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Taking the Heat: Potential Fetal Health Effects of Hot Temperatures

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Exposure to periods of extreme heat has been linked to a variety of adverse health outcomes, including cardiovascular disease, respiratory diseases, kidney disease, and mental illness.[1,2] Now researchers are investigating the potential effects of heat exposure in the fetus.

Several epidemiological studies over the past five years have reported associations between high temperatures and adverse pregnancy outcomes, including preterm birth, stillbirth, and low birth weight (LBW),[3,4] as well as congenital heart defects.[5] (At least two studies have also examined ambient temperature in relation to neural tube defects.[6,7]) Each study has its strengths, weaknesses, and caveats, but experts point toward the consistent and concerning signal that's starting to materialize in the literature.

"When more and more studies start to pile up and coalesce around the same conclusion, we have to pay attention, especially when there's biological plausibility behind the outcome," says Nathaniel DeNicola, an obstetrician–gynecologist at the George Washington University Hospital in Washington, DC, and environmental health expert for the American College of Obstetricians and Gynecologists.

Although this area of research is relatively new, obstetricians have long known that natural gestational changes in thermoregulation can make pregnant women vulnerable to heat exposure.[3,8] Weight gained during pregnancy lowers the ratio of body surface area to body mass, which may make it harder for pregnant women to dissipate internal heat.[9] The metabolic demands of the growing fetus may create heat, leading to a slight increase in a pregnant woman's core body temperature.[9] Pregnant women are also more susceptible to dehydration, which in the late stages of pregnancy could trigger uterine contractions and, potentially, early labor.[10]

However, beyond these basic physiological changes, exactly how maternal heat exposure might contribute to birth defects or adverse obstetrical outcomes is not yet clear. The mechanism would likely differ for different outcomes, say researchers.

Animal studies suggest that heat exposure during early pregnancy could interfere with normal protein synthesis through the

Taken together, a growing body of evidence hints at a spectrum of heat-related vulnerabilities across pregnancy. Some studies have suggested that heat exposures in the first trimester, when the major organs form, could contribute to certain birth defects, whereas exposure in the second or third trimester, when the fetus undergoes rapid growth, may contribute to preterm birth or stillbirth. Heat exposure throughout pregnancy may contribute to low birth weight. Image: © iStockphoto/lemonadelucy.

production of heat-shock proteins.[11] Disrupting protein homeostasis could lead to fetal cell damage, potentially altering fetal development.[5] Previous research in the general (nonpregnant) population shows that circulating levels of markers of inflammation and oxidative stress are associated with ambient temperatures.[12,13,14,15] If temperature were similarly linked to inflammation and oxidative stress in pregnant women, these changes could potentially decrease uterine and placental–fetal blood flow, which ultimately could slow fetal growth and lead to LBW.[16]

