

VIRAL INFECTION AS A TRIGGER OF AUTISM

Increased susceptibility to infection is a common problem during pregnancy due to various pathophysiological and mechanical changes and immune system adaptation necessary to keep the fetus in utero and prevent expulsion. Therefore, there is an increased chance of asymptomatic and symptomatic viral infection during pregnancy. Some viruses can cross the placental barrier, reaching the fetus and causing devastating developmental fetal effects. Infection is an important trigger for immune activation. Viruses can directly infect the brain, causing neuron cell death by cell lysis, the release of free radicals, or apoptosis induction, inducing a systemic inflammatory response that affects the brain or alters the maternal or their offspring's immune status, which could influence autism development. Viral-induced immune activation causes elevated levels of pro-inflammatory cytokine IL-6, which changes brain gene expression in the offspring, driving abnormal behaviour development. Maternal immune activation increases maternal pro-inflammatory cytokines, activates maternal T-helper-17 cells, and increases IL-6 mRNA and protein in the fetal brain and the placenta making specific placental tissue changes commonly observed in patients who developed ASD (Autism Spectrum Disorder). Some viruses, such as rubella and cytomegalovirus, may have a teratogenic effect on the fetus, impairing brain functions and causing autism. The brain and immune system are not fully developed in fetuses and young infants, so they are at high risk of viral-induced brain damage. Therefore, maternal viral infection and inflammation during critical periods of pregnancy could result in an unfavourable intrauterine environment and alter the brain structure and function, raising the risks of having a child with autism. Certain viruses are known to be more commonly associated with the development of autism.

Rubella: Rubella is a well-known RNA virus that can cause various congenital malformations when contracted, especially during the first trimester of pregnancy. Intellectual disabilities, including autism, are common among children with congenital rubella infection. Different mechanisms were proposed, including infection-induced hypervitaminosis A. Acute rubella infection induces mild liver dysfunction altering the liver metabolism of vitamin A with the spilling of the stored vitamin A complexes into the circulation, resulting in an endogenous type of hypervitaminosis A, which serves as a teratogen causing mitochondrial damage, DNA alteration, and apoptosis; inducing autism development. In addition, the rubella virus can invade and replicate inside the brain cells. It also can cause cerebral vascular lesions and haemorrhages and fulminant degeneration of leptomeninges with significant brain volume loss and destruction of white matter. Therefore, many manifestations of congenital rubella syndrome, such as congenital heart defects, spasticity, deafness, and visual impairment, are common in children with autism.

Influenza viruses: Influenza is associated with increased morbidity and mortality in high-risk groups, including pregnant women, and during the first two postpartum weeks, reliant on pre-existing immunity. Some studies showed an increased risk of adverse neurodevelopmental outcomes such as autism or schizophrenia when pregnant ladies encounter influenza during pregnancy. Mahic et al found a statistically non-significant increase in the risk of autism in the offspring of seropositive mothers with

symptoms of influenza during mid-pregnancy compared to seronegative mothers. In addition, the influenza virus can trigger a cascade of acute-phase reactions, including fever which by itself increases the risk of autism, together with a systemic increase in cytokine expression. However, many recent studies showed no increased risk of developing autism with influenza infection or vaccination during pregnancy in the offspring. In addition, Zerbo et al showed no significant association between influenza infection and the risk of autism in the offspring. Meanwhile, they found a statistically non-significant increased risk of autism in the offspring when pregnant ladies received influenza vaccination during the first trimester. However, they emphasized that this observation should not call for any change in vaccination policy or practice. A more recent study by Becerra-Culqui et al reported the same finding when they found no association between prenatal influenza infection or vaccination and increased risk of autism in offspring. They strongly recommended influenza vaccination to pregnant ladies to protect themselves and their offspring.

