile, the majority of the literature has refuted the association of vaccination with ASD, and the scientific research, conducted in recent years, confirms the inconsistency of the relationship between MMR vaccine and autism.\(^2,7-9\)

In this respect, many epidemiologic studies among large-size populations have shown that neither thimerosal nor MMR vaccine causes autism, and in concert with the biological implausibility that vaccines overwhelm a child’s immune system, they have effectively dismissed the notion that vaccines cause autism.\(^9\)

Despite an abundance of scientific evidence that shows no causal effect between any vaccine and autism, sizable segments of the public still champion Wakefield’s view. To understand what causes such persistent reliance on patently incorrect information,\(^1\) we share the opinion that some relevant data about ASD, early childhood development, and child-mother attachment, as well as the vaccination schedule, should be considered in more detail.

The Etiology and Physiopathology of ASD: The Role of Stress
ASD includes a range of neurodevelopmental disorders that are characterized by deficits in social communication and interactions, as well as by repetitive behaviors and restrictive interests, with onset in early development.\(^10\) Although the detailed mechanisms of ASD remain unclear, many possible explanations and potential causative factors have been reported, such as genetics, sex, and environmental factors.\(^11\) Current studies have identified a significant positive genetic correlation between autism and various measures of cognition.\(^12\) Notably, family studies have demonstrated a genetic contribution to ASD etiology, with a concordance ranging from 83% in monozygotic twins to at least 7% among siblings.\(^10,13\) Rare genetic variation is found as small insertions and deletions, which can be inherited from a paternal and/or maternal origin or they may appear de novo on the X chromosome of the affected subject.\(^10,13\)

Meanwhile, suggested environmental cofactors in the development of ASD are gut microbiota, regenerations deficit of gut epithelia, etc., which may lead to inflammatory processes and disorders of the limbic system.\(^5,6\) Studies on the environment’s role and social behavior have evidenced the similarity between anxiety and ASD, leading to the conclusion that stress can be a supplemental cofactor in the development of these disorders.\(^14-16\) Thus, animal models of pregestational maternal stress exposure resulted in limbic and hypothalamic-pituitary-adrenal (HPA) changes due to epigenetic mechanisms.\(^15,17,18\)

Based on primarily animal model research, it is postulated that prenatal maternal stress may alter the intrauterine environment and exert effects on placental structure and function during a time of rapid organ development, leading to physiological adaptations in the developing fetus that have ongoing effects throughout postnatal development.\(^19\) In this context, the significantly higher serum cortisol response and prolonged duration of recovery of cortisol elevation following the blood-stick stressor in children with autism suggest increased reactivity of the HPA axis to stress and novel stimuli in children with autism.\(^20\)
The association of the autistic-like behavior during psychological stress with deviations on HPA cortisol response and limbic increase of brain-derived neurotrophic factor (BDNF) is explained by the fact that the limbic area of the amygdala integrates and processes incoming information pertinent to reward and to emotions such as fear and anxiety that promote survival by warning of potential danger.\cite{21-25} Apart from increased reactivity, the elevated stress in children with autism could be associated with their difficulty to tolerate novel environment(s), whereas some environmental stressors can lead to excessive behavioral reactivity to situations that could be associated with a concurrent rise in cortisol and BDNF level.\cite{20,26} In this respect, observations in rat hippocampus suggest that BDNF is involved in neonatal isolation-induced anxiety and autism-like behaviors (cognitive impairment, etc), underlying the ASD development as a persistent and lasting condition.\cite{27,28} The lateral part of the amygdala communicates bi-directionally with brain regions affecting cognition, motivation, and stress responses including the prefrontal cortex, hippocampus, nucleus accumbens, and hindbrain regions that trigger norepinephrine-mediated stress responses.\cite{23} Changes in its local regulation excitability underlie behavioral disturbances characteristic of disorders including post-traumatic stress syndrome, ASD, attention-deficit hyperactivity disorder, and stress-induced relapse to drug use. Converging evidence indicates that chronic stress causes limbic principal output neurons to become hyperexcitable or the state of hyperreactive flee-or-fight responses (hypervigilance) when the autistic person finds him or herself outside their comfort zone.\cite{14,23}