Preterm Birth and LBW

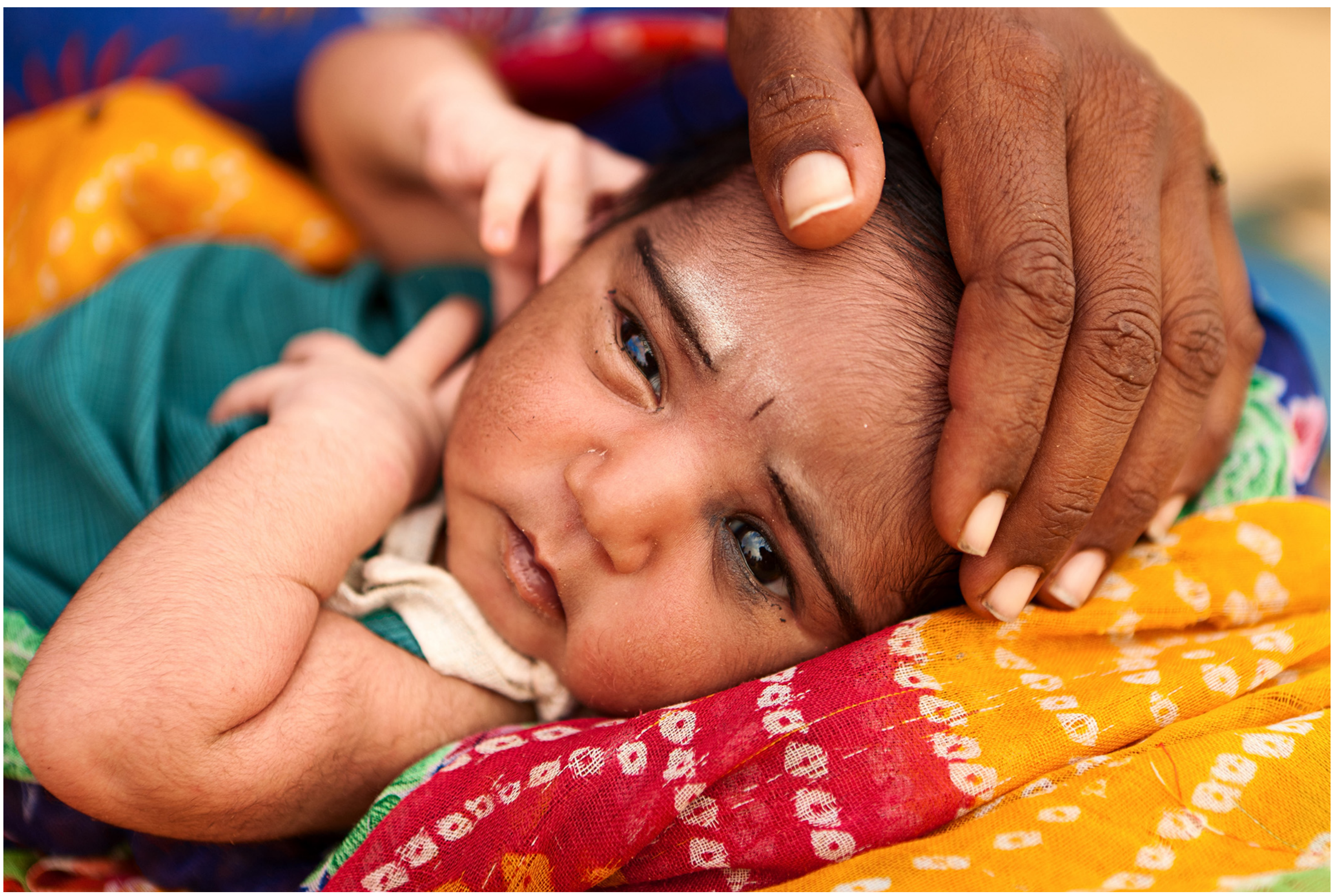
Epidemiological studies investigating the relationship between ambient temperature and preterm birth (before 37 weeks' gestation) or LBW (less than 5 lb 8 oz, or 2.5 kg) have produced intriguing but largely inconclusive findings. As one recent review[3] pointed out, the variety of study designs, statistical approaches, temperature indicators, windows of exposure, and geographical settings employed so far make it difficult to perform meta-analyses.

However, the work continues. Most recently, in 2019, researchers at the Brown University School of Public Health published two reports based on data from the National Center for Health Statistics on approximately 30 million singleton births across 403 U.S. counties.[9,17] In their study of preterm birth,[9] the researchers defined "extreme heat" as temperatures above the 95th percentile of each county-specific temperature distribution. In their cohort, 9.3% of babies were born preterm, and the risk of preterm birth increased by an estimated 2.5% in the four days following a single day with extreme heat. The authors estimated that if the association were causal, about 0.2% of all preterm births in the study could be attributed to extreme heat exposure.[9] That fraction translates into about 150 excess premature births per 1 million deliveries.

In a second study using this data set, the researchers looked at the relationship between average ambient temperatures across the entire pregnancy and markers of fetal growth.[9] They concluded that among full-term babies, those whose mothers were exposed to outdoor temperatures above the 90th percentile, averaged across the pregnancy, tended to have a slightly lower birth weight—equivalent to a mean 15 g (about 0.5 oz).[17] Similar associations were reported for the second and third trimesters.

Such small changes in birth weight are not necessarily important at the individual level, says senior study author Greg Wellenius, an epidemiologist at Brown. However, he continues, applied to a large population, even small changes can have a meaningful impact on long-term public health.

Both of these studies suggest that time and location of pregnancy matters. Extreme heat was most strongly associated with preterm birth in drier or colder climate zones, especially the U.S. Southwest and Midwest.[9] In the study of fetal growth,[9] being small for gestational age was most strongly associated with extreme heat in counties with cold or very cold climates. When estimated according to region, the associations were strongest for the Northwest and Northeast. That association is likely due to



Advances in neonatal intensive care over the past several decades have led to better outcomes for infants born too early or small. Nevertheless, preterm birth complications remain the leading cause of death globally among children under age 5, according to the World Health Organization.[37] Babies born prematurely or with low birth weight may have trouble breathing, eating, gaining weight, or fighting off infections. Over the long term, they may face problems with growth, behavior, and cognition.[38] Image: © iStockphoto/Bartosz Hadyniak.

local adaptation, says Wellenius. People in Maine, for instance, may be less prepared to deal with a 90°F (32°C) day than are people in Miami. However, not all studies agree. For example, a study in Germany[18] did not find a link between warmer-than-average temperatures and markers of fetal growth.

