that basal mLVs provide the main route for macromolecule uptake and for drainage of CSF and interstitial fluid from the brain directly into the peripheral lymphatic system.

The flow in lymphatic vessels that carry fluid drained from the CSF to lymph nodes in the periphery was previously reported to be slower in older compared with younger mice[7], and such a decline in drainage function might have implications for age-related neurological diseases[1,2,5]. The authors therefore compared basal and dorsal mLVs in young mice (3 months old) with those in aged mice (24–27 months old). Whereas dorsal mLVs in aged mice showed deterioration, basal mLVs in aged mice were enlarged and more numerous. The basal mLVs in older mice also had fewer luminal valves compared with younger mice, and the junctions between the endothelial cells that form the vessel walls in older mice showed signs of disintegration. The authors confirmed that these age-related changes in basal-mLV morphology correlated with reductions in the drainage of macromolecules from the CSF in the aged mice.

A decline in mLV function has been suggested to lead to a build-up of proteins in the brain and to contribute to cognitive deficits and brain pathology in Alzheimer's disease[5]. One way of counteracting age-dependent reductions in drainage function might be to stimulate mLV growth and to increase the diameter of mLVs. The endothelial cells that compose the mLVs in adult mice express the receptor VEGFR3, which is activated by the growth factor VEGF-C, and treating adult mice with VEGF-C induces growth and widening of mLVs[4,9]. The authors used a genetic manipulation to remove VEGFR3 from all lymphatic vessels, including mLVs, in adult mice. This approach revealed that, consistent with previous findings[9], when VEGF-C signalling is lost, dorsal mLVs deteriorate more rapidly than do basal mLVs. However, it remains unclear whether VEGF-C–VEGFR3 signalling is affected in ageing and whether it could be targeted to counteract the observed ageing-associated changes in mLV function.

Besides clearing CNS macromolecules, mLVs also drain immune cells to lymph nodes[4,6], where immune responses are initiated. Indeed, dorsal mLVs were previously identified on the basis that they contained immune cells[4], and Ahn *et al.* also observed such cells in the basal mLVs. A previous study[6] showed that disrupting dorsal mLVs attenuated inflammatory responses in a mouse model of the neurological disorder multiple sclerosis, indicating that mLVs might have a role in neuroinflammatory diseases. Future experiments should investigate whether, independently of their drainage function, mLVs might also promote immune tolerance (that is, a dampening of immune responses to recognized substances), as do the lymphatic vessels in lymph nodes[10].

We still need a better understanding of the mechanisms that enable entry of fluid to the basal mLVs and of how mLVs cooperate with the other systems that clear waste from the CNS. Nevertheless, the identification of the precise exit routes for fluids leaving the brain is a crucial step towards understanding how waste is cleared from the CNS. This finding might eventually enable the development of therapies that promote CNS drainage to combat pathological processes in neurological diseases. ■

**Taija Mäkinen** *is in the Department of Immunology, Genetics and Pathology, Uppsala University, 751 85 Uppsala, Sweden.*
*e-mail: taija.makinen@igp.uu.se*

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CLIMATE SCIENCE

# Weak sensitivity of cloud water to aerosols

**Human activities produce tiny airborne particles called aerosols. The discovery that the average impact of these aerosols on the water content of low-level clouds is minimal will lead to more-reliable models of future climate.** **See Article p.51**

ANNA POSSNER

Ever since humans first harnessed fire, we have emitted microscopic particles called aerosols into the atmosphere. These particles remain suspended in the air and alter the amount of sunlight that reaches Earth's surface. Low-level clouds efficiently cool the planet by reflecting sunlight back into space and are readily exposed to human-made aerosols. Such particles can change the reflectance of clouds, and the associated cooling, by modifying the size of droplets[1] or the amount of water[2] in the clouds. On page 51, Toll *et al.*[3] provide compelling evidence that human-made aerosols cause a weak average decrease in cloud water content compared with unpolluted clouds. This result provides an important constraint on the overall cooling effect of aerosol emissions and reduces one of the key uncertainties in climate science.

Earth's global mean temperature is governed

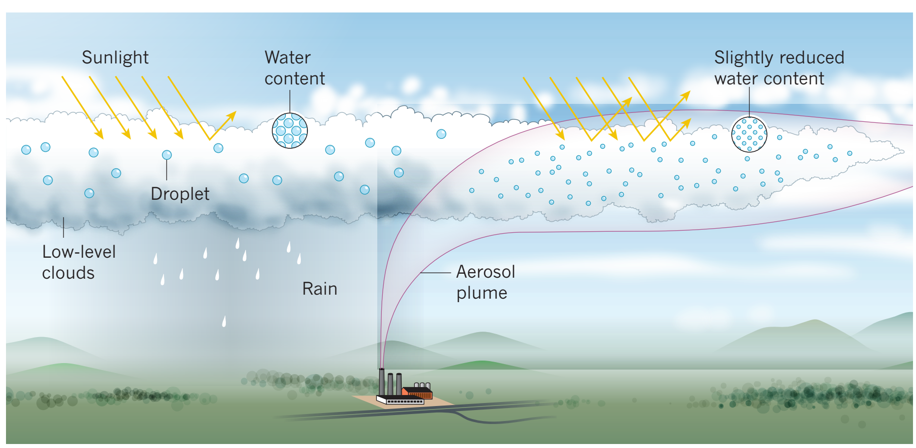


**Figure 1 | Impact of human-made aerosols on low-level clouds.** Microscopic particles called aerosols are released into the atmosphere by human activity; an aerosol plume from a factory is shown here. Low-level clouds that form in the presence of these particles contain droplets that are smaller and more numerous than usual. As a result, these clouds reflect more sunlight, and have a greater cooling effect on Earth, than do unpolluted clouds. Toll *et al.*[3] show that human-made aerosols also lead to a weak average reduction in cloud water content (and therefore in the frequency of rain) compared with unpolluted clouds. This effect slightly reduces the overall aerosol-induced increase in cloud reflectance.

by the interplay of competing warming and cooling processes. Since 1850, there has been a net warming owing to greenhouse-gas emissions from human activity[4]. Over this time, the global mean temperature has increased[5] by 0.9 °C, although the warming caused by greenhouse-gas emissions has been partially compensated for by the cooling effect of aerosol emissions. Therefore, a precise quantification of this cooling could have profound implications for projections of future climate.

