Study points to genetic link in apnea of prematurity

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A potentially life-threatening challenge characterized by pauses in breathing that can last for more than 20 seconds, apnea of prematurity (AOP) affects more than 50 percent of premature infants and is almost universal in the smallest of preemies. Caused in part by an underdeveloped central nervous system that can't adequately regulate breathing outside of the womb, especially during sleep, AOP is not yet fully understood by scientists and remains a grave concern among neonatologists and parents alike. New research published in the October issue of *Pediatrics* by clinical scientists at the University of Massachusetts Medical School suggests that heredity may play a strong role in determining an infant's susceptibility to AOP and could lead to the development of more effective treatments and screening methods.

Because it causes gaps in breathing, AOP can lead to reduced oxygen levels and a slowed heart rate in premature infants, as well as permanent disabilities and long-term damage to internal organs. Requiring around-the-clock monitoring, infants with AOP often must be gently jostled or rubbed to encourage inhalation and continued breathing, but such activities wake the baby, depriving it of much needed sleep. In severe cases, pharmaceutical interventions, such as caffeine, may be required. While the permanent consequences of AOP and its treatments have yet to be fully studied, infants with AOP are more likely to have cognitive and behavior problems, and other long-term disabilities.

"AOP is a medical puzzle," said David Paydarfar, MD, professor of neurology and physiology at the University of Massachusetts Medical

School. "Our research seeks to explain why there is so much variability in the incidence and severity of apnea in premature infants and why some infants outgrow the problem much sooner than others."

Elisabeth B. Salisbury, PhD, assistant professor of neurology, Paydarfar, and colleagues compared the rates of AOP in 217 identical and fraternal twin pairs to determine whether heredity played a role in the condition. Using advanced statistical models, they calculated the correlation of the onset of AOP in twins born before 36 weeks gestational age to determine if a genetic component was responsible. What they discovered was that in same-gender twin cases where one fraternal twin suffered from AOP, the other twin had a 62 percent likelihood of also having AOP. In identical twins, the correlation of AOP diagnosis among identical twin pairs was significantly higher – 87 percent.

These findings indicate that genetic influences shared by identical twins play a significant part in developing AOP. "While other factors, including environmental ones, contribute to AOP, our study suggests a surprisingly strong genetic predisposition for AOP. Further research is needed to confirm our results and to find the specific gene or group of genes that are linked to this common developmental disorder of breathing," said Paydarfar.

The next step for Paydarfar, Salisbury, and colleagues is to conduct a genome-wide study of AOP among premature infants in order to identify the gene or genes responsible for the condition. "Our work could lead to future insights on the genetic basis of the disease and ultimately more effective treatments for breathing problems in infants. If we can identify the genes involved, it's possible we could develop screening methods for AOP and to test whether these biomarkers are predictive for respiratory conditions later in life," said Paydarfar.