That said, the new results from Wellenius et al. suggest that environmental factors may be important determinants of premature birth and issues with fetal growth during the later stages of pregnancy. Some earlier studies support that view. A 2018 study of more than 2 million births in California found risk of term LBW increased in association with increases in "apparent temperature" (a measure that takes both heat and humidity into account) either over the entire pregnancy or during the second or third trimester, the last month, or the last two weeks of pregnancy.[19] At the same time, there was an inverse relationship between premature birth and higher apparent temperature during the first trimester.

A 2017 analysis of 220,572 singleton births across 12 U.S. sites estimated that the risk of full-term LBW was 2.5 times higher when average temperatures during the second and/or third trimesters were above the 95th percentile, whereas there was no association with high average temperature during the first trimester.[20] In addition, a 2015 study conducted across 19 African countries indicated that average birth weights were 0.9 g (0.03 oz) lower with each additional day with an average temperature over 100°F (38°C) during the second trimester. In comparison, average birth weights were 0.6 g (0.02 oz) and 0.4 g (0.01 oz) lower with each additional hot day during the first and third trimesters, respectively.[21]

Furthermore, heat may also shorten pregnancy, even within the normal range for term birth. A study led by Nathalie Auger, an epidemiologist at the University of Montreal Hospital Research Centre, reported in 2014 that hot temperatures were associated with a shorter length of pregnancy among Quebec women who delivered between 37 and 40 weeks.[22] "This is important to know," she explains, "because births at 37 or 38 weeks have more adverse outcomes than births at 40 weeks of pregnancy."

Stillbirths

Stillbirth affects about 1% of U.S. pregnancies each year.[23] Causes of stillbirth are varied and may include problems with the placenta, umbilical cord, or fetus; maternal medical conditions; or other obstetric complications.[24]

Fewer studies have investigated extreme heat with respect to risk of stillbirth. Part of the reason may be that stillbirth is a less-common outcome than premature birth or LBW, says Elaine Symanski, an epidemiologist and director of the Southwest Center for Occupational and Environmental Health at UT Health School of Public Health in Houston.

Nevertheless, at least four studies have reported associations between stillbirth and higher temperatures during the week before delivery for warm-weather births.[25,26,27,28] The most recent, led by Symanski, looked at 708 pregnant women in the Houston

Both time and location of pregnancy appear to matter when it comes to the potential adverse impacts of extreme heat. Local adaptation likely plays a role—people in cooler climates may be less prepared to cope with heat waves, in comparison with people who live in hotter locales. Image: © iStockphoto/courtneyk.

metropolitan area and found that from May through September, each 10°F increase in apparent temperature in the week preceding delivery was associated with a 45% increase in stillbirth, relative to baseline risk.[25] Furthermore, the Texas investigation found that associations between stillbirth and high summer temperatures appeared to be limited to Hispanic and non-Hispanic black women, with no association seen in non-Hispanic white women.[25]

These disparities possibly reflect differences in socioeconomic status, says Symanski. Factors related to the social environment could include education level, access to health care, food insecurity, exposure to violence, and availability of air conditioning in the home, she explains. As such, the factors may be specific to a given study population. For example, a study conducted in California reported the strongest associations for white and black mothers, in comparison with Hispanic and Asian mothers—although the latter two groups were very similar to each other.[27]

"Any one and probably a combination of these factors might explain the [racial or ethnic] differences we observed," Symanski says. She adds that future studies focusing on what makes certain groups of pregnant women more susceptible than others to heat stress will be important for designing targeted public health interventions.

Congenital Heart Defects

Although extreme heat may affect fetal growth late in pregnancy, exposure to hotter-than-usual weather early in pregnancy may affect other aspects of fetal development. For instance, two recent studies have reported an association between maternal heat exposure during the first few weeks of pregnancy—when fetal heart development begins—and congenital heart defects.[29,30]

Congenital heart defects occur in nearly 1% of U.S. births each year.[31] The causes of most of these defects are not clear, though previous research has suggested that factors such as maternal smoking and diabetes may increase risk.[32] Maternal fever during the first trimester also has been associated with congenital heart defects in some human studies.[33,34]

In a 2017 study, Auger et al. showed that, in babies conceived in Quebec between the months of April and September, exposure to at least 15 hot days during weeks 2–8 of pregnancy was associated with a 37% higher prevalence of atrial septal defects, in comparison with no exposure to hot weather.[29] "Hot days" were defined as those on which maximum outdoor temperatures reached 86°F (30°C) or higher.