Clouds that form in the presence of high aerosol concentrations contain droplets that are smaller and more numerous than usual (Fig. 1). These droplets therefore have a large total surface area for sunlight to bounce off. Consequently, the reflectance of polluted clouds is greater than that of unpolluted ones[1]. As a result of the aerosol emissions of the early twenty-first century, as opposed to pre-industrial conditions, this enhanced reflectance generates a substantial cooling effect on Earth's climate[6].

Whether cloud reflectance is increased or decreased by changes in water content, and to what extent, has been highly uncertain. A greater water content in polluted clouds than in unpolluted ones could enhance the net cooling effect of aerosol emissions[2]. This possibility is suggested by many global climate models[7]. Some scientists have argued that the increase in cloud water content, and the associated cooling effect, caused by aerosols might be even larger than these models indicate[8]. By contrast, other evidence suggests that there could be considerably less water in polluted clouds than in unpolluted ones, which would reduce the net cooling effect substantially[9].

To address this uncertainty, Toll and colleagues looked at features of polluted clouds called pollution tracks (see Fig. 1 of the paper[3]). These features were produced downwind of sources of human-made aerosols such as coal-fired power plants, oil refineries, smelters, cities, ships and wildfires. Like the cloud trails that form behind aircraft at high altitudes, these pollution tracks in low-level clouds are visible from space. As a result, polluted and less polluted cloudy regions can be clearly distinguished. Observed changes in droplet size or cloud water content can, therefore, be unequivocally attributed to variations in aerosol concentrations.

Using 15 years of high-resolution satellite data of near-global coverage, the authors built an unprecedented database of thousands of such tracks across Earth's climate zones. Overall, they found that the average droplet size was at least 30% lower in polluted clouds than in unpolluted ones. Although differences in cloud water content varied, the mean water content was slightly lower in polluted clouds than in unpolluted ones (Fig. 1). This finding suggests that the effect of aerosols on cloud water content slightly reduces the overall aerosol-induced increase in cloud reflectance.

Toll *et al.* then extrapolated their findings to all low-level clouds across Earth, considering global changes in aerosol emissions from human activity. They estimate that the identified decrease in cloud water content offsets only 23% of the net cooling effect caused by the reduction in droplet size. However, the precise estimate remains uncertain. Although the authors sampled thousands of pollution tracks, these features are scarce. For example, it is extremely rare for a ship to leave a pollution track in its wake[10], and probabilities of track generation for the other sources of human-made aerosols are likely to be similarly low. This rarity raises the question of whether observations made using pollution tracks can be generalized to all other conditions in which pollution tracks are not seen.

The most common hypothetical situations in which pollution tracks are not identified are: when clouds are already bright, so that added aerosols have no impact on reflectance; and when cloud properties are rapidly varying because of changes in humidity, stability or horizontal winds. The aerosol-induced decrease in cloud water content might therefore be smaller or larger than is estimated from pollution tracks. However, there is no a priori reason for the clouds to respond in a fundamentally different manner in conditions in which pollution tracks are not observed. Toll and colleagues' work therefore strongly suggests that the sensitivity of cloud water content to changes in the concentration of human-made aerosols might not be accurate in many current global climate models, and that large cooling effects caused by variations in cloud water content are unlikely. ■

**Anna Possner** *is at the Institute for Atmospheric and Environmental Sciences, Goethe University, 60438 Frankfurt, Germany.*
*e-mail: apossner@iau.uni-frankfurt.de*

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MEDICAL RESEARCH

# Deep learning detects impending organ injury

**Organ damage is often detected late, when treatment options are limited. The use of artificial intelligence to continuously monitor a patient's medical data can identify people at risk of imminent kidney injury.** **See Letter p.116**

ERIC J. TOPOL

Acute injury to the kidneys occurs in one in five patients in US hospitals[1]. It is a common condition in hospital patients because it can be caused by a number of factors, including abnormal blood pressure or blood volume. But the ability to predict whether or when acute kidney injury will happen is limited. For people who are at high risk of developing this condition, the standard clinical approach is daily assessment of their laboratory test results, including the concentration of creatinine in their blood, because high levels of this molecule are a hallmark of kidney problems.

Tomašev *et al.*[2] report on page 116 that an approach involving artificial intelligence makes it possible to identify impending acute kidney injury, for most patients, one or two days before the condition would be diagnosed using standard clinical tests. Kidney injury is usually spotted only at a late stage, when irreversible damage has occurred that could lead to death or the need for temporary or long-term dialysis. Being able to catch the condition early would be a major step forward in enabling effective treatment.

In the artificial-intelligence method known as deep learning, an algorithm is developed to identify patterns in the data that are associated with an outcome of interest — in this case, the development of acute kidney injury. The authors used this approach on data collected between 2011 and 2015 from more than 700,000 adults treated in 172 hospitals and 1,062 outpatient clinics run by the US Department of Veterans Affairs — a health-care provider for military workers and their families. The anonymized information