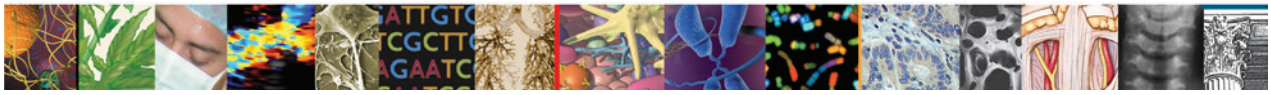

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Perspective

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The Case of *Juliana v. U.S.* — Children and the Health Burdens of Climate Change

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On June 4, 2019, the Ninth Circuit Court of Appeals will hear oral arguments in *Juliana v. United States* to determine whether the case will proceed to trial in district court in Oregon.

Nearly 4 years ago, 21 children and adolescents between 8 and 19 years of age, including Kelsey Juliana from Oregon, filed suit against the federal government, charging that the government's inaction on addressing climate change violated their constitutional right to life, liberty, and property.[1] To date, no such lawsuit against the federal government has succeeded in the United States, despite a sharp increase in the number of similar suits filed by young people, municipalities, and state governments. Indeed, none of these lawsuits has gone to trial.

As the *Juliana* plaintiffs argue — and we agree — climate change is the greatest public health emergency of our time and is particularly harmful to fetuses, infants, children, and adolescents.[2,3] The adverse effects of continued emissions of carbon dioxide and fossil-fuel–related pollutants threaten children's right to a healthy existence in a safe, stable environment. It is for this reason that we, together with nearly 80 scientists and physicians and 15 health organizations including the American Academy of Pediatrics, submitted an amicus brief to help educate the Ninth Circuit about this extraordinary threat.[4] More frequent and longer heat waves, increasing intensity of extreme weather events such as droughts and wildfires, worsening infectious-disease exposures, food and water insecurity, and air pollution from fossil-fuel burning all threaten to destabilize our public health and health care infrastructure.[3]

Developing fetuses, infants, and children are more biologically and psychologically vulnerable than adults to the effects of climate change and to exposure to particulate matter and air pollutants that are emitted during the production and combustion of fossil fuels.[4] Their increased susceptibility is a product of their ongoing developmental processes and growth; underdeveloped systems for temperature regulation, immune responses, and detoxification; and inability to care for themselves. The World Health Organization has estimated that 88% of the global health burden of climate change now falls on children less than 5 years of age.[4]

Exposure to extreme heat in utero is associated with an increased risk of pregnancy complications and birth defects.[4] Climate-sensitive infections are on the rise because of the spread of vectors, such as the *Aedes aegypti* mosquito that transmits Zika virus. The 2015–2016 Zika outbreak in the

United States was linked to a 21% increase in birth defects in affected regions.[4] The combustion of coal at power plants produces mercury, a known potent neurotoxin for fetuses that can lead to reduced cognitive ability and motor function even at low levels of exposure.[4] Infants are especially vulnerable to the effects of heat in the first week of life, and one study found that infant mortality increased by 25% on extremely hot days.[4]

As children grow into toddlers and begin school, their developing organs remain vulnerable to insults.[4] Their higher respiratory rates and increased outdoor exposure as compared with adults make children especially susceptible to air pollution, including particulate matter from fossil-fuel combustion and ozone, which forms more rapidly at higher temperatures. Exposure to air pollutants has been linked to increased mortality, school absenteeism, asthma-related emergency department (ED) visits and admissions, and cognitive and behavioral effects.[4] Early-life exposure to such pollutants increases a child's likelihood of developing asthma and of having diminished lung function as a teenager.

Some health risks associated with climate change vary depending on geographic region or socioeconomic status. For example, children in the western United States are facing more days of wildfire smoke exposure, which increases rates of hospitalizations for asthma exacerbations.[4] Children between 5 and 9 years of age have the highest incidence of Lyme disease, the most common tickborne disease, and exposures are being documented in an increasing number of regions.[4] Children of lower socioeconomic status are more likely to be heavily exposed to air pollution and are anticipated to be more affected by the reduced nutritional content of crops and by water insecurity than children from wealthier families.[4] As for older children, heat-related exertional injuries disproportionally affect teenage athletes, and ED visits for such injuries increased by 134% between 1997 and 2006.[4]

Today's children are expected to have poorer health as they age than today's adults do, because of the worsening and intensifying effects of climate change. We have only scratched the surface in terms of our understanding of the range of health harms associated with climate change and related increases in air pollution over the lifetime of a child born in the past decade or two. For example, recent studies revealed early associations between extreme heat and increasing antibiotic resistance, worsening mental health, and impaired cognitive function.[4] These adverse health effects may be further exacerbated by climate-change–related destabilization of U.S. health care infrastructure, as illustrated by the intravenous saline shortage that occurred after Hurricane Maria.

