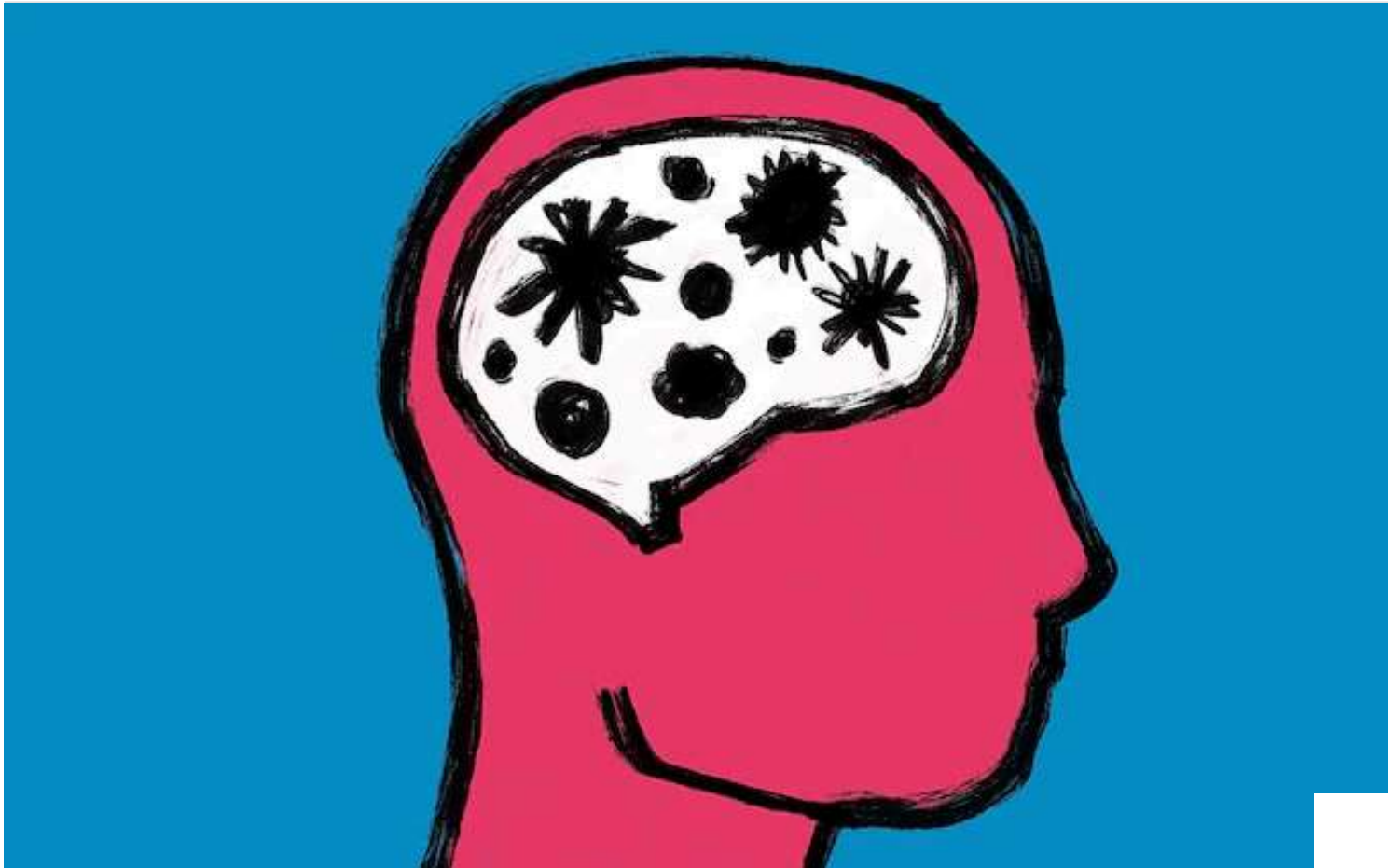


Life



The four viruses linked to autism

A study has found that children who are infected with a common herpes virus in the womb are more likely to be autistic

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As a doctor at a children's hospital in Michigan, Dr Megan Pesch has found herself becoming all too familiar with the damage the infection cytomegalovirus (CMV) can wreak on newborn babies.

Cytomegalovirus (CMV) is a little known but surprisingly common [herpes virus](#). According to the NHS, around one in 200 children in England are born with a so-called congenital CMV infection which they contracted in their mother's womb. Capable of invading the brain, around one in 1,000 children develop some form of lifelong disability because of such an infection, the most common being [hearing loss](#).