A second analysis, published in 2018, used data from eight research centers across the United States that participate in the National Birth Defects Prevention Study. Associations with atrial and ventral septal defects varied by season (spring or summer), exposure metric (any exposure to at least two consecutive hot days, numbers of such exposures, and the longest number of consecutive hot days during gestational weeks 3–8), outcome (atrial versus ventral septal defects), and region.[30] The results suggested stronger associations between hot spring days and ventral septal defects at centers in the South (Arkansas and Texas) and

Some studies looking at the effects of hotter-than-usual temperatures on birth outcomes also have looked at the effects of extreme cold.[3] "At the molecular level, animal studies have shown that exposure to both extreme heat and extreme cold can contribute to oxidative stress and systemic inflammation," says Sandie Ha, an epidemiologist at the University of California, Merced. However, fewer studies have focused on cold exposures during pregnancy.[3] Image: © iStockphoto/AlexLinch.

Northeast (New York), and between hot days during both seasons and atrial septal defects at the Northeast center.

Even if causality were to be proven eventually, not every pregnant woman who is exposed to hot weather will have a child with a birth defect, emphasizes Shao Lin, an epidemiologist at the University of Albany, State University of New York. "Certain women probably have other factors that make them more susceptible to the effects of heat," she explains. Her team now is beginning to look at how heat exposure interacts with other known or suspected risk factors for congenital heart defects. "We want to identify who those susceptible people are and whether certain behaviors interact with heat to compound risk," Lin says. "We cannot change the weather, but maybe we can change the behavior."

Challenges, Caveats, and Recommendations

Most current studies on maternal heat exposures and pregnancy complications or birth defects share a similar set of limitations. "The major weakness in this field has been the lack of our ability to measure personal exposure to temperature," says Sandie Ha, an epidemiologist at the University of California, Merced.

Studies to date have relied primarily on ambient temperature data collected at a single or a few outdoor locations in a county or city. However, this type of data may not paint a very accurate picture of an individual's actual exposure. For instance, does a woman spend most of her time indoors in an air-conditioned building, or does she work outdoors in the summer heat? These distinctions are important in fully understanding the potential links between outdoor temperature and complications of pregnancy.

"In the ideal study, women would wear a temperature monitor throughout pregnancy," says Ha. Personal monitoring studies in relation to temperature are starting to proceed on a small scale, she says, but they have traditionally been difficult to organize for the large cohort sizes that would be needed to identify risk factors for uncommon health outcomes. However, advances in wearable technologies could help to make this type of large-scale personal monitoring study feasible in the near future, she adds.

The role of coexposures, especially to air pollution, is one of the many unresolved questions in this area. Some evidence suggests that exposure to high levels of various outdoor air pollutants may increase the risk of congenital heart defects[35] as well as adverse birth outcomes and other pregnancy complications.[4] Meanwhile, hotter days are associated with higher concentrations of ground-level ozone.[36]

In most studies to date of the health effects of temperature, investigators have attempted to account for potential effects of air pollution in their statistical analyses. However, to completely disentangle the two factors may be impossible. In addition, says Frederica Perera, a molecular epidemiologist and founding director of the Columbia Center for Children's Environmental Health in New York City, "Future studies should look at temperature and air pollution and the cumulative effects and nature of those joint impacts. This is a gap in our current knowledge," she says.

Doctors and public health authorities generally recommend that pregnant women take precautions against becoming overheated. When possible, they should avoid long periods of exposure to extreme heat, avoid strenuous activity outside during the hottest parts of the day, wear loose-fitting clothing, and stay hydrated.[10] "Pregnant women almost cannot drink too much water in extreme heat situations," says DeNicola.

However, beyond these commonsense measures, making evidence-based recommendations based on the available body of literature is impossible. Studies to date have not identified specific levels of temperature-related exposures, activities, or behaviors that may put some women more at risk than others. "We do not have a good sense of how much heat exposure is bad and how important a risk factor it is for various pregnancy complications," says Alisse Hauspurg, a maternal–fetal medicine expert at the University of Pittsburgh Medical Center Magee-Womens Hospital. Hauspurg stresses the need for more granular, detailed data to help practitioners better counsel patients.

Practitioners in other fields have started to look at how extreme weather affects their ability to optimize patient outcomes, says DeNicola. For example, doctors preferentially schedule high-risk pulmonary patients for procedures during times of the year when allergy season is less active, he explains. With concern about climate change growing, along with the likelihood of extreme temperature events, the obstetrics community, too, is now paying more attention to this topic.

"As physicians, as providers, we have an obligation to prepare patients for extreme weather and things that can cause insults to health," DeNicola says. "In some parts of the country already, summer has become [one of those things]."

Lindsey Konkel is a New Jersey-based journalist who reports on science, health, and the environment.

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