SARS-CoV-2 viruses: COVID-19 is caused by infection by SARS-CoV-2, one of the beta coronaviruses, which caused the pandemic coronavirus COVID-19, posing a severe threat worldwide. SARS-CoV-2 can spread from the respiratory tract to the central nervous system through the olfactory bulb. COVID-19 induces brain structural changes that cause various neurologic complications that could last long. There is a rising concern about the potentially harmful effects of SARS-CoV-2 on pregnancy that could affect the pregnant lady and her fetus. Currently, there is no proof of SARS-CoV-2 vertical transmission from the mother to her fetus, which could be due to the preventive effect of placental lactoferrin. However, the virus could be transferred postnatally via the mother's air droplets or during breastfeeding. Severe gestational COVID-19 induces uncontrolled inflammatory cytokine storm release and maternal immune activation, causing possible fetal organ damage, including the brain, that could manifest later with autism symptoms. The induced inflammation causes amygdala neurodegenerative changes by "short-circuiting the electrical system," producing emotional feeling ability impairment and abnormal fear regulation due to an abnormal hypothalamic-pituitary-adrenal axis system.

These changes can explain the increase in the rate of autism during the COVID-19 pandemic. Edlow et al showed that in-utero exposure to SARS-CoV-2 infection might be associated with increased neurodevelopmental disorder rates in some offspring. However, Brynne et al showed that the increased association of autism and other intellectual disabilities in the offsprings of mothers infected with SARS-CoV-2 during pregnancy does not necessarily reflect the causal relationship but is more probable to be related to common familial conditions such as shared genetic and environmental factors. To lessen the influence of gestational COVID-19, pregnant women should have adequate amounts of n-3 polyunsaturated fatty acids, vitamin D, folic acid, and a high choline and luteolin supplement. These supplements benefit brain development and function in the offspring of women who encounter viral infections during early pregnancy.

Fonte: Adaptado de: Al-Beltagi M, Saeed NK, Elbeltagi R, Bediwy AS, Aftab SAS, Alhawamdeh R. **Viruses and autism: A Bi-mutual cause and effect.** World J Virol 2023; 12(3): 172-192. Disponível em: [Viruses and autism: A Bi-mutual cause and effect \[wjnet.com\]](http://www.wjnet.com) Acesso em: 13 Set 2023.

AUTOMOTIVE TECHNOLOGY DEVELOPMENT

There are over 900 million vehicles worldwide on the road today. **Since** long, the fuel **used** for propulsion purposes for almost all vehicles has been produced from fossil fuel. It is estimated on record that this number of vehicles on the road is **likely** to increase appreciably to 1.1 billion vehicles **by** 2020 due to high economic expansion in China and India. This **likely** situation would have a detrimental effect on global crude oil demand and for the worldwide CO₂ emissions. **Since** an increase in demand of oil and CO₂ production proportional to the projected number of vehicles is not sustainable for financial, ecological and political reasons, every implementation strategy must aim at the replacement of fossil fuel as a source of energy for automotive applications. One strategy that was **used by** General Motors is the electrification of the automobile, the displacement of gasoline by alternative energy carriers. This will lead to a drastic reduction in fuel consumption, reduced emissions and also increased energy security through geographic diversification of the available energy sources.

This strategy was first established in 1996 during the development of the first electric vehicle: GM EV1. This design was a pure battery electric vehicle (BEV), but failed to rise or compete on the market— hence the need for its modification in the subsequent years. EV1 drivers coined the term “range anxiety” describing their omnipresent concern or the fear of becoming stranded with a discharged battery in a limited-range vehicle, away from an electric infrastructure. These concerns remain one of the main challenges which still hinder the progress of the BEV on the market even till now. However, most of the EV-enabling electric components and systems have found utility in the meantime by adapting them for the usage in mild and fully hybrid electric vehicles (HEVs). These vehicles often do not provide power by exclusively using electric motor and therefore the power and energy level requirements for the system components are reduced in comparison with a conventional BEV.

The conventional hybrid improves vehicle efficiency and thus reduces power generated from an onboard liquid medium. The on-board electrical engine and the storage system are only used to shift the operating point of the internal combustion engine (ICE) to a more favourable point on the efficiency map and to enable recuperation. Thus, HEVs unfortunately provide no additional pathways to utilize CO₂-neutral renewable energy sources. Partially, these drawbacks may be resolved by introducing the so-called extended-range electric vehicles (EREVs). Zero-emission vehicles using an electric powertrain system based on hydrogen fuel cells or purely battery-electric systems that are fully competitive to conventional vehicles regarding performance and ease-of-use represent the ultimate target of the GM strategy. A further important step into this direction was the start of mass production of the Chevrolet Volt at the end of 2010, as well as the introduction of other vehicles like the Opel Ampera which are also based on the VOLTEC technology.

