

Looking on the brighter side of childhood asthma

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Credit: Pavel Losevsky / fotolia.com

The effect of a widespread genetic variant that increases the risk for childhood asthma can be neutralized. A new study shows that young infants are particularly responsive to the positive influence of exposure to farm dust.

Asthma researchers from Ludwig-Maximilians-Universitaet (LMU) in Munich have shown, for the first time, that specific environmental

influences can neutralize the effect of a prevalent genetic variant that increases risk for childhood asthma. The new study shows that carriers of this particular variant are also especially responsive to environmental factors that confer long-term protection against asthma. Bearers of the risk variant who had been exposed to airborne micro-organisms in animal sheds on farms before their first birthday were found to be significantly less likely to show symptoms of infections of the lower respiratory tract than were carriers who had had no contact with farm animals in early life. "We can conclude from this observation that these children are also less likely to develop asthma later on than carriers who did not benefit from the 'farm effect,'" says LMU's Markus Ege, Professor of Pulmonary Epidemiology at Dr. von Hauner's Children's Hospital. Ege, together with Professor Erika von Mutius (Director of the Outpatient Clinic for Asthma and Allergy at the same hospital), first author Dr. Georg Loss (a member of the von Mutius research group) and an international team of co-authors report their findings in the *American Journal of Respiratory and Critical Care Medicine*.

In the new paper, the LMU researchers report the results of their analysis of data obtained in the course of the long-term epidemiological study "Pasture". The data were drawn from weekly diaries, in which almost 1000 mothers, recruited for the project and resident in predominantly rural regions, recorded details of the early development of her children from birth up until the age of 6. Among other things, these diaries contained information on the incidence of respiratory illnesses and noted how much time the children spent in stables, cowsheds, pigsties and poultry yards. The researchers focused on the data relating to the frequency of infections of the lower respiratory tract. These are usually caused by viruses and result in telltale symptoms that include wheezing. When the researchers focused on those children who carried a known risk variant for asthma, located in region q21 on chromosome 17, they made a remarkable discovery: Carriers of the variant who had been exposed as infants for at least 2 hours per week to

the air in animal sheds showed an 80% reduction in the incidence of wheeze, relative to carriers reared in non-farm settings. "It turns out that this risk genotype is especially responsive to protective environmental influences," says Markus Ege.

Better able to fight infection

These findings argue that farm children who are regularly brought into animal sheds before they are weaned can cope more effectively with viral infections than other kids. Based on the analysis of other variables, such as the incidence of viral illnesses in older siblings, the researchers deduced that the infants are exposed to the same infection risk as children reared in non-agricultural environments. "But they react differently to infection and show no overt symptoms of acute illness," says Georg Loss. The data gathered in the course of the "Pasture" study give researchers a unique opportunity to observe the development of these children over a period of several years. As a result, they were also able to confirm that carriers of the risk variant who displayed no symptoms of infection of the [lower respiratory tract](#) during their first year of life also have a lower risk of developing asthma later on. "The protective effect of the appropriate environment is so strong that it effectively neutralizes the normally deleterious influence of the risk variant. It's as if these children didn't have the genetic variant at all," says Ege.

Children who regularly play in close contact with farm animals inhale minute particles of hay and grass. These carry with them a complex mixture of micro-organisms – bacterial and fungal cells and spores – and pollen grains into the airways. When these come into contact with the respiratory epithelium lining the airways, "the micro-organisms evidently modulate the course of the inflammatory response in the body," says Loss. The researchers' ultimate goal is to identify precisely what triggers the so-called farm effect, as this would make it possible to develop

active strategies to inhibit the development of asthma. The genetic variant on chromosome 17, which is one of several that are known to increase susceptibility to [childhood asthma](#), is not at all rare. "Actually some 75% of the population carry this variant and are at increased risk of developing [asthma](#). We assume that these carriers would benefit from the farm effect if exposed to it in very early childhood," says Ege.

More information: Georg J Loss et al. The Early Development of Wheeze: Environmental Determinants and Genetic Susceptibility at 17q21, *American Journal of Respiratory and Critical Care Medicine* (2015). [DOI: 10.1164/rccm.201507-1493OC](https://doi.org/10.1164/rccm.201507-1493OC)

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