NEWS

Newborn blood may reveal early immune signs of autism

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Blood spots: Samples taken at birth suggest that the immune system is dampened overall in children later diagnosed with autism.

Children diagnosed with autism tend to have low blood levels of several immune molecules at birth, according to an epidemiological study published in August in the *Journal of Immunology*[1].

Studies have found **differences in the immunological profiles** of children and adults with autism, as well as in the mothers of children with autism during pregnancy, but only a **handful of studies** have examined this issue in newborns.

“There’s something altered about the immune status of these offspring that’s different from [that of typical] children,” says **Paul Patterson**, professor of biology at the California Institute of Technology, who was not involved in the study.

Similar changes, when observed in children and adults with autism, could be attributed to differences in experiences or stress levels, he says. “What’s important about the newborns is they don’t have any life experience yet.”

The researchers measured levels of cell signaling molecules called cytokines in dried blood

samples taken at birth from 359 people later diagnosed with autism and 741 controls. The samples are from heel pricks conducted during routine newborn screening in Denmark between 1982 and 2000.

“The advantage of using the Scandinavian system, where you have everything registered in a central biobank, is that these samples are collected routinely,” says lead investigator **Morsi Abdallah**, a researcher at Statens Serum Institute and Aarhus University-Health in Denmark.

The researchers measured the levels of 16 cytokines in the samples and found that 9 of them are at about half the levels in children later diagnosed with autism compared with controls. The children with autism tended to have lower levels at birth of both T helper 1 (Th-1) cytokines, which promote inflammation, and Th-2 cytokines, which quell it.

The results together suggest that the immune system in these children is dampened overall, says Abdallah. The study is the first to suggest that, early in life, children with the disorder have “a hypoimmune pattern,” he says.

A study by the same group of researchers published in early October hinted at low amounts of three nerve growth factors in neonatal bloodspots from children with autism compared with controls. The finding may point to impairment in the brain’s ability to adapt to new information[2].

Up or down:

Researchers don’t yet have a clear picture of the immune system’s role in autism. Some studies have found that people diagnosed with autism have **elevated or reduced levels** of various immune molecules. Mouse studies support the role of immune system dysregulation in autism[3], and some hint that disrupted levels of **cytokines** and **antibodies** may affect behavior.

The new results follow up on the group’s previous work on samples from the same biobank, published last year. That study found **raised cytokine levels in the amniotic fluid** of women whose babies were later diagnosed with autism. “During pregnancy, the picture is totally the opposite,” says Abdallah. The new study relies on blood samples from many of the same individuals with autism.

Patterson and others laud the Danish study’s large sample size, but warn that the findings should be interpreted with caution.

One key caveat, noted in the paper, is that the blood spots were collected at least ten years ago. “[Cytokines] are very small molecules that are susceptible to degradation,” says **Carlos Pardo-Villamizar**, associate professor of neurology and pathology and Johns Hopkins University in Baltimore, who was not involved in the study.

The researchers attempted to control for the degradation by matching the samples from children with autism with control samples taken the same year.

Pardo-Villamizar says it's also unclear whether the findings suggest an under-active immune system. "The immune system doesn't work with units; it works with pathways and interactions between molecules," he says. "So the fact that some molecules are down doesn't mean the immune system is down." Using blood spots as a measure of a baby's immunological activity also requires validation, he adds.

Another potential for noise in the data is how long after birth a heel prick is done, which can depend on birth complications and labor time, says **Judy Van de Water**, professor of clinical immunology at the University of California, Davis, who was not involved in the study.

"That's probably the single biggest factor that changes what the immune profile would look like," she says. "The minute you hit the pavement when you're born, your immune system is exposed to things and starts being activated and developing."

Still another concern is diagnosis. The study relied on diagnostic information in old files. Because Denmark changed its definition of autism after 1993, some individuals in the control sample may have later met the criteria for the disorder.

The association between the disorder and cytokine level is complex and subtle, says Van de Water, who is conducting a similar study on blood spots from newborns in California. "We see a difference [in cytokines] between full autism and those that are just on the spectrum."

Abdallah's next study may address this concern. He and his colleagues are planning to examine blood spots from a different Danish cohort of 400 children. In this study, child psychologists will first validate the diagnosis based on clinical information from the children's medical records.

The researchers also plan to examine *in utero* and newborn levels of vitamins including **vitamin D**, which has been implicated in autism, and **oxidative stress**, which might reflect protection from inflammatory triggers, Abdallah says.

Epidemiological studies such as this one don't provide insight into mechanisms that might explain the proposed link between immunological factors and autism — for that, researchers must look to animal models. "This kind of work is really only getting started," says Van de Water.

References:

1: Abdallah M.W.*et al. J. Neuroimmunol.* **252**, 75-82 (2012) **PubMed**

2: Abdallah M.W. *et al. Acta Psychiatr. Scand.* Epub ahead of print (2012) **PubMed**

3: Garay P.A. *et al. Brain Behav. Immun.* Epub ahead of print (2012) **PubMed**