It is virtually impossible to discuss electric cars without considering the key role hydrogen might play in the whole process. As discussed previously, it is possible to use hydrogen as an on-board fuel for motive

power either through internal combustion engine or fuel cell to generate electricity that can be used to power an electric traction motor. Hydrogen is often considered as CO₂-free energy if produced from renewable and nuclear energy. But with the latest technologies for hydrogen production, storage, transportation and distribution, as well as fuel cell emissions, if the hydrogen is from renewable energy sources, the hydrogen vehicle generates zero emission CO₂, while plug-in hybrids are still not fully green as they are hybrid models— only partially reducing emissions.

Lately in Europe, electric vehicles have been making serious strides. In London, for instance, the then mayor of the city, Boris Johnson, fleshed out his ambition to turn the metropolis into the electric car capital of Europe by promising that every Londoner would be within a one mile's reach of an electric car charging point within five years. The mayor of London claimed that electric cars were a way of reducing harmful emissions, but he made clear that he expected funding support from the government to turn his ambition for mainstream use of zero carbon electric vehicles into a reality. The mayor is under pressure to find solutions to London's poor air quality – which is among the worst in Europe. Johnson announced his plans to introduce 100,000 cars to the capital's streets by building the charging point infrastructure to incentivize drivers to go electric and then make London the ultra-low emission vehicle capital of Europe. He plans to lower the congestion charge further for low-emission vehicles and to give decommissioning grants to taxis that are more than 10 years old, in an effort to encourage drivers to take up zero emission vehicles. He also signaled a private-public membership scheme so that electric car users can register their vehicle in their borough. The mayor plans to buy 1,000 electric vehicles for the Greater London authority fleet.

FONTE: Adaptado de: T. Wilberforce et al. *Developments of electric cars and fuel cell hydrogen electric cars*, in **International Journal of Hydrogen Energy**. Disponível em: <https://www.sciencedirect.com/science/article/abs/pii/S036031991732791X>. Acesso em 15 nov 2019.

QUESTÕES

As questões de 1 a 5 referem-se ao TEXTO 1:

1) NÃO constitui fator de aumento de risco de se ter filhos com autismo:

- (A)** Uma resposta inflamatória sistêmica causada pela morte das células neurais decorrente da contração de algum vírus.
- (B)** O aumento da citocina IL-6 e de proteína no cérebro fetal e na placenta.
- (C)** Um efeito teratogênico no feto prejudicial às funções cerebrais.
- (D)** O baixo risco de dano cerebral causado pelas infecções em fetos e bebês.

2) Segundo os autores, quais danos cerebrais podem ser causados pela infecção por rubéola congênita?

3) Quais similaridades foram apontadas pelos resultados em ambas as pesquisas de Zerbo et al e Becerra-Culqui et al?

4) TODOS os 3 tipos de vírus citados no texto têm em comum:

- (A) São sintomáticos durante a gravidez.
- (B) Podem causar alterações cerebrais e complicações neurológicas.
- (C) Ocorrem nos 3 primeiros meses de gravidez.
- (D) São causas significativas de desenvolvimento de autismo apontadas por todos os pesquisadores.

5) Analise as seguintes afirmativas sobre possíveis tratamentos mencionados no texto:

- I. A vitamina A pode evitar a infecção por rubéola.
- II. A vacina para influenza deve ser evitada por gestantes.
- III. Suplementos são indicados para gestantes com COVID-19.
- IV. A lactoferrina placentária pode ter efeito preventivo na infecção do feto por COVID-19.

São VERDADEIRAS:

- (A) I e III, apenas.
- (B) I, II e IV, apenas.
- (C) II e III, apenas.
- (D) III e IV, apenas.