Finally, there is evidence that the mental health effects experienced by children today may have a long-lasting impact that extends to future generations. Among the 200,000 children who were displaced because of Hurricane Katrina, 50% of preschool-aged children and 71% of middle school–aged children met the criteria for post-traumatic stress disorder.[4] Severe storms and other extreme weather events related to climate change will substantially increase toxic stress, which not only impairs children's healthy development but can alter gene expression and therefore result in changes that are passed on to future generations.[5]

The failure of the federal government to reduce the United States' reliance on fossil fuels and reduce emissions of greenhouse gases and other dangerous pollutants has put our children in danger. We believe this failure represents a breach of our collective responsibility to our children. Young people are entitled to a safe and healthy environment in which to grow, bear children, and live to an old age. As evidenced by *Juliana*, children are becoming increasingly vocal about the adverse health effects of climate change on them and on future generations.

Courts in the Netherlands and Colombia have recently recognized the fundamental rights of children to demand that their governments reduce greenhouse-gas emissions. We hope the Ninth Circuit will at least allow Juliana and the other plaintiffs their day in court. They, and the rest of the country, deserve to hear the expert environmental and health testimony that would be presented during a trial.

Regardless of the outcome of this case, we believe the medical and public health community should recognize, acknowledge, and speak out about the health burdens of climate change and their disproportionate effects on children. As scientists, physicians, and residents of the United States, we owe all children a duty of trust and care.

Disclosure forms provided by the authors are available at NEJM.org.

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A Temporizing Solution to "Artemisinin Resistance"

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Antimalarial drug resistance has arisen frequently in the past, causing familiar treatment regimens to fail, with sometimes devastating consequences. Resistance has eventually been managed when new treatments have been developed, but drug discovery is a painstaking process that takes decades of effort and considerable investment.

Despite successes of malaria-eradication campaigns launched by the World Health Organization in the 1950s, the emergence of drug-resistant parasites in many malaria-endemic areas resulted in failures of response to inexpensive drugs such as chloroquine. These failures stimulated investments in drug-discovery programs, including a national project set up by the Chinese government to consolidate its research resources. The dedication of hundreds of scientists and decades-long efforts (as part of Project 523) led to our discovery of artemisinins.

Artemisinin derivatives, used in carefully developed combinations, have since served as the first-line drugs against most uncomplicated malaria infections. Artemisinins are combined with other drugs so that the fast-acting artemisinin can immediately reduce parasitemia, allowing remaining parasites to be removed by a long-acting partner drug. Monotherapy with the artemisinin compound artesunate is used for initial management of severe disease. In geographic areas where artemisinin combinations work, there is no need to modify treatments.

A slowdown in the clearance of parasites in patients treated with artesunate sounded alarms when it was first reported from Cambodia. Subsequently, similar delays in parasite clearance were noted in countries in Asian territories, including Myanmar, Thailand, Laos, and China, collectively referred to as the Greater Mekong Subregion.[1] It was determined that parasites that were cleared more slowly after artemisinin treatment carried mutations in the propeller domain of the malarial *kelch13* (*K13*) gene. Although *K13* mutations are not reliably associated with increased risk of treatment failure, parasites bearing these mutations are now called "artemisinin-resistant." Phenotypically, "artemisinin resistance" is defined as a delay in parasite clearance. These parasites recrudesce more frequently than artemisinin-sensitive parasites after standard 3-day therapeutic courses with artemisinin combination treatments (ACTs).

However, 3-day courses do not contain the full treatment doses of artemisinins needed to cure infections, which last 7 to 10 days, according clinical studies conducted in China. When a 7-day treatment course of artesunate is used, it is effective even when early parasite clearance is delayed.[2] The same is not true of resistance to other classes of antimalarials, which results in a failure to cure the infection after a full treatment course.

Should a delay in parasite clearance with artemisinin treatments be defined as drug "resistance" or "tolerance"? Either way, 3-day therapeutic courses are losing their efficacy against malarial parasites in the Greater Mekong Subregion. So what matters most to patients and populations at risk is how we handle this emerging threat.

We propose that the continued rational and strategic use of ACTs is the best, and possibly the only, solution to treatment failures for the foreseeable future. This proposition is based on two considerations related to artemisinins and their contribution to successful antimalarial therapies.

The first consideration is that current artemisinin resistance continues to manifest as delayed parasite clearance with no evidence of full resistance phenotypes. Artemisinins remain effective, even if they require a longer treatment