Now in a recent [study](#), Dr Pesch has revealed one of the longer-term consequences of congenital CMV infection on the developing brain. Through examining the medical records of more than three million children in the United States stored in Medicaid and Children's Health Insurance Program databases, she found that these children are two and a half times more likely to go on to [develop autism](#).

"CMV is such a brutal virus," says Dr Pesch. "In utero, CMV really attacks and invades the placenta, so it can lead to decreased blood flow and nutrients. It's also really drawn to the foetal central nervous system, so it gets in there and it not only infects those early foetal brain cells but modifies how the brain develops."

Dr Laetitia Davidovic, a research director at the French National Centre for Scientific Research, described the findings as having important public health implications. She says that they point to a need for systematic antibody testing to screen for CMV during pregnancy and around birth.

But CMV is far from the only viral infection to have been implicated in the development of autism.

Which viruses are linked to autism?

Perhaps the most well-known link of all is between rubella and autism. Rubella can lead to various forms of organ dysfunction in the foetus, especially when contracted during the first trimester of pregnancy. The autism rate in children born with a rubella infection is more than [200 times higher](#) than the general population. Like CMV, this has been linked to the fact that rubella can invade and replicate inside foetal brain cells.

Other so-called neurotropic viruses which can invade the brain, like Zika, a tropical virus which spreads through mosquito infection, [have also been implicated](#) as possible risk factors for autism by affecting brain development. Children born to mothers who are HIV-positive

have also been found to be three times more likely to be diagnosed with either autism, developmental delay or [attention disorders](#).

But not all viruses need to even penetrate the brain of the foetus to cause problems. Genital herpes, a sexually transmitted infection which is carried by around 15 per cent of women of childbearing age, has been found to induce the release of inflammatory molecules which alter foetal brain structure, leading to abnormal growth in the cerebral neocortex. The cerebral neocortex comprises around half the brain's total volume and is involved in attention, thought, perception and episodic memory. [One study](#) in Norway showed that male babies born to women who contracted genital herpes from their partner during the first 18 weeks of their pregnancy were twice as likely to be diagnosed with autism.

[Other data](#) has also shown an increased risk of autism, intellectual disabilities and schizophrenia in cases where the mother was hospitalised with influenza during her pregnancy. "This definitely makes you wonder about the link between an inflammatory state and autism in the child, especially for a foetus who might have some genetic propensities toward autism in the first place," says Dr Pesch.

How can viruses affect brain development and function?

In some cases, the presence of viruses like CMV will cause direct injury to the developing brain. "For example, some foetuses with severe congenital CMV infection have severe brain injury from the infection and may not survive the pregnancy," says Dr Sarah Mulkey, a prenatal-neonatal neurologist at Children's National Hospital in the US.

But in other cases, the impact of viruses on the delicate structures of brain cells are perhaps subtler than might be expected. Rather than killing these cells, they merely modify their behaviour, from how they form connections to how they arrange themselves in a precise architecture as the brain grows and expands. Dr Pesch says that many of the changes are not always visible on brain imaging scans.

Dr Pesch says that CMV is also capable of regulating certain genes so that the brain doesn't acquire its characteristic folds. This results in developmental delay as the brain has a smaller surface area and so fewer cells.

"There is a gene that CMV can suppress in the foetal brain and when you knock out that gene, it can sometimes result in a really smooth brain," she says. "So CMV does change how brains form."

Another possibility is that some congenital viral infections could affect the microbiome of the developing baby, which in turn impacts the brain through [the gut-brain axis](#); the many

communication networks which link the brain to our intestines. At a recent conference, Mark Schleiss, a paediatrics professor at the University of Minnesota, presented findings showing alterations in [the gut microbiome](#) of babies with CMV.

How inflammation and the immune system impacts the baby

But we now know that a virus doesn't even need to directly infect the foetal brain to cause disruption. One of the reasons why autism rates are higher in the children of pregnant women who have been hospitalised with an infection is because severe infections can unleash widespread inflammation in the mother's body, something known as a cytokine storm.

When the mother's immune system is generating high rates of inflammatory molecules called cytokines, these molecules can reach the brains of unborn babies and initiate abnormal brain development. For the same reason, pregnant women with autoimmune conditions such as Sjögren's syndrome and rheumatoid arthritis, [are thought](#) to be more likely to have autistic children.

The reason why chronic viral infections, such as HIV and genital herpes, are linked to autism is also related to the immune system, but in a very different way. Just as our immune system produces antibodies which attack foreign infections, we now know that when it goes awry, it can also produce autoantibodies which attack the body's own tissues.

Between [10 and 12](#) per cent of mothers of children with autism have been found to have autoantibodies. One theory is that viruses which have embedded themselves deep within the DNA, such as [HIV](#) and herpes, can overstimulate the immune system in a way that stimulates the production of autoantibodies, which then attack the developing foetus.