As questões de 6 a 10 referem-se ao TEXTO 2:

6) Em relação aos termos destacados no 1º parágrafo, é CORRETO afirmar que ambas as ocorrências de

- (A) “since” podem ser substituídas por “seeing that”, sem comprometimento de significado das orações.
- (B) “used” podem ser substituídas por “operated”, sem comprometimento de significado das orações.
- (C) “likely” podem ser substituídas por “possible”, sem comprometimento de significado das orações.
- (D) “by” podem ser substituídas por “for”, sem comprometimento de significado das orações.

7) O que é o efeito “range anxiety” e como ele afeta o mercado de BEVs?

8) Qual estratégia a GM e a Chevrolet têm em comum para superar as limitações dos HEVs?

9) De acordo com as informações constantes no 4º parágrafo, o uso de hidrogênio na indústria automobilística poderá

- (A) ensejar a produção de carros com emissão zero de CO₂.
- (B) ser viável apenas em carros com motores a combustão.
- (C) ter um papel menos relevante em um futuro próximo.
- (D) tornar os veículos elétricos mais baratos e acessíveis.

10) No plano de Boris Johnson para o incentivo ao uso de carros elétricos, estavam incluídos

- I. a criação de novos impostos.
- II. a minoração do problema da poluição do ar em Londres.
- III. a proibição da circulação de táxis antigos em Londres.
- IV. o envolvimento da iniciativa privada.
- V. os veículos oficiais.

Estão CORRETOS os itens:

- (A) I e III, apenas.
- (B) I, III e V, apenas.
- (C) II e IV, apenas.
- (D) II, IV e V, apenas.

RASCUNHO

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CHAVE DE RESPOSTAS

QUESTÃO	
1	<input type="radio"/> (A) <input type="radio"/> (B) <input type="radio"/> (C) <input checked="" type="radio"/>
2	O vírus da rubéola pode invadir e se replicar dentro das células cerebrais. Pode ainda causar lesões vasculares cerebrais, hemorragias e degeneração fulminante das leptomeninges com perda significativa de volume cerebral e destruição da substância branca.
3	Zerbo et al não mostraram associação significativa entre a infecção por influenza e o risco de autismo nos filhos. Entretanto, eles encontraram um risco aumentado estatisticamente não significativo de autismo nos filhos quando as mulheres grávidas receberam a vacinação contra a gripe durante o primeiro trimestre. Ainda assim, eles enfatizaram que essa observação não deve exigir qualquer mudança na política ou prática de vacinação. Becerra-Culqui et al relataram o mesmo achado quando não encontraram associação entre infecção pré-natal por influenza ou vacinação e aumento do risco de autismo nos filhos. Eles recomendam fortemente a vacinação contra a gripe para mulheres grávidas para protegerem a si mesmas e seus descendentes e afirmaram que o tratamento ou a profilaxia contra influenza durante a gravidez não representaram um risco significativo de autismo.
4	<input type="radio"/> (A) <input checked="" type="radio"/> (B) <input type="radio"/> (C) <input type="radio"/> (D)
5	<input type="radio"/> (A) <input type="radio"/> (B) <input type="radio"/> (C) <input checked="" type="radio"/>
6	<input type="radio"/> (A) <input type="radio"/> (B) <input checked="" type="radio"/> (C) <input type="radio"/> (D)
7	Trata-se de uma expressão criada para descrever o medo que motoristas de carros elétricos têm de a bateria subitamente descarregar em um local muito distante de uma instalação elétrica. Esse sentimento resulta em desconfiança desse tipo de veículo e afeta o mercado de BEVs desde o seu lançamento até hoje em dia.
8	As companhias têm em comum a estratégia de produção de EREVs - veículos de emissão zero que dispõem de um sistema de trem de força elétrico baseado em células a combustível de hidrogênio ou de sistemas elétricos a bateria, o que torna esses veículos competitivos em comparação aos carros convencionais no que diz respeito ao desempenho e à facilidade de uso.
9	<input checked="" type="radio"/> (A) <input type="radio"/> (B) <input type="radio"/> (C) <input type="radio"/> (D)
10	<input type="radio"/> (A) <input type="radio"/> (B) <input type="radio"/> (C) <input checked="" type="radio"/>