The Development of Child Attachment
Indepedently to the clinical of psychological situation, the early childhood psychomotor development passes in several stages, which can influence the social behavior.\cite{29,30} In this respect, the attachment behavior in adults towards the child includes responding sensitively and appropriately to the child’s needs.\cite{29} The importance of the child-mother relationship is considered as important in terms of social, emotional, and cognitive child development. During the first half-year, infants indiscriminately enjoy human company and most babies respond equally to any caregiver.\cite{50} But along the third quarter, the baby looks to particular familiar people for security, comfort, and protection. Distinguishing the family members to other close relatives, it shows stranger fear and unhappiness when separated from a special person (separation anxiety) at the end of the mentioned interval.\cite{30} During the fourth quarter, he has usually formed its specific attachment to mother and family relatives. Along the following stage that begins at the end of the first life year, the attachments were most likely to form with those who responded accurately to the baby's signals, not the person they spent more time with.\cite{29,30}

The Vaccination Schedules
The vaccination is a situation in which every child finds him or herself outside their comfort zone because of the eventual separation from the mother. Everyone (especially babies and young children) consider the parenteral injection per se a main stressful event because of painful experience. According to the World Health Organization and Centers for Disease Control and Prevention schedules, a combined vaccine of diphtheria, pertussis, and tetanus is applied in parenteral route at age of 2, 4 and 6 months, whereas the MMR vaccine is administrated at the age of 1 year in the same way.\cite{31,32} Also, these schedules recommend the parenteral vaccination along with early childhood for varicella, influenza, or hepatitis B.

The ASD-Vaccination Association as Attachment-related Trauma
In concert, the afore-mentioned findings may suggest that the relationship between MMR (and/or other vaccines administrated in the parenteral route during the second half-year of life) and the subsequent development of ASD could be a surrogate of disturbances on the mother-child attachment. Taken into account that the ASD patients are characterized by limbic hyperexcitability and the state of hyperreactive hypervigilance (especially when the autistic person finds him or herself outside their comfort zone),\cite{14,23} they also should be in such state
even during the parenteral vaccine administration. Especially in the case of MMR vaccination, the one-year-old child has formed its specific attachment to its mother, which represents the symbol of security, comfort, and protection against the stranger pediatrician (or assisting personnel).\[30\] In contrast to the developmentally disabled children, the children with autistic disorder stayed closer toward their mothers compared with their responses to strangers.\[33\] The missed expected maternal protection against the painful injection (despite her presence in the medication room), may lead to an “apocalypse” with concern to the mother-child attachment, as well as to the child’s disappointment and frustration. In the next time, the autistic child will show fear of strangers in a deviated mode and the relationship to closer relevant(s) will be not the same as compared to the previous life stages. Taken into account that the autism is hereditary predisposed,\[11-13\] it could be suggested that the parenteral vaccination in the presence of the mother and the violation of the child by the stranger pediatrician (and/or collaborators) serve only as an apparent trigger that makes the autism behavior distinguishable and expressive for the parents and caregivers. This is the ground that the ASD diagnosis happens within the childhood vaccination schedule (mostly after MMR vaccination); so, it is likely that the parents will have some recent vaccine to point to when looking for factors that seem to correlate with the onset of autism.\[8,34\]

Our point-of-view agrees with wide known arguments, which are reported in the literature. Thus, ASD etiology is very complex, but the heredity is the main factor, and the stress seems to be a trigger or exposes the clinical situation to caregivers and physicians.\[10,13,16,20,35\] The early signs of autistic personality may be detected during the second half the first year; however, the ASD is generally diagnosed during the third life year.\[8,36\] This contrasts with the international schedules, in which the majority of vaccines are given before the age of 2, many in fact at or before 12 months (see Figure 1).\[31,32,34,37\] Especially, the MMR does not come “in their first 12 months of life.”, but at the very earliest it comes at 12 months, which obviously cannot be responsible for symptoms that are present by 12 months.\[34\] Therefore, the association of the parenteral vaccination with ASD occurrence among genetically-predisposed children can be considered an attachment-related trauma and maybe an important traumatic experience related to the clinical development of the autism.\[16\]