“Viral infections can activate the maternal immune system, causing it to produce autoantibodies,” Dr Pesch says. “They might cross the placenta and target the developing foetal brain.”

What can you do?

Dr Davidovic says that these emerging findings really highlight the need to ensure that all pregnant women are vaccinated against common viral infections like influenza and rubella – with the goal of reducing the risk of autism and other neurodevelopmental disorders. She also points to the need for education on the importance of good hygiene measures to prevent CMV exposure, such as regular hand washing and not sharing drinks during pregnancy (as CMV is carried in body fluids like saliva and urine).

Dr Pesch's findings have also reinforced the importance of developing a vaccine for CMV, something which may become a reality in the near future – as Pfizer and Moderna, among others, are believed to be working on a jab against the virus.

For pregnant women infected with genital herpes, doctors advise taking antiviral medication to reduce the chances of the baby being affected. While for those who are HIV positive, antiretrovirals are vital.

Dr Blake Turner, a psychiatric epidemiologist at Columbia University agrees that, in theory, vaccines against common pregnancy infections could greatly reduce autism rates. Given the complexity of autism and other contributing factors, which also include genetics and possible dietary and environmental factors, it may not be quite so straightforward.

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“The results of a study we did suggests that elimination of maternal infections during pregnancy would have a large effect on the incidence of autism, mostly because of how common these infections are,” he says. “But vaccines and antivirals may have their own effects [on the developing foetus]. That would be important to study.”

Dr Pesch is hopeful that her results will lead to greater awareness among both healthcare providers and the public about the potential risks of maternal infections, and ultimately perhaps better monitoring and screening of pregnant women.

Given the many connections between the gut and the brain, and the possibility that these infections may initiate brain developmental changes through disrupting the microbiome, Dr Pesch has begun recommending giving probiotics to toddlers as a possible mitigating strategy, albeit one which isn't really evidence-based. “It's just a shot in the dark,” she says. “But it certainly won't hurt.”

‘My autistic daughter was born with a CMV infection’

Dr Megan Pesch was in the middle of investigating the possible connection between CMV and autism when her three-year-old daughter [was diagnosed as being autistic](#).

“I had suspected it,” she says. “It was Covid time, so she wasn’t going to nursery, but around two-and-a-half, she started being a little less engaged with faces. She wouldn’t check in with me quite as much, and she was really focused on doing her own thing.”



Dr Pesch only found out that her daughter had been infected with CMV after doctors discovered that she was deaf at the age of three months

There was a certain irony to the diagnosis, which arrived at a time when Dr Pesch was putting together the results of her analysis. Unlike her other two children, her daughter had been born with a CMV infection. She had been inspired to launch the study through her work at a paediatric clinic, where she had seen many other children suffering the long-term effects of congenital CMV.

Dr Pesch only found out that her daughter had been infected after doctors discovered that she was deaf at the age of three months. “I asked if she had CMV and they said it was unlikely,” she says. “I requested a test anyway, but they didn’t know how to test her. She’d had the heel prick newborn screening test done, and they still had some of the dried blood left over. I asked them to send it to the University of Washington for testing and they found CMV in it. So we are lucky that she got a CMV diagnosis at all. Most babies are missed.”



Dr Pesch's daughter has a strong connection to her baby doll stroller and likes to take it everywhere

Initially, she did not notice any signs of developmental issues, apart from language delay. “That was understandable as she didn’t have any access to sounds,” says Dr Pesch. “But as she’s gotten older, her autistic features, such as not loving eye contact, and her passion for certain special topics and items, have become more obvious.”

In particular, she says that her daughter is fixated on her baby carriage for her doll, something which “goes absolutely everywhere.” While this might sound very similar to the

interests of other toddlers, particularly girls, Dr Pesch says that her daughter takes it to a more intense level.

“She feels so strongly and passionately about it,” she says. “That stroller comes absolutely everywhere with us, and if you say, “No, we can’t bring it into the grocery store or through security onto the plane,” she gets so upset. It’s almost like she’s been morally injured. It’s very hard for her to understand why she can’t do something she feels so strongly and passionately about. But it’s also very charming, if atypical.”

While Dr Pesch recommends [probiotics](#) to other parents with toddlers, she’s chosen not to give them to her daughter, deciding to accept and embrace her differences.

“We feel like her autism is part of who she is, just as with her deafness,” she says. “I think when it’s a family with infants who were born with congenital CMV and who are not [yet] displaying any risk factors for autism, it’s something where I think, maybe you could try this. As an autism researcher, I think I would have tried it if someone had suggested it to me when she was a toddler, but now she is who she is, and we’re just on that journey with her.”

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