**Figure 1: The timeline of parenteral vaccines, child social attachment and ASD**\[30-32\]

![Figure 1: The timeline of parenteral vaccines, child social attachment and ASD](image-url)
Legend:
1* The schedule of parenteral vaccines: Vaccines before 6 months (start age of any social attachment) and after 3 years (commonly age of ASD diagnosis) are not shown.
2* MMR - Measles, Mumps, Rubella; DTP – Diphtheria, Tetanus, Pertussis.
3* The varicella vaccine could be given in infants from 12 months, together with other live viral vaccines (MMR); it should be administered at a minimum interval of 28 days.31
4* The attachment stages: From 1.5 months until the age of 7 months infants indiscriminately enjoy human company and most babies respond equally to any caregiver. From 7 until 9 months baby develops specific attachment or preference for a single person, especially his/her mother, in the need for security, comfort, and protection. The fear of strangers and unhappiness/anxiety when separated from the special person, are seen as evidence that the baby has formed an attachment. This is usually developed by one year of age. From 10 months and onward the baby starts several attachments to other family members (multiple attachments) - father, sibling(s), grandparents, but still, the mother remains the principal attachment figure for half of the babies. The key of this attachment is not who feeds and changes the child, but who plays, respond, and communicate with him/her.
5* The parent/caregiver may have the first suspicion for the child’s autism directly after his 1st birthday; however, the medical diagnosis is determined generally during the child’s 3rd year.8,34

The Perspective of our Reflections
To testify our argument, we suggest enrollment of longitudinal studies about the development of ASD in children that are vaccinated through parenteral and non-parenteral (i.e. digestive, etc) route. That means the development of vaccines administrable in alternative routes is mandatory to compare the respective results (to testify our argument). A significant difference in the reduction of ASD among non-parenteral vaccinated subjects could agree with the theory of attachment-related trauma, not with the casual association of vaccines with autism. Alternatively, to respond this question we can observe the expected data evidenced in the established animal models and compare the provided results between genetically modified and wild type animals (in such way as during the parenteral sensitization with ovalbumin A and/or the exposure to various stressful events).38-40 The consistent similarity or difference between the established findings in both cases may be reflected even in the behavioral response to stress, is therefore a potential agreement or contradiction to our explanation.

CONCLUSIONS
The present study has addressed the pertinent case of misinformation about vaccines and autism. In our opinion, the relationship between MMR (including other vaccines administrated in the parenteral route) and the subsequent development of ASD could be a surrogate of disturbances on the mother-child attachment. Being in the situation of limbic hyperexcitability and hypervigilance, the one-year-old autistic child experiences the lack of expected maternal protection against the painful injection as “apocalypse” that leads to persistent disappointment. This unexpected violation in the presence of the mother can serve only as an apparent trigger that makes the autism behavior distinguishable and expressive for the parents and caregivers. Consequently, the association of parenteral vaccination with the ASD occurrence among genetically-predisposed children can be considered an attachment-related trauma and maybe the decisive traumatic experience related to the clinical development of autism.

Despite this appearance, the clinical data clearly shows that there is no real etiologic association between the vaccines and autism, even in case of most often implicated vaccine – MMR. This review also supports other evidence that the onset of autism occurs earlier than many parents observe and much earlier than formal diagnosis, which calls into question any casual observations about the timing of onset to any potential triggers. Given that correction of vaccine misinformation remains an urgent priority to assure the continued success of the immunization programs, this work emphasizes the need for further studies on the autism cause(s) and their focus on more-promising leads.
Ethical Responsibilities
The authors declare that the manuscript has not been submitted to more than one journal for simultaneous consideration. The manuscript has not been published previously (partly or in full) unless the new work concerns an expansion of previous work. No data, text, or theories by others are presented as if they were the author’s own (“plagiarism”). Authors whose names appear on the submission have contributed sufficiently to the scientific work and therefore share collective responsibility and accountability for the results. Other statements do not apply to this work.

Compliance with Ethical Standards and Disclosure of Potential Conflict of Interests
Authors declare that anyone has received research grants or any financial support from funding agencies, individuals, or programs, and they have any potential conflict of interest to declare. Other statements do not apply